The PQQ biosynthetic operons and their transcriptional regulation in Pseudomonas aeruginosa
N Gliese, V Khodaverdi, H Görisch - Archives of microbiology, 2010 - Springer
... 1992), while in Methylobacterium extorquens AM1, the pqq genes are clustered in two separate operons (Toyama et al. 1997): the pqqABC/DE operon and the pqqFG genes, which form an operon together with 3 other genes (Zhang and Lidstrom 2003). ...
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Aging Skin Microbiology
DL Charbonneau, YL Song, CX Liu - Textbook of Aging Skin, 2010 - Springer
... 5]. The community composition of resident skin biota is believed to be as essential to the health of the skin as gut microorganisms are to overall health of the individual [2]. Resident biota promote health through pathogen inhibition, immune ... Methylobacterium. M. extorquens.
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Construction of a genome-scale kinetic model of mycobacterium tuberculosis using generic rate equations
DA Adiamah, JM Schwartz - Metabolites, 2012 - mdpi.com
The study of biological systems at the genome scale helps us understand fundamental biological processes that govern the activity of living organisms and regulate their interactions with the environment. Genome-scale metabolic models are usually analysed using constraint-based ...
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P Gilbert, AH Rickard, AJ McBain, AT Stead - pdfs.semanticscholar.org
... 2.1 198 Mycobacterium mucogenicum 594 99.7 AJ626883 2.2 198 Methylobacterium fujisawae 593 97.4 AJ6268649 2.3 198 Varivox paradoxx 631 99.8 AJ626865 4.7 65 Bacillus sphaericus 668 98.3 AJ627395 4.8 65 Methylobacterium fujisawae 593 98.1 AJ627396 ...
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A new modified ortho cleavage pathway of 3-chlorocatechol degradation by Rhodococcus opacus 1CP: genetic and biochemical evidence
OV Moiseeva, IP Solynikova... - Journal of..., 2002 - Am Soc Microbiol
... cycloisomerase YkFB from Bacillus subtilis (AJ002571) were used. For panel D, ORF2 from Methylobacterium extorquens AM1 (UT7662) and Usf from Aquifex pyrophilus from Ko15a (U17575), both with unknown function, were used.
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Expression of green fluorescent protein fused to magnetosome proteins in microaerophilic magnetotactic bacteria
C Lang, D Schüller - Applied and environmental microbiology, 2008 - Am Soc Microbiol
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A structural model of anti-anti-σ inhibition by a two-component receiver domain: the PhyR stress response regulator
J Herrou, R Foreman, A Fiebig... - Molecular..., 2010 - Wiley Online Library
... PhyR consists of an amino-terminal ECF σ-like domain (hereafter referred to as the SL domain) and a carboxy-terminal TCS receiver domain, and was first described in Methylobacterium extorquens AM1 as a protein that regulates expression of genes involved in general stress ...
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Identification of a methanol-inducible promoter from Rhodococcus erythropolis PR4 and its use as an expression vector
Y Kagawa, Y Mitani, HY Yun, N Nakashima... - Journal of bioscience..., 2012 - Elsevier
The genus Rhodococcus exhibits a broad range of catalytic activity and is tolerant to various kinds of organic solvents. This property makes rhodococci suitable.
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https://scholar.google.com/scholar?start=260&q=methylobacterium+extorquens+pathogenicity+plant&hl=en&as_sdt=0,22
Detection of legionellae in hospital water samples by quantitative real-time LightCycler PCR
N Wellinghausen, C Frost, R Marre - Applied and Environmental ..., 2001 - Am Soc Microbiol

... all strains (described in Table 1), as well as with Legionella-like amoebal pathogen (LLAP) 10 ...
40 PCR cycles was seen with 10 pg of DNA from a Methylobacterium sp., isolated ... The target
sequences of the 16S rRNA gene primers forMethylobacterium extorquens are depicted in ...
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LABORATORY PROCEDURE
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... Miniaturized microbiological methods. Academic Press, New York. 6. Sanders, AC, Faber,
Using Paper Discs," Appl. Microbiol. 5:36-40. 7. Synder, ML 1954. ...
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Phenotypic variation in metabolic functions of Escherichia coli in mixed-substrate environments
N Nikolic - Nela Nikolic, 2013 - e-collection.library.ethz.ch
... Page 116. 108 We also used a natural isolate of Escherichia coli, an enteroaggregative
Pole age affects cell size and the timing of cell division in Methylobacterium extorquens AM1. ...
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Metabolic modeling of a mutualistic microbial community
S Stoliar, S Van Dijk, KL Hillesland... - Molecular systems ..., 2007 - msb.embopress.org
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Metabolic engineering of Corynebacterium glutamicum for methanol metabolism
S Witthoff, K Schmitz, S Niedenfuhr, K Noh... - Applied and ..., 2015 - Am Soc Microbiol
... Whereas Gram-negative methylotrophic bacteria such as Methylobacterium extorquens employ
pyrroloquinoline quinone (PQQ)-dependent and periplasmic methanol dehydrogenases (MDHs)
to oxidize methanol (24), Gram-positive thermotolerant Bacillus strains usually use ...
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Prokaryotic Systems Biology
A Schmid, N Baliga - Systems Biology, 2007 - Springer
... prokaryotes because of its genetic tractability, fast generation time, and medical relevance as
a major enteric pathogen in human ... 27 Using a similar strategy, metabolic models have been
constructed for several other organisms, including Methylobacterium extorquens AM1, 31 ...
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Characterization of a two-peptide plantaricin produced by Lactobacillus plantarum MBSa4 isolated from Brazilian salami
MS Barbosa, SD Todorov, IV Ivanova, Y Belguemia... - Food Control, 2016 - Elsevier
... Ross, & Hill, 2012). Some studies have also reported on activity against unrelated
strains, especially those that are pathogenic and responsible for food spoilage
(Forrest, Settanni, & Van Sinderen, 2004). Although a variety ...
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Methylotrophic bacterium for the production of recombinant proteins and other products
... [0009]. Such methods would include a non-pathogenic prokaryotic microbial system, as
an alternative to E. coli, for recombinant peptide or ... [0016]. In another embodiment of the present
invention the methylotrophic bacterium is Methylobacterium extorquens ATCC 55366.
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Parallelism and Epistasis in the de novo Evolution of Cooperation between Two Species
SM Douglas - 2014 - search.proquest.com
... 7. Wong, A., Rodrigue, N. & Kassen, R. Genomics of adaptation during experimental evolution
of the opportunistic pathogen Pseudomonas aeruginosa. ... identifies candidate pathogenicity genes.
Nat. ... throughput culturing methods for Methylobacterium extorquens. PLoS One 8, ...
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Frequency and fitness consequences of bacteriophage Φ6 host range mutations
BE Ford, B Sun, J Carpino, ES Chapler, J Ching... - PloS one, 2014 - journals.plos.org
... mutations and their frequency of appearance would be important parameters governing the probability of emergence of a potential human pathogen. ... This type of prioritization is critical before allocating resources to interdict potential pathogenic viruses before they emerge. ...
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Methods for rapid identification of bacillus cereus
... BACKGROUND OF THE INVENTION Bacillus cereus is gram-positive, spore-forming, motile, aerobic rod which inhabits in soil and has been recognized as an opportunistic food poisoning pathogen. ... cloaceae. Methylobacterium, 11048, 12234, 2, 0, 2. extorquens. ...
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Update and evaluation of 16SpathDB, an automated comprehensive database for identification of medically important bacteria by 16S rRNA gene sequencing
S Yeuang, 極兆恩 - HKU Theses Online (HKUTO), 2013 - hub.hku.hk
... the pathogenic role of the pathogens. For example, the invasive Streptococcus iniae infection, which was recognized in North America before, now reported in Asia (Weinstein et al., 1997; Lau et al., 2003). By using the conventional phenotypic tests, the rare pathogen may be ...
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Actinomyces oris fimbriae: an adhesive principle in bacterial biofilms and tissue tropism
HTon-That, A Das, A Mishra - Oral Microbial Communities: ..., 2011 - books.google.com
... HELPFUL WEB RESOURCES • Oral Pathogen Sequence Databases (http://www. ... Different type 1fimbrial genes and tropism of commensal and potentially pathogenic Actinomyces spp. ... sortase anchors a class of surface protein during Staphylococcus aureus pathogenesis. ...
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Transport genes and chemotaxis in Laribacter hongkongensis: a genome-wide analysis
SKP Lau, RYY Fan, GKM Wong... - Cell & ..., 2011 - cellandbioscience.biomedcentral. ...
... available (Table 2). Moreover, a homologue of urea transporter responsible for urea uptake (LHK_01044) was also present in L. hongkongensis (Table 2), while this protein was absent in C. violaceum and the pathogenic Neisseria spp. ... Methylobacterium extorquens PA1. ...
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A two-component system, an anti-sigma factor and two paralogous ECF sigma factors are involved in the control of general stress response in Caulobacter ...
RF Lourenco, C Kohler, SL Gomes - Molecular microbiology, 2011 - Wiley Online Library
... In fact, a molecular system involved in this response was recently identified in Methylobacterium extorquens, Bradyrhizobium japonicum and Sinorhizobium meliloti (Francez-Charnol et al., 2009; Gourion et al., 2009; Bastiat et al., 2010). ...
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Processes and Rates of Bacterial Evolution
N Delaney - 2013 - search.proquest.com
... 5, I used genome re-sequencing to examine the genetic changes that occurred in a population of pathogenic Mycoplasma gallisepticum. ... Methylobacterium extorquens. ... &KDSWHU. ... pathogen, Mycoplasma gallisepticum ...
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Poly (3-hydroxybutyrate) fuels the tricarboxylic acid cycle and de novo lipid biosynthesis during Bacillus anthracis sporulation

MR Sadykov, JS Aan, TJ Widhelm... - Molecular,..., 2017 - Wiley Online Library

... (Singh et al., 2009), the specific requirements for PHB during sporulation in any given species might reflect adaptations to different life styles, including distinct metabolism-based mechanisms of pathogenesis and resistance, as well as specialized morphological features of the ...

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Costs of antibiotic resistance—separating trait effects and selective effects

AR Hall, DC Angst, KT Schiessl... - Evolutionary,..., 2015 - Wiley Online Library

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Methylotrophic bacterium for the production of recombinant proteins and other products


... [0011]. Such methods would include a new non-pathogenic prokaryotic microbial system, as an alternative to E. coli, for recombinant peptide or ... [0019]. In another embodiment of the present invention the methylotrophic bacterium is Methylobacterium extorquens ATCC 55396...

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Applications of cellular fatty acid analysis.

DF Welch - Clinical Microbiology Reviews, 1991 - Am Soc Microbiol

Page 1. CLINICAL MICROBIOLOGY REVIEWS, Oct. 1991, p. 422-438 Vol. 4, No. 4 0893-8512/91/040422-17502.00/0 Copyright © 1991, American Society for Microbiology Applications of Cellular Fatty Acid Analysis DAVID...

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(2S)-Methylsuccinyl-CoA dehydrogenase closes the ethylmalonyl-CoA pathway for acetyl-CoA assimilation

TJ Erb, G Fuchs, BE Alber - Molecular microbiology, 2009 - Wiley Online Library

... We recently described the outlines of the ethylmalonyl-CoA pathway, a new acetyl-CoA assimilation strategy that operates in a number of bacteria such as Rhodobacter sphaeroides, Methylobacterium extorquens and streptomyces and replaces the glyoxylate cycle. ...

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Building better drugs: developing and regulating engineered therapeutic proteins

C Kimchi-Sarfaty, T Schiller... - Trends in,..., 2013 - Elsevier

Most native proteins do not make optimal drugs and thus a second- and third-generation of therapeutic proteins, which have been engineered to improve product at...

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Metabolic and stress responses of Acinetobacter oleivorans DR1 during long-chain alkane degradation

C Park, B Shin, J Jung, Y Lee... - Microbial,..., 2017 - Wiley Online Library

... This unexpected result suggests that DR1 cells might have additional alternative pathways to the glyoxylate shunt during alkane metabolism as seen in Rhodobacter sphaeroides and Methylobacterium extorquens AM1 (Ensign, 2006). Thus, growth defect of the DaeA mutant ...

Cite Save

A Low-Molecular-Weight Alginate Oligosaccharide Disrupts Pseudomonal Microcolony Formation and Enhances Antibiotic Effectiveness

MF Pritchard, LC Powell, AA Jack... - Antimicrobial Agents,..., 2017 - Am Soc Microbiol

... The opportunistic Gram-negative pathogen Pseudomonas aeruginosa is found in a range of chronic human respiratory diseases, including chronic obstructive pulmonary disease and cystic fibrosis (CF) (1). CF is a life-threatening, autosomal recessive genetic disorder affecting ...

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... Another object of the present invention is to provide a method and system for identifying lethal gene deletions. Yet another object of the present invention is to provide a method and system for identifying gene therapeutic candidates for pathogenic microbes ...

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A Kashiwagi, R Sugawara, FS Tsushima... - Journal of..., 2014 - Am Soc Microbiol
... Recently, whole-genome analysis has been performed for experimental evolution using DNA and RNA viruses, Escherichia coli, Methylobacterium extorquens, Saccharomyces cerevisiae, and Drosophila melanogaster (1-16). ...
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Asymmetric, bimodal trade-offs during adaptation of Methylobacterium to distinct growth substrates
MC Lee, HH Chou, CJ Marx - Evolution, 2009 - Wiley Online Library
... Here, we use adaptation of experimental populations of the model methylotroph, Methylobacterium extorquens AM1, to C 1 (methanol) or multi-C (succinate) compounds to investigate specialization and trade-offs between these two metabolic lifestyles. ...
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Methods for treating bacterial infections
... enteragg aggressive E. coli; EHEC=enterohemorrhagic E. coli; EIEC=enteroinvasive E. coli; EPEC=enteropathogenic E. coli; ETEC=enterotoxinogenic E. coli; ExPEC=extraintestinal pathogenic E. coli ... Methyllobacteriaceae.—Methyllobacterium extorquens group; Methyllobacterium ...
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The dynamics of diverse segmental amplifications in populations of Saccharomyces cerevisiae adapting to strong selection
C Payen, SC Di Rienzi, GT Ong... - G3: Genes, Genomes,..., 2014 - g3journal.org
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L Chistoserdova - Environmental Microbiology, 2011 - Wiley Online Library
... A MDH first characterized in Methyllobacterium extorquens (Anthony, 1962; 2004) and later detected in most of the model methylotrophs was a heterotetramer consisting of subunits encoded by genes designated mxAFI, contained pyrroloquinoline quinone (PQQ) as cofactor and ...
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Untersuchungen zur Interaktion epiphyller Bakterien mit Blattoberflächen und Veränderungen in der Phyllosphäre während der Vegetationsperiode
U Krimm - Mathematisch-Naturwissenschaftliche Fakultät,..., 2005 - hss.ulb.uni-bonn.de
... 2002). Arten der Gattung Methyllobacterium, va Methyllobacterium mesophilicum können Methanol metabolisieren (Holland et al. ... In der Regel werden antagonistische Organismen auf die Pflanze oder das Erntegut aufgebracht, bevor das Pathogen sich ansiedeln kann. ...
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SM Douglas, LM Chubb, WR Harcombe, FM Ytreberg... - PloS one, 2016 - journals.plos.org
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The ability of flux balance analysis to predict evolution of central metabolism scales with the initial distance to the optimum

WR Harcombe, NF Delaney, N Leiby... - PLoS computational, 2013 - journals.plos.org

Author Summary The most common method of modeling genome-scale metabolism, flux balance analysis, involves using known stoichiometry to define feasible metabolic states and then choosing between these states by proposing that evolution has selected a metabolic flux that...

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Biological costs and benefits of antibiotic resistance

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S Lal, DV Raje, S Cheema, A Kapley, HJ Purohit... - Microbial Factories, 2015 - Springer


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Current approaches to the prevention of catheter-related infections

B Jansen - INFECTIOUS DISEASE AND THERAPY SERIES, 1997 - books.google.com

... These include the pathogenesis and epidemiology as well as patient risk factors and are intensively discussed in the respective chapters elsewhere in this book. 1, eg, the nature and specific abilities of the pathogen involved are important. ...

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Increasing avermectin production in Streptomyces avermitilis by manipulating the expression of a novel TetR-family regulator and its target gene product

W Liu, Q Zhang, J Guo, Z Chen, J Li... - Applied and... , 2015 - Am Soc Microbiol

... TFRs have been shown to participate in such important cellular processes as multidrug resistance, antibiotic biosynthesis, morphogenesis, osmotic stress, biofilm formation, catabolic pathways, nitrogen uptake, and pathogenicity (19), but the functions of many of them in ...

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Characterization of microbial populations in the subsurface

MP Buttner, P Cruz, JI Steffenbach, AJ Smieciinski - 2006 - digitalscholarship.unlv.edu

Page 1. Publications (YM) Yucca Mountain 12-2006 Characterization of microbial populations in the subsurface Mark P. Buttner University of Nevada, Las Vegas, mark.buttner@unlv.edu Patricia Cruz University of Nevada, Las Vegas, patricia.cruz@unlv.edu...

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Expression bakterieller Gene zur PHA-Synthese in Arxula adeninivorans und Untersuchungen zum Stoffwechsel der Hefe

A Scholz - 2000 - deutsche-digitale-bibliothek.de

... PHB-Synthese aus C. necator wie auch um das PHA-Synthasegen aus Methylobacterium extorquens. 3-Hydroxybutyrate 3-Hydroxyvalerate 3-Hydroxy-4-pentenoate 3-Hydroxy-8, 9-epoxy-5,6-cis-tetradeconoate 3-Hydroxy- 5-cyclohexylyvalerate ...

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A mutational hotspot and strong selection contribute to the order of mutations selected for during Escherichia coli adaptation to the gut

M Lourenço, RS Ramiro, D Güleresi... - PLoS ..., 2016 - journals.plos.org

Author Summary The relative contribution of random loss and migration versus de novo mutation to the overall diversity of the gut microbiota is far from understood. Population sizes of bacterial communities inhabiting the gut can be very large and therefore, both weak and strong ...

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https://scholar.google.com/scholar?start=300&q=methylobacterium+extorquens+pathogenicity+plant&hl=en&as_sdt=0.22
RNA-seq Based Transcriptomic Analysis of Single Cyanobacterial Cells
Page 1. 4 RNA-seq Based Transcriptomic Analysis of Single Cyanobacterial Cells Zixi Chen1,2,3, Jiangxin Wang1,2,3, Lei Chen1,2,3 and Weiwen Zhang1,2,3* Laboratory of Synthetic Microbiology, School of Chemical Engineering ...
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Two-tiered histidine kinase pathway involved in heat shock and salt sensing in the general stress response of Sphingomonas melonis Fr1
A Kaczmarczyk, R Hochstrasser, JA Vorholt... - Journal of..., 2015 - Am Soc Microbiol
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Умеренно гапалкалофильные аэробные метилобактерии
ЮА Троценко, НВ Дорохина, ЦЛ Лих, АС Решетников - Микробиология, 2007 - elibrary.ru
... Leisingera methylalcoholovorans ATCC BAA-92 T (AY005463) Methylophilus capsulata IM1 ATCC 700716 T (AF004844) Methylophilus multivorans ATCC 51890 T (AF004845) Methylobacterium extorquens JCM 2802 T (D32224) Methylobacterium organophilum NCIMB 11278 ...
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WrpA is an atypical flavodoxin family protein under regulatory control of the Brucella abortus general stress response system
J Herrou, DM Czyz, JW Willett, HS Kim... - Journal of..., 2016 - Am Soc Microbiol
... Next Section. ABSTRACT. The general stress response (GSR) system of the intracellular pathogen Brucella abortus controls the transcription of approximately 100 genes in response to a range of stress cues. The core genetic ...
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Extractoplasmic function Sigma factors in Bacillus Species
T Wecke - 2011 - edoc.pub.uni-muenchen.de
... often extended by a repeating oligosaccharide, called O-antigen (Bos et al., 2007).
Lipoplysaccharides can play a role in pathogenicity since they are responsible for the ... formation (Brandt et al., 2005). The Corynebacterineae, including the important pathogen ...
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Glyoxylate Metabolism in Mycobacterium smegmatis
LN Merkoff - 2006 - digitalcommons.rockefeller.edu
... feasible, or easily executable, with pathogenic M. tuberculosis. Page 13. 5 ... They are high-GC (~ 85%) and lack pathogenicity strains typical of many bacterial pathogens. ... 1998), the clinical isolate CDC1951 (Fleischmann et al., 2002), the animal pathogen M. bovis (Garnier et al. ...
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Newly discovered bacterium in the family acetobacteraceae
SM Holland, DE Greenberg, A Zelazny... - US Patent ..., 2015 - Google Patents
... X7517). The 16S rDNA sequence similarity between the subject's isolate and other commonly encountered pathogenic Gram-negative rods was very low (~80%). A phylogenetic tree of Granulibacter bethesdenis based on its 16S RNA sequence is shown in FIG. 1. ...
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Protein with recombinase activity for site-specific DNA-recombination
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Mycobacterial diagnostics
V Kapur, JP Bannantine, LL Li, Q Zhang... - US Patent..., 2011 - Google Patents
... The pathogenesis of M. paratuberculosis has been recently reviewed by Harris and Barletta (2001, Clin. Microbiol. Rev., 14:489-512)... During the clinical phase of infection, fecal shedding of the pathogen is high and can exceed 10 10 organisms/g of feces. ...
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Evolutionary consequence of a trade-off between growth and maintenance along with ribosomal damages

BW Ying, T Honda, S Tsuru, S Seno, H Matsuda... - PloS one, 2015 - journals.plos.org

Microorganisms in nature are constantly subjected to a limited availability of resources and experience repeated starvation and nutrition. Therefore, microbial life may evolve for both growth fitness and sustainability. By contrast, experimental evolution, as a powerful approach to ...

Chapitre V

FM Medie, R Ghodbane, B Henriassat, D Raoult... - Le rôle des cellules..., 2011 - theses.fr

... A novel pathogenic taxon of the Mycobacterium tuberculosis complex, Canetti: characterization of an exceptional... Lactobacillus reuteri JCM 1112 Lactobacillus reuteri SD2112 Methylobacterium dichloromethanicum DM4 Methylobacterium extorquens AM1 Methylobacterium ...

Wearable Computing: Designing a Solution to Enhance User Interactions


... reduced) NAD (P) NAD+ or NADP+ NAD (P) H NADH or NADPH ATP adenosine triphosphate

PHB poly-β-hydroxybutyrate BHB-Coa β-hydroxybutyryl-CoA EMC ethylmalonyl-CoA Gly glycine

Glyc glyoxylate Abstract In Methylobacterium extorquens AM1, mechanisms to ...

Identification and characterisation of bacterial TIR domains, with particular focus on yersinia pestis: Study Data

AM Spear - 2011 - datacompass.ishkm.ac.uk

Bacterial Results,..., O1,Phylum,Family,Genus,Species,Protein ID,Description,E-Value
9470501,Acidobacteria,Acidobacteriaceae,Acidobacteria bacterium Ellin345,YP_592549.1. Toll-interleukin receptor [Acidobacteria bacterium Ellin345] >g|94552556|gb|ABF42475.1| Toll ...

Biochemische und molekularbiologische Untersuchungen zu Lacton-Hydrolasen des bakteriellen Aromaten-und Halogenaromen-Abbaus

IS Hinnen - 1996 - books.google.com


Accurate microbial genome annotation using an integrated and user-friendly environment for community expertise of gene functions: the microscope platform

E Belda, D Veillnet, C Médigue - ..., Genomic and System Analyses of Pure ..., 2017 - Springer

... into the MicroScope platform, 1,702 are freely available, including several bacterial genomes of interest in the context of hydrocarbon microbiology (Pseudomonas and Acinetobacter species, Acidothermus cellulolyticus, Clostridium species, Methylobacterium extorquens, etc.). ...

Compounds and methods of treating infections


The invention provides compounds of Formula (I), and methods of treating or preventing a bacterial infection in a subject using a compound of Formula (I). The invention also provides the use of a compound of Formula (I) in the manufacture of a medicament for the treatment of a ...

UNIVERSIDAD AUTÓNOMA DEL ESTADO DE MEXICO

DDEA RESIDUALES, QF BIÓLOGO, EM ZARATE - iaee.org

... Otros microorganismos que han demostrado ser también resistentes a la radiación ionizante, se encuentran: Deinococos radioduranus (Wackeet, 1998), Deinococcus proteolyticus, Pseudomona radiata (Matanabe et al., 1984), Methylobacterium extorquens (Nogueira et al., 1998 ...

Genetically modified bacteria and methods for genetic modification of bacteria


... 30. The genetically modified bacteria of claim 1, wherein the nucleic acid encoding a mammalian growth factor or a mammalian cytokine is inserted into or a part of an endogenous gene encoding a pathogenic protein. 31. ...

https://scholar.google.com/scholar?start=320&q=methylobacterium+extorquens+pathogenicity+-+plant&hl=en&as_sdt=0,22
Molecular basis for trimethoprim and sulphonamide resistance in Gram negative pathogens
M Grape - 2006 - openarchive.ki.se

... Integrons can insert and express gene cassettes conferring resistance to various different antibiotics and are thus important tools for spread of resistance in pathogenic bacteria. ... Only a limited number of E. coli strains are pathogenic ...
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Bazı Stres Faktörlerinin Aerobik Oksalat Bakterinin Kültüre Edilebilirliği ve Canlılığı Üzerine Etkileri
M Oskay, AÜ Tamer, G Saracaloğlu - dergipark.gov.tr

... Bessalik [3], ilk kez literatürde tanımlanan, oksalatı kullanan Methylobacterium sp. ... [3] Basalik, K. Über die verarbeitung der oxalsaure durch Bacillus extorquens n sp. Jahrb. Wiss. ... [23] Browne, N.; Dowds, BCA Heat and Salt Stress in the Food Pathogen Bacillus cereus. J. Appl. ...
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https://scholar.google.com/scholar?start=320&q=methylobacterium+extorquens+pathogenicity+plant&hl=en&as_sdt=0,22
The genomic prediction and characterization of transmembrane β-barrels in Gram-negative bacteria
TC Freeman Jr - 2009 - search.proquest.com
The genomic prediction and characterization of transmembrane β-barrels in Gram-negative bacteria. Abstract. Transmembrane β-barrels (TMBB) are a special structural class of proteins predominately found in the outer membranes ...
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Infections associated with urinary catheters
CE Chenoweth, S Saint - Catheter-Related Infections, 2005 - researchgate.net
... PATHOGENESIS The normal urinary tract has a number of defense mechanisms that prevent attachment of potential pathogens to the ... Enterococci have remained a significant pathogen, especially with the emergence and spread of vancomycin-resistant enterococci (43, 93–95 ... Cited by 2 Related articles All 4 versions Cite Save More

Aerosol Collection Apparatus and Methods
The lifetime of aerosol monitoring, concentration and collection equipment is extended by acoustic cleaning of accreted particle deposits from internal surfaces where fouling occurs by application of acoustic energy to the particle accretion surface, optionally in combination with a ...
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Tradeoffs, Mobile Genetic Elements and Horizontal Gene Transfers in Microbial Evolution
MC Lee - 2011 - search.proquest.com
... Here we use adaptation of, experimental populations of the model methylotroph, Methylobacterium extorquens. AM1, to C (methanol) or multi-C (succinate) compounds to investigate. ... The a-proteobacterium Methylobacterium extorquens AM1[94], which grows on a ...
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G Syzc - 2015 - digital.ufc.br/cecn.ufl.br
... They are the causative agent or brucellosis, a zoonotic infection that causes miscarriage and infertility in animals, and a febrile disease in humans. Brucella is a facultative intracellular pathogen, which resides in a replicative niche derived from the endoplasmic reticulum. ...
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Evolutionary Trajectories to Daptomycin Resistance in Enterococcus faecalis
C Miller - 2013 - scholarship.rice.edu
... Initially isolated from a stool sample, whole genome sequence analysis suggests Symbiobacterium thermophilum 1 can likely trace its lack of pathogenicity to large deletions in virulence ... While pathogenesis will ... pathogen and the patient, the biochemical foundations of antibiotic resistance need not. ...
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Methanocaldococcus jannaschii and the Recycling of S-adenosyl-L-methionine
DV Miller - 2017 - vtechworks.vt.edu
... 630 0.62% Bacteroides fragilis YCH46 0.73% Methylobacterium extorquens AM1 0.41% Escherichia coli K12 0.44% Saccharomyces cerevisiae (Baker's yeast) 0.05% Table 2. Kinetic parameters of Dald with 5'-dA, MTA, SAH, and Ad Substrate KM (mM) kcat (s-1) kcal/KM (M ...
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Identificação de genes de isolados clínicos de Porphyromonas gingivalis expressos diferencialmente na formação de biofilme, usando differential display PCR.
D Higashi - teses.usp.br
Page 1. DANIELA HIGASHI IDENTIFICAÇÃO DE GENES DE ISOLADOS CLÍNICOS DE Porphyromonas gingivalis EXPRESSOS DIFERENCIALMENTE NA FORMAÇÃO DE BIOFILME, USANDO DIFFERENTIAL DISPLAY PCR ...
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A New Approach to Controlling Epilepsy
VA Herrera - The McNair Scholars Journal of the University of ..., 2013 - depts.washington.edu
Page 122. 113 A New Approach to Controlling Epilepsy Vicky A. Herrera Abstract
Epilepsy is a neurological disease characterized by recurring seizures, and it affects millions. We hypothesize that modulation of p38 mitogen ...
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Cross-Talk tra Bifidobacterium e intestino umano: impatto sulle attività health promoting
SCF Dipalo - 2010 - amsdottorato.unibo.it
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Elements of P1B-type ATPase structure and function. Abstract. P-type ATPases are
membrane-bound proteins that couple hydrolysis of ATP to transport a substrate
across cellular membranes, often against a gradient. Three ...
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as vaccine candidates and imaging targets
R Brady - 2007 - search.proquest.com
... The pathogenesis of osteomyelitis has been explored clinically and different types of osteomyelitis ...
If antimicrobial therapy directed at the responsible pathogen is begun prior to ...
mobile genetic elements called SaPIs (Staphylococcus aureus pathogenicity islands), ...
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N Kim - 2012 - etheses.whiterose.ac.uk
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Lymphocyte Specificity and Degeneracy
V Rubio-Godoy - 2002 - doc.rero.ch
... peptides to the T cells composing the actual repertoire so that all pathogenic peptides are
recognized by the immune system. Also, the frequency of T lymphocytes that can recognize
peptides from pathogen origin has to be large enough to assure an efficient ...
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Optimisation de la production d’acide succinique chez methylobacterium extorquens par
le biais de petits arn regulateurs
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... OPTIMISATION DE LA PRODUCTION D’ACIDE SUCCINIQUE CHEZ METHYLOBACTERIUM
EXTORQUENS PAR LE BIAIS DE PETITS ARN REGULATEURS Par ...
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S Patarai - 2012 - deposotnce.tu-berlin.de
Page 1. Acknowledgment Partitioning of cytochrome c in multicomponent lipid
membranes vorgelegt von Salome Patarai, M.Sc Georgia, Tbilisi Von der Fakultät
II - Mathematik und Naturwissenschaften der Technischen Universität ...
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Page 1. Az anyagcsere szerkezetének hatása a genetikai interakciókra és a genomszerveződésre
Ph.D. értekezés Kovács Károly Témavezető: Papp Balázs Biológia Doktori Iskola MTA Szegedi
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Aerosol collection apparatus and methods


An apparatus or device for collecting aerosol particles from a gas stream, having a collector body enclosing a collector channel, a particle trap in the collector channel, and an injection duct for injecting a discrete microdroplet of an elution reagent. The particle trap may be a centrifugal...
Formate metabolism in sulfate reducing bacteria
SIM Silva - 2011 - search.proquest.com
... the ability of some pathogenic bacteria, such as Helicobacter pylori or Salmonella enterica to efficiently use H2 as an energy source, constitutes a virulence factor [75, 76]. This subject is further discussed in Chapter 6, where the energy metabolism of the opportunistic pathogen ...

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Genetics and physiology of ammonia catabolism by the methane-oxidizing bacterium, Methyloccoccus capsulatus Bath
A Poret-Peterson - 2009 - search.proquest.com
... 2000). In general, cytochrome P460-like enzymes have been found in denitrifying bacteria and pathogenic bacteria, where they are thought to function in protection from host-generated NO (Zumft, 2005; Elmore et al. 2007) ...

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Probiotic potential of lactic acid bacteria isolated from rainbow trout (Oncorhynchus mykiss, Walbaum) and rearing environment. Importance in the prevention of fish ...
CAD Araujo - 2016 - search.proquest.com
... Taking into consideration that most LAB are currently considered as safe microorganisms for human and animal consumption (EFSA, 2006a; 2005b; 2007), and that some bacteriocin-producing strains inhibit pathogenic microorganisms responsible for human and animal ...

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Evalúacion Microbiológica de las aguas termales del balneario las Peñas, cantón Baños, provincia Tungurahua.
P.J Cabrera Aguayo - 2016 - dspace.es.poch.edu.ec
... The analysis resulted in a water hole contaminated with Gram negative bacteria corresponding 33% to Cardiobacterium sp and similar Methyloobacterium mesophilicus percentage. ... Thereby establishing that exist in these waters a predominance of Gram negative pathogenic ...

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Evaluación y diseño de bacterias lácticas (BAL) de origen alimentario y de otros hospedadores como factorías celulares de producción de bacteriocinas
JJ Martinez - 2015 - eprints.ucm.es
... But, with no doubt the progress in the development and evaluation of biological strategies to eliminate, reduce or control in food the presence of food-borne pathogenic microorganisms and, specially, Listeria monocytogenes, should rely on the development and evaluation of ...

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AB Gilbert - 2008 - search.proquest.com
Improving biotechnological processes through automated flow cytometry. Abstract.
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System and tools to support a Bayesian approach to improving large-scale metabolic models
X Shi - 2008 - search.proquest.com
...

Modeling molecular mechanisms of mammalian mineralization
JA Horst - 2010 - search.proquest.com
...
Pathogenicity is discernable from patterns of interactions between a missense mutation, the...

In silico analysis of microbial biosynthetic capabilities at the genome-scale
M Imielinski - 2007 - search.proquest.com
...
For example, one may identify a critical set of reactions whose knockout disables the production of a pathogenic factor or induces the ...
Appendix 6-2: Methylobacterium extorquens toxicity

A Google Scholar search “Methylobacterium toxicity” on October 31, 2017 yielded ~5900 hits.

A Google Scholar search limiting to the species of Methylobacterium extorquens and toxicity yielded 1960 hits. Most of these papers were related to plant toxicity.
A Google Scholar search “Methylobacterium extorquens toxicity -plant”, yielded 569 hits most of which were not relevant to any alleged toxicity of Methylobacterium species (for reasons discussed below), and none of which were relevant to M. extorquens. Several papers were already identified in the “pathogenicity” search (Appendix 6-1). Among the reasons for ruling out most of the references in this search were that the search picked up references to the toxicity of methanol or formaldehyde, or irrelevant references to other toxic molecules not found in or produced by Methylobacterium. In fact, several papers reported that Methylobacterium species could reduce the toxicity of metallic waste streams.

Previous Google searches using the same or similar keywords also provided no hits relevant to mammalian or human toxicity. The only reference found by KnipBio that is remotely relevant is (Balachandran et al., 2012), who reported a Methylobacterium soil isolate which they called Methylobacterium sp. (ERI-135), which showed promising antibacterial and cytotoxic activity in vitro.

Objective To assess the antimicrobial and cytotoxic effects of Methylobacterium sp. isolated from soil sample of Doddabetta forest, Nilgiris, Western Ghats of Tamil Nadu.

Results

Ethyl acetate extract showed activity against bacteria such as Bacillus subtilis, Klebsiella pneumoniae (K. pneumoniae), Pseudomonas aeruginosa, Salmonella typhimurium, Shigella flexneri, Enterobacter aerogenes, Staphylococcus aureus and Staphylococcus epidermidis (S. epidermidis) and fungi such as, Candida albicans and Trichophyton rubrum. The lowest minimum inhibitory concentrations were: 250 μg/mL against S. epidermidis and 250μg/mL against K. pneumonia. The isolate had the ability to produce enzymes such as protease. The exyract showed cytotoxic effect in human adenocarcinoma cancer cell line (A549). GC-MS analysis showed the presence of isovaleric acid (3.64%), 2-Methylbutanoic acid (5.03%), isobutyramid (5.05%), N,N-oimethylformamide-di-t-butylacetal (9.79%), benzeneacetamide (15.56%), octyl butyl phthalate (3.59%) and diisooctyl phthalate (5.79) in the extract.

Conclusions

Methylobacterium sp. (ERI-135) showed promising antibacterial and cytotoxic activity. This is the first report in the antimicrobial and cytotoxic effect of Methylobacterium sp."

The following pages list all the 569 references.
Production of poly-β-hydroxybutyrate from methanol: characterization of a new isolate of *Methylobacterium extorquens*  
D Bourque, B Ouellette, G Andre, D Groleau - Applied Microbiology and ..., 1992 - Springer  
... concentration at its optimal value (1.7 g/l) to minimize both the toxic effects of ... Using methanol as substrate has two characteristics: potential toxicity and volatility. Tests done with our *Methylobacterium extorquens* isolate showed that methanol concentrations above 1.7 g/l ...  
Cited by 71  Related articles  All 4 versions  Cite  Save

High-cell-density production of poly-β-hydroxybutyrate (PHB) from methanol by *Methylobacterium extorquens*: production of high-molecular-mass PHB  
D Bourque, Y Pomerleau, D Groleau - Applied Microbiology and ..., 1995 - Springer  
... and characterization of a new isolate of the methylorophic bacterium *Methylobacterium extorquens*, which is ... to be very efficient at low concentrations and showed no obvious sign of toxicity. ... Our M. extorquens strain was able to synthesize PHB of very high molecular mass, up ...  
Cited by 100  Related articles  All 7 versions  Cite  Save

Formaldehyde-detoxifying role of the tetrahydromethanopterin-linked pathway in *Methylobacterium extorquens* AM1  
... the idea of cytoplasmic formaldehyde rather than periplasmic formaldehyde being responsible for toxicity. ... of a C 1-H 4 MPT intermediate(s) is either toxic and/or ... Genetic organization of the mau gene cluster in *Methylobacterium extorquens* AM1: complete nucleotide sequence ...  
Cited by 77  Related articles  All 11 versions  Cite  Save

A systems biology approach uncovers cellular strategies used by *Methylobacterium extorquens* AM1 during the switch from multi-to single-carbon growth  
E Skovran, GJ Crowther, X Guo, S Yang, ME Lidstrom - PLoS One, 2010 - journals.plos.org  
... *Methylobacterium extorquens* AM1 is a facultative methylorophic bacterium capable of growth on single-carbon compounds such as methanol ... must be poised to quickly adapt, capturing available methanol while preventing buildup of its subsequent toxic oxidation product ...  
Cited by 44  Related articles  All 12 versions  Cite  Save

Alternative route for glyoxylate consumption during growth on two-carbon compounds by *Methylobacterium extorquens* AM1  
Y Okubo, S Yang, L Chistoserdova, ... - Journal of ..., 2010 - Am Soc Microbiol  
... Next Section. ABSTRACT: *Methylobacterium extorquens* AM1 is a facultative methylorophic bacterium capable of growth on both single-carbon and multicarbon compounds. ... Since glyoxylate is toxic to this bacterium, it seemed likely that a system is in place to keep it from accumulating. ...  
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Heterologous extracellular production of enterocin P from Enterococcus faecium P13 in the methylorophic bacterium *Methylobacterium extorquens*  
J Gutiérrez, D Bourque, RC Criado, YJ Choi, ... - FEMS microbiology, 2005 - academic.oup.com  
... Article Navigation. Heterologous extracellular production of enterocin P from *Enterococcus faecium* P13 in the methylorophic bacterium *Methylobacterium extorquens*. Jorge Gutiérrez Jorge Gutiérrez. Departamento de Nutrición ...  
Cited by 29  Related articles  All 17 versions  Cite  Save

Production and characterization of polyhydroxyalkanoates by recombinant *Methylobacterium extorquens*: combining desirable thermal properties with functionality  
P Höfer, P Vermette, D Groleau - Biochemical engineering journal, 2011 - Elsevier  
... a model that allowed for on-line estimation of toxic co-substrate ... Functionalized polyhydroxyalkanoates; *Methylobacterium extorquens*; Methanol; Alkenoic acid; Automatic substrate feeding; Thermo-mechanical ... bonds are cheaper and generally exhibit less toxicity ...  
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... of a heterologous protein, haloalkane dehalogenase, in a poly-β-hydroxybutyrate-deficient strain of the facultative methyloroph *Methylobacterium extorquens* AM1  
KA Fitzgerald, ME Lidstrom - Biotechnology and ..., 2003 - Wiley Online Library  
... Methanol is a relatively inexpensive (http://www.methanex.com/methanol/currentprice.htm) substrate, and has the added advantages of high solubility in water and low toxicity. ... An attractive strain for this purpose is *Methylobacterium extorquens* AM1. ...  
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QscR-mediated transcriptional activation of serine cycle genes in *Methylobacterium extorquens* AM1
... The levels of XyIE in these mutants declined during longer incubation periods, presumably due to formaldehyde toxicity. ... 1993. Genetics of serine pathway enzymes in *Methylobacterium extorquens* AM1: phosphoenolpyruvate carboxylase and malyl coenzyme A lyase. ...
Cited by 29 Related articles All 15 versions Cite Save

Determination of the Gene Sequence and the Three-dimensional Structure at 2.4 Å Resolution of Methanol Dehydrogenase from *Methylophilus* W3A1
Z Xia, W Dai, Y Zhang, SA White, GB Boyd... - Journal of molecular... 1996 - Elsevier
... The refined structure of the quinoprotein methanol dehydrogenase from *Methylobacterium extorquens* at 1.94 Å. A molecular level mechanism for uranium (VI) toxicity through Ca²⁺ displacement in pyrroloquinoline quinone-dependent bacterial dehydrogenase. ...
Cited by 140 Related articles All 6 versions Cite Save

Metabolic engineering of *Methylobacterium extorquens* AM1 for 1-butanol production
B Hu, ME Lidstrom - Biotechnology for biofuels, 2014 - biotechnologyforbiofuels...
... *Methylobacterium extorquens* AM1 is a facultative methylotrophic α-proteobacterium capable of using both one-carbon (C1) 1-butanol toxicity to microorganisms is one of the important factors that limit. Therefore, the growth rates of *M. extorquens* AM1 wild type in the presence of 1 ...
Cited by 15 Related articles All 14 versions Cite Save More

Novel formaldehyde-activating enzyme in *Methylobacterium extorquens* AM1 required for growth on methanol
JA Vorholt, CJ Marx, ME Lidstrom... - Journal of... 2000 - Am Soc Microbiol
... Formaldehyde is toxic for all organisms from bacteria to humans due to its reactivity with biological macromolecules. In the α-proteobacterium *Methylobacterium extorquens* AM1, we found a previously unknown enzyme that efficiently catalyzes the removal of formaldehyde: it ...
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Formaldehyde-limited cultivation of a newly isolated methylotrophic bacterium, *Methylobacterium* sp. MF1: enzymatic analysis related to C 1 metabolism
R Mitsui, M Omori, H Kitazawa, M Tanaka - Journal of bioscience and... 2006 - Elsevier
... Since formaldehyde is highly toxic, it must be oxidized or assimilated immediately ... 6 and 7). This transformant is capable of effectively overcoming the toxicity of formaldehyde. ... The facultative serine pathway-utilizer, *Methylobacterium extorquens* AM1, has well-devised systems for ...
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Production of functionalized polyhydroxyalkanoates by genetically modified *Methylobacterium extorquens* strains
P Höfer, YJ Choi, MJ Osborne... - Microbial cell... 2010 - microbialcellfactories.biomedcentral... ...
... The proprietary, wildtype strain *Methylobacterium extorquens* ATCC 55368 was used throughout this study [24]. ... The two M. *extorquens* strains (Figure 4A and Figure 5A) continued to grow, although ... addition of the respective carboxylic acid, due to the well-known toxicity of such ...
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Heterologous expression of heterotrophic nitrification genes
LC Crossman, JW Moir, JJ Enticknap... - ... 1997 - mic.microbiologyresearch.org
... Further, when expressed in the methylotroph *Methylobacterium extorquens* AM1, the AM0 endows on this organism the ... The heterotrophic nitrification genes are moderately toxic in M. *extorquens*, more toxic in Ps. ... Toxicity is due to the activity of the gene products in M. *extorquens* ...
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Biosynthesis of polyhydroxybutyrate/valerate with different molecular weights during the growth of *Methylobacterium extorquens* G-10 on a methanol-pentanol mixture
VA Ezhov, NV Doronina, YA Trotsenko - Applied biochemistry and... 2013 - Springer
... weight (MW) of the polyhydroxybutyratervalerate (PHBV) copolymer synthesized by *Methylobacterium extorquens* G 10 ... Consequently, the MW of PHB synthesized by methylotobacteria depended on the carbon ... of the pentanol concentration on the growth of M. *extorquens* G 10 ...
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https://scholar.google.com/scholar?start=0&q=methylobacterium+extorquens+toxicity+plant&hl=en&as_sdt=0,22
Biochemical characterization of a dihydromethanopterin reductase involved in tetrahydromethanopterin biosynthesis in Methylobacterium extorquens AM1
... dmrA mutants grow on succinate but not on C 1 compounds, and the mutants are highly sensitive to methanol toxicity. ... 2003. Methylothrophy in Methylobacterium extorquens AM1 from a genomic point of view. J. Bacteriol. 185:2980-2987. ...
Cited by 14 Related articles All 9 versions Cite Save

... role of the methylene-tetrahydromethanopterin dehydrogenase MtdA in the tetrahydromethanopterin-dependent oxidation pathway in Methylobacterium extorquens ...
NC Martinez-Gomez, S Nguyen... - Journal of ..., 2013 - Am Soc Microbiol
... The metabolism of one-carbon compounds in the facultative methylothroph Methylobacterium extorquens AM1 (Fig. ... in cell extracts of M. extorquens, suggesting that M. extorquens has the ... to allow sufficient carbon flux from formaldehyde to formate to avoid formaldehyde toxicity. ...
Cited by 11 Related articles All 8 versions Cite Save

Methylobacterium genome sequences: a reference blueprint to investigate microbial metabolism of C1 compounds from natural and industrial sources
S Vuilleumier, L Chistoserdova, MC Lee, F Bringel... - PloS one, 2009 - journals.plos.org
... Leading metrics. Open Access. Peer-reviewed. Research Article. Methylobacterium Genome Sequences: A Reference Blueprint to Investigate Microbial Metabolism of C1 Compounds from Natural and Industrial Sources. Stéphane Vuilleumier, ...
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Flux analysis uncovers key role of functional redundancy in formaldehyde metabolism
CJ Marx, SJ Van Dien, ME Lidstrom - PLoS biology, 2005 - journals.plos.org
... of a gapped genome sequence for a model methylothrophic bacterium, Methylobacterium extorquens AM1, has ... responses is important for assessing and possibly ameliorating toxicity problems in ... each metabolic module in methylothrophic metabolism in M. extorquens AM1 during ...
Cited by 64 Related articles All 37 versions Cite Save More
Development of improved versatile broad-host-range vectors for use in methylotrophs and other Gram-negative bacteria

CJ Marx, ME Lidstrom - Microbiology, 2001 - mic.microbiologyresearch.org

... *Methylobacterium extorquens* AM1 is an example of an organism for which improved genetic tools are needed. ... Expression vector pCM110, was created that would provide minimal expression in E. coli to allow toxic genes to be introduced into *M. extorquens* AM1 (Fig. ... Cited by 249 Related articles All 10 versions Cite Save

Closed-loop control of bacterial high-cell-density fed-batch cultures: production of mcl-2PHAs by *Pseudomonas putida* KT2442 under single-substrate and cofeeding ...

MB Kellerhals, B Kessler - - Biotechnology and ..., 1999 - Wiley Online Library

... Efficient production of mcl-2PHAs on such toxic substrates therefore requires control of the ... show that this control system is suitable for avoiding substrate toxicity and supplying the molecular mass of poly(3-hydroxybutyrate) produced by *Methylobacterium extorquens* and Alcaligenes ... Cited by 56 Related articles All 5 versions Cite Save More

Catheter infection caused by *Methylobacterium* in immunocompromised hosts: report of three cases and review of the literature

KM Kaye, A Macone - - Clinical infectious diseases, 1992 - academic.oup.com

... t Organisms were not identified, but their description was consistent with *Methylobacterium*. ... Our series shows that *M. extorquens* is among the organ... Except in the treatment of patients demonstrating severe toxicity, no evidence supports the addition of a second antibiotic to ... Cited by 42 Related articles All 9 versions Cite Save More

Use of oligodeoxynucleotide signature probes for identification of physiological groups of methylotrophic bacteria.

HC Tsien, BJ Bratina, K Tsuiji - - Applied and ..., 1990 - Am Soc Microbiol

... Some of them are toxic chemicals that are on the high priority list of toxic environmental pollutants of the Environmental Protection Agency (21, 32). Methanotrophs * Corresponding author.  * *Methylobacterium extorquens* 25 Methanol 37 NCIMB ... Cited by 141 Related articles All 9 versions Cite Save

Dichloromethane metabolism and C1 utilization genes in *Methylobacterium* strains

MF Kayser, Z Uncurum, S Vuilleumier - Microbiology, 2002 - mic.microbiologyresearch.org

... Formaldehyde, the product of dehalogenation, certainly constitutes a toxic burden to the methylotrophic cell ... in both pathways of C " oxidation and assimilation recently discovered in *M. extorquens* AM1 (Chistoserdova et al ... *Methylobacterium*: DCM metabolism and C " utilization ... Cited by 51 Related articles All 5 versions Cite Save

Development of an optimized medium, strain and high-throughput culturing methods for *Methylobacterium extorquens*

NF Delaney, ME Kaczmarek, LM Ward, PK Swanson - - PLoS ..., 2013 - journals.plos.org

... Peer-reviewed. Research Article. Development of an Optimized Medium, Strain and High-Throughput Culturing Methods for *Methylobacterium extorquens*. ... Development of an Optimized Medium, Strain and High-Throughput Culturing Methods for *Methylobacterium* ... Cited by 35 Related articles All 13 versions Cite Save More

Formaldehyde damage to DNA and inhibition of DNA repair in human bronchial cells


... Abstract. Cultured bronchial epithelial and fibroblastic cells from humans were used to study DNA damage and toxicity caused by formaldehyde. Formaldehyde caused the formation of cross-links between DNA and proteins, caused ... Cited by 195 Related articles All 8 versions Cite Save

Characterization of a second methylene tetrahydromethanopterin dehydrogenase from *Methylobacterium extorquens* AM1

CH Hagemeyer, L Chistoserdova - - The FEBS ..., 2000 - Wiley Online Library

... The methylotrophic α-proteobacterium *Methylobacterium extorquens* AM1 possesses tetrahydrofolate (H 4 F) and diphospho ... As formaldehyde is a necessary but toxic intermediate during growth on C 1 ... Whereas wild-type *M. extorquens* AM1 could grow on succinate in the ... Cited by 67 Related articles All 5 versions Cite Save
Antioxidant protein 2 prevents methemoglobin formation in erythrocyte hemolysates
KM Stuhlmeier, JJ Kao, P Wallbracht... - The FEBS ..., 2003 - Wiley Online Library
... Previous article in issue: The tungsten-containing formate dehydrogenase from Methylobacterium extorquens AM1: Purification and properties. ... Evolving antioxidant defence systems to protect against O2 toxicity has been a prerequisite for an organism's use of O2 for efficient ...
Cited by 46 Related articles All 7 versions Cite Save

Electro-biocatalytic production of formate from carbon dioxide using an oxygen-stable whole cell biocatalyst
H Hwang, YJ Yeon, S Lee, H Choe, MG Jang... - Bioresource ..., 2015 - Elsevier
... Electro-biocatalytic CO2 reduction with 8 species of Methylobacteria (1.3 g wet cells, 5... Oxygen-stable Methylobacterium extorquens AM1 in the electro-biocatalytic CO2 reduction system (1.3 g wet... Additionally, the varied concentration of M. extorquens AM1 as a whole cell was ...
Cited by 12 Related articles All 7 versions Cite Save

Cofactor-dependent pathways of formaldehyde oxidation in methylo trophic bacteria
JA Vorholt - Archives of microbiology, 2002 - Springer
... A central feature of the metabolism of methylo trophic bacteria is that carbon flow proceeds via the central intermediates formaldehyde (Fig.1), which is highly toxic due to its nonspecific... The H4F-dependent pathway and its encoding genes in Methylobacterium extorquens AM1 ...
Cited by 155 Related articles All 10 versions Cite Save

Parallel and divergent evolutionary solutions for the optimization of an engineered central metabolism in Methylobacterium extorquens AM1
SM Carroll, LM Chubiz, D Agashe, CJ Marx - Microorganisms, 2015 - mdpi.com
... Microorganisms 2015, 3(2), 152-174; doi:10.3390/microorganisms3020152. Article. Parallel and Divergent Evolutionary Solutions for the Optimization of an Engineered Central Metabolism in Methylobacterium extorquens AM1 ...
Cited by 5 Related articles All 12 versions Cite Save More

Comprehensive molecular characterization of Methylobacterium extorquens AM1 adapted for 1-butanol tolerance
B Hu, YM Yang, DAC Beck... - Biotechnology ..., 2016 - biotechnologyforbiofuels ...
... The toxicity of alcohols is one of the major roadblocks of biological fermentation for biofuels production. Methylobacterium extorquens AM1, a facultative methylo trophic a-proteobacterium, has been engineered to generate 1-butanol from cheap carbon feedstocks through a ...
Cited by 4 Related articles All 17 versions Cite Save More

Metabolomics in systems microbiology
ML Reaves, JD Rabinowitz - Current opinion in biotechnology, 2011 - Elsevier
... Elucidation of the methanol assimilation pathway in Methylobacterium extorquens AM1... needed, both to optimize long-term fluxes and to avoid immediate toxicity due to... the ability to inactivate glutamine synthetase by covalent modification suffers toxic ... metabolic derangements ...
Cited by 94 Related articles All 13 versions Cite Save

Phylogeny poorly predicts the utility of a challenging horizontally transferred gene in Methylobacterium strains
... product into its native one-carbon metabolic pathways to minimize any resulting toxicity (28)... transfer of the dcmA gene to two other strains of M. extorquens, AM1 and... addressed these questions by transferring dcmA into a broad range of Methylobacterium strains, quantifying ...
Cited by 13 Related articles All 12 versions Cite Save

Growth and formation of poly (hydroxybutyric acid) by Methylobacterium rhodesianum at methanol concentrations of above 25 g/l
EJ Bormann, M Leissner, B Beer - Engineering in Life Sciences, 1997 - Wiley Online Library
... poly(hydroxybutyric acid) using Methylobacterium organophilum [8], Pseudo - monas K [9], Protomonas extorquens [ 101, Methylobacterium rhodesianum Z [11] and Methylobacterium sp. ... But generally, the main problem results from the toxicity of the methanol ...
Cited by 8 Related articles All 3 versions Cite Save More
Asymmetric, bimodal trade-offs during adaptation of Methylobacterium to distinct growth substrates
MC Lee, HH Chou, CJ Marx - Evolution, 2009 - Wiley Online Library

Methylobacterium extorquens AM1, to C 1 (methanol) or multi-C (succinate) compounds to investigate specialization and trade-offs between these two metabolic lifestyles. ...
Cited by 66 Related articles All 14 versions Cite Save More

Methylobacterium extorquens microorganism useful for the preparation of poly-ß-hydroxybutyric acid polymers

The above mentioned strain of Methylobacterium extorquens of the present invention, grows well in a minimal ... achieve this goal since a concentrated culture medium may be (partially) toxic to the ... The toxicity may be caused either by the high concentration of the carbon source ...
Cited by 10 Related articles All 3 versions Cite Save

Ethylmalonyl coenzyme A mutase operates as a metabolic control point in Methylobacterium extorquens AM1

Methylobacterium extorquens AM1 is a facultative methylotroph capable of growth on single-carbon (C 1 ... dynamic growth environment (4, 5). In this niche, M. extorquens must acclimate ... substrate availability while preventing the lethal accumulation of the toxic methanol oxidation ...
Cited by 3 Related articles All 10 versions Cite Save

Analysis of the 3′-region of the dcmA gene of dichloromethane dehalogenase of Methylobacterium dichloromethanicum DM4
YE Firsova, DN Fedorov, YA Trotsenko - Microbiology, 2011 - Springer

dichloromethanicum DM4 and DCM degraders Methylophilus multivorans DM15 and Methylobacterium extorquens DM 17 ... DNA of the strains M. dichloromethanicum DM4 (1), M. extorquens DM17 (2) ... these genes were expressed during the growth of methylobacteria on DCM. ...
Cited by 7 Related articles All 6 versions Cite Save
Overview of bacterial expression systems for heterologous protein production: from molecular and biochemical fundamentals to commercial systems
K Terpe - Applied microbiology and biotechnology, 2006 - Springer
... Enterococin P, a strong antilisterial pediocin-like bacteriocin from Enterococcus faecium P13, was produced by Methylobacterium extorquens (Gutierrez et al. ... Furthermore, the tight repression of the nir promoter upon induction allowed the production of the toxic oncoprotein E6. ...
Cited by 700 Related articles All 17 versions Cite Save

Widespread genetic switches and toxicity resistance proteins for fluoride
JL Baker, N Sudarsan, Z Weinberg, A Roth... - ..., 2012 - science.sciencemag.org
... of species encode at most 2 fluoride riboswitches, the bacterium Methylobacterium extorquens DM4 encodes ... fluoride anions and require a more robust fluoride sensor and toxicity mitigation response ... why some species carry sensor and mitigation systems for toxic metals such ...
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MtdC, a novel class of methylene tetrahydromethanopterin dehydrogenases
Cited by 18 Related articles All 15 versions Cite Save

Just add lanthanides
ESKovran, NC Martinez-Gomez - Science, 2015 - science.sciencemag.org
... in the environment (8). Transcription of the mxAF genes in M. extorquens AM1 requires ... M. fumarophilicum SolV differed from those previously described for XoxF from Methylobacterium ... species: Methanol ... cleanup of REE mining sites, and to reduce the potential for toxicity in our ...
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Production of 2-Hydroxyisobutyric Acid from Methanol by Methylobacterium extorquens AM1 Expressing (R)-3-Hydroxybutyryl Coenzyme A-Isomerizing Enzymes
MT Rohde, S Tischer, H Harms... - Applied and ..., 2017 - Am Soc Microbiol
... A well-studied representative is Methylobacterium extorquens AM1, a pink-pigmented, aerobic alphaproteobacterium first ... In addition, a toxicity of the mutase proteins has not been previously observed when ... on recombinant AM1 (25, 32, 39-41) or other M. extorquens strains (29 ... Cited by 3 Related articles All 4 versions Cite Save

Calorespirometric feeding control enhances bioproduction from toxic feedstocks—Demonstration for biopolymer production out of methanol
MT Rohde, S Pauffer, H Harms... - Biotechnology and ..., 2016 - Wiley Online Library
... A methylotrophic model bacterium is the strictly aerobic, facultative methylotroph Methylobacterium extorquens AM1. ... a pathway for the production of biofuels in M. extorquens (Hu and ... processes has two main shortcomings: Its high volatility and toxicity for microorganisms. ...
Cited by 4 Related articles All 4 versions Cite Save More

Amperometric detection of methanol with a methanol dehydrogenase modified electrode sensor
... An amperometric enzyme electrode was developed by immobilizing the quinoprotein methanol dehydrogenase from Methylobacterium extorquens AM1 onto a ... automobile fuel [1]. However, methanol exposure via inhalation and skin absorption may lead to toxic effects from ...
Cited by 31 Related articles All 6 versions Cite Save

Detection of dichloromethane with a bioluminescent (lux) bacterial bioreporter
NLopes, SA Hawkins, P Jogier, FM Menn... - Journal of industrial ..., 2012 - Springer
... Fatal intoxication due to DCM inhalation as well as numerous cases of non-fatal ... have reduced the estimated risks but the mechanisms of DCM toxicity continue to ... by employing the evolutionary adaptation of the methylotrophic bacterium Methylobacterium extorquens (formerly M ...
Cited by 6 Related articles All 14 versions Cite Save
Adaptation of aerobic *methylbacteria* to dichloromethane degradation  
ML Torgonskaya, YE Firsova, NV Doronina... - Applied Biochemistry ..., 2007 - Springer  
... consumption of DCM by these degraders but not by transconjugants *Methylbacterium extorquens*  
AM1, expressing... Our experiments showed that *methylbacteria* able to grow on DCM were more  
stress [11, 13], we suggested that faster adaptation of methylbacterial cells to...  
Cited by 3 Related articles All 7 versions Cite Save

Metabolomics revealed an association of metabolite changes and defective growth in  
*Methylbacterium extorquens* AM1 overexpressing ecm during growth...  
J Cui, NM Good, B Hu, J Yang, Q Wang, M Sadilek... - PloS one, 2016 - journals.plos.org  
... *Methylbacterium extorquens* AM1 is a facultative methylotroph capable of growth on both  
single-carbon... is one of the central assimilatory pathways in *M. extorquens* during growth. Moreover,  
glyoxylate, a toxic and highly regulated essential intermediate, was determined to be...  
Cited by 2 Related articles All 11 versions Cite Save More

Formaldehyde metabolism in *Methylbacterium extorquens* AM1  
CJ Marx - 2003 - digital.lib.washington.edu  
... *Methylbacterium extorquens* AM1 possess two pterin-linked C1 transfer pathways that are critical  
for methylotrophic growth... metabolism that has elucidated an elegant metabolic loop through which  
*M. extorquens* AM1 maintains formaldehyde below toxic levels while...  
Cited by 1 Related articles All 2 versions Cite Save More

Novel, versatile, and tightly regulated expression system for *Escherichia coli* strains  
YJ Choi, L Morel, T Le Françoise... - Applied and..., 2010 - Am Soc Microbiol  
... The construct of the cymu switch in *E. coli* described herein is a simplified and more flexible  
version of the *Methylbacterium extorquens* cymu switch. In order to avoid cellular toxicity caused  
by the CymR in *M. extorquens*, expression levels were reduced by integrating...  
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Effects of DNA-damaging agents on aerobic *methylbacteria* capable and incapable of  
utilizing dichloromethane  
YE Firsova, ML Torgonskaya, NV Doronina... - Applied Biochemistry ..., 2005 - Springer  
... way—*Methylbacterium dichloromethanum* DM4 VKM V-2191 (=DSM 5343), *Methylbacterium*  
extorquens AM1 VKM... conditions allowed us to find out whether the methylbacterial DNA was...  
out how efficiently the DNA damage was repaired in the *methylbacteria* capable or...  
Cited by 3 Related articles All 9 versions Cite Save

Proteomic analysis of differentially expressed proteins in human lung cells following  
formaldehyde treatment  
YM Jeon, JC Ryu, MY Lee - Molecular and Cellular Toxicology, 2007 - koreascience.or.kr  
... C. J. Christoserdova, L. & Lidstrom, ME Formaldehyde- detoxifying role of the  
tetrahydrodiaminoethinoprotein-linked pathway in *Methylbacterium extorquens* AM1... Dowling, VA &  
Sheehan, D. Proteomics as a route to identification of toxicity targets in environmental toxicology...  
Cited by 3 Related articles All 2 versions Cite Save More

Physiological and biochemical analysis of the transformants of aerobic *methylbacteria*  
expressing the dcmA gene of dichloromethane dehalogenase  
YE Firsova, NV Doronina, YA Trotsenko - Microbiology, 2004 - Springer  
... Because of its high toxicity, carcinogenicity, volatility, solubility in water, and persistence, DCM  
is included on the list of... of Aerobic *Methylbacterium* Expressing the dcmA Gene... DM4  
(DM4-2cr/pME 8220 and DM4-2cr/pME8221) and of *Methylbacterium extorquens* AM1 (AM1)...  
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Genetics and regulation of C1 metabolism in methylotrophs  
ME Lidstrom, L Christoserdova, S Stolyar... - ... Electron Transfer Chains... 1998 - Springer  
... monophosphate cycle intermediates [2]. In the methylotrophs, the central metabolic intermediate  
is formaldehyde, a toxic compound... approach to study formaldehyde production and consumption  
systems in the a-proteobacterial methylotroph, *Methylbacterium extorquens* AM1...  
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Functionality of the xoxF gene in *Methylbacterium dichloromethanicum* DM4  
YE Firsova, ML Torgonskaya, YA Trotsenko - Microbiology, 2016 - Springer  
... is required for expression of methanol dehydrogenase in *Methylbacterium extorquens* AM1,  
J. ... Doronina, NV, and Trotsenko, Yu.A., Adaptation of aerobic methylbacteria to dichloromethane  
W. Gruffaz, C., Haugen, E., Hourcade, E., et al., *Methylbacterium* genome sequences...  
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https://scholar.google.com/scholar?start=40&q=methylbacterium+extorquens+toxicity+plant&hl=en&as_sdt=0,22
Aerobic methyllobacteria as the basis for a biosensor for dichloromethane detection
YV Plekhanova, YE Firsova... - Applied ... 2013 - search.proquest.com
... Characteristics. *Methyllobacterium* dichloromethanicum DM4. relationships presented in Fig. 2 allow one to detect DCM by the *methyllobacteria* M. dichloromethani cum DM4, *M. extorquens* DM17, M. helvetica DM8, and A. dichloromethanicus DM16, which use ...
Cited by 2 Related articles All 9 versions Cite Save

Biotechnological potential of the ethylmalonyl-CoA pathway
BE Alber - Applied microbiology and biotechnology, 2011 - Springer
... Other considerations include secretion of products, possible toxicity, yields, and downstream processing of the desired ... organisms already considered for biotechnological applications contain the ethylmalonyl-CoA pathway: R. sphaeroides and *Methyllobacterium extorquens* ...
Cited by 50 Related articles All 12 versions Cite Save

Direct immunofluorescence and enzyme-linked immunosorbent assays for evaluating organic contaminant degrading bacteria
RL Brigmon, MM Franck, JS Bray, DF Scott... - Journal of..., 1998 - Elsevier
... 35069, Methylosinus sporium 43645, *Methyllobacterium extorquens*. SRS cultures.
S4A/1Bd, Methanotroph. S3C2AB, Methanotroph. ... ATCC 35069, Methylosinus sporium, -, -, -
-, +, -, ATCC 43645, *Methyllobacterium extorquens*, -, -, -, +, -, ...
Cited by 18 Related articles All 5 versions Cite Save
Creating auxotrophic mutants in Methylophilus methylo trophus AS1 by combining electroporation and chemical mutagenesis
CS Kim, TK Wood - Applied microbiology and biotechnology, 1997 - Springer

... Although ethyl methanesulfonate has had success in mutating Methylobacterium extorquens AM1 (Morris et al. ... mutagenesis treatment for E. coli BK6 since MNNG is much more toxic to this ... to no MNNG exposure or electroporation); therefore, there was no increase in toxicity. ...
Cited by 5 Related articles All 13 versions Cite Save More

Biosensors and biofuel cells: Research focused on practical application
AN Reshetilov - Applied biochemistry and microbiology, 2015 - search.proquest.com

... interest and are the most promising for assessment of the toxicity of goods; the possibility to assess acute and chronic toxicity could be ... Out of four strains of methylobacteria, Methylobacterium dichloromethanum DM4, Methylobacterium extorquens DM17, Methylophila ...
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Exploring C1-metabolism-shotgun proteomics of the methylo trophic prokaryote
Methylobacterium extorquens AM1
G Bosch, T Wang, J Miller, E Skovran, G Crowther...
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Anti-alcoholic and anti-narcotic action of Methylobacterium extorquens UCM B-3368
TP Kryshata, VO Romanov's k, NA Stashnii ... - (Kiev, Ukraine; 1993), 2008 - europepmc.org

... Anti-alcoholic and anti-narcotic action of Methylobacterium extorquens UCM B-3368. (PMID:19938614), PMID:19938614. ... Abstract. The paper deals with action efficiency of microbial biomass on characteristic indicators at alcohol and morphine organism intoxication. ...
All 2 versions Cite Save More

Functional activity of the modA2 gene in Methylobacterium dichloromethanicum DM4
YE Firsova, YA Trotsenko - Microbiology, 2014 - Springer

... Aerobic methylobacteria can mineralize DCM due to dichloromethane dehalo genase DcmA, a cytoplasmic ... of DCM dehalogenase, dcmA and dcmR, from the degrader Methylobacterium dichloromethanicum DM4 to ... ("DCM island") which is not present in M. extorquens AM1 [3 ...
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Physiology and Evolution of Methylamine Metabolism across Methylobacterium extorquens strains
DD Nayak - 2014 - search.proquest.com

... homolog that has been suggested to play a regulatory role in M. extorquens (Skovran et al ... in the build-up of (potentially toxic) C1 intermediates ... basis for these effects, and to determine whether they hold for other strains of Methylobacterium. ...
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Synthetic microbial ecology for biofuel production from lignocellulose
M Thommes, A Lubbe, J Lee - orau.gov

... produced by the demethoxylation of lignin monomers can inhibit microbial growth due to its toxicity. ...
In order to demethylate and cleave complex aromatics, we have genetically engineered M. extorquens to express the vanABK operon from Methylobacterium nodulans ...
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GENETICS AND REGULATION OF CI METABOLISM IN METHYLOTROPHS
AJL SPRINGER - ... Electron Transfer Chains; Genetics, Composition, and ..., 1996 - Springer

... monophosphate cycle intermediates [2]. In the methylothrophs, the central metabolic intermediate is formaldehyde, a toxic compound, ... approach to study formaldehyde production and consumption systems in the a-proteobacterial methylothroph, Methylobacterium extorquens AM1. ...
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ME LIDSTROM, L. CHISTOSEROLOVA, S. STOLYAR
AL SPRINGER - ... Chains: Genetics, Composition and Mode of ..., 2012 - books.google.com

... monophosphate cycle intermediates [2]. In the methylothrophs, the central metabolic intermediate is formaldehyde, a toxic compound, ... approach to study formaldehyde production and consumption systems in the a-proteobacterial methylothroph, Methylobacterium extorquens AM1 ...
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https://scholar.google.com/scholar?start=60&q=methylobacterium+extorquens+toxicity+-+plant&hl=en&as_sdt=0,22
Cloning and characterization of dichloromethane dehalogenase from *Methylobacterium rhodesianum* for dichloromethane degradation
J Yu, Q Liu, L Liu, J Chen - Bioremediation Journal, 2017 - Taylor & Francis
... Functional genomics of dichloromethane utilization in *Methylobacterium extorquens* DM4 ... and biochemical analysis of the transformants of aerobic *methylobacteria* expressing the...
*Methylobacterium* and *Hypromicrobium* were isolated from industrial wastewater with DCM as ...
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Direct measurement of oxygen consumption rates from attached and unattached cells in a reversibly sealed, diffusively isolated sample chamber
TJ Strovas, SC McQuaide, JB Anderson... - ... in bioscience and..., 2010 - ncbi.nlm.nih.gov
... effects of stimuli on cells in the investigation of stress response and toxicity studies. ... Measurement of respiration rates of *Methylobacterium extorquens* AM1 cultures by use of a ... Optical oxygen microrespirometry as a platform for environmental toxicology and animal model studies ...
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Synthesis of high-molecular-mass polyhydroxybutyrate from methanol in *Methylophilic* halotolerans C2
VA Ezhev, NV Doronina, MN Shmareva... - Applied Biochemistry ..., 2017 - Springer
... condition of PHB biosynthesis from methanol is the maintenance of a low methanol concentration (to avoid the toxic effects of ... An increase in PHB MM to 900–1800 kDa could be achieved for *Methylobacterium extorquens* via the maintenance of methanol concentration at a low ...
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Effective utilization of dichloromethane by a newly isolated strain *Methylobacterium rhodesianum* H13
DZ Chen, DJ Ouyang, HX Liu, J Chen... - ... Science and Pollution ..., 2014 - Springer
... DCM has a high toxicity, has been proven to be carcinogenic, and has ... Among the genus *Methylobacterium*, another DCM-degrading strain *Methylobacterium* dichloromethanicum DM4 was investigated ... In fact, even belonging to the same species *M. extorquens*, strain DM4 and ...
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Upregulated transcription of plasmid and chromosomal ribulose monophosphate pathway genes is critical for methanol assimilation rate and methanol tolerance in ...
ØM Jakobsen, A Benichou, MC Fickinger... - Journal of ..., 2006 - Am Soc Microbiol
... and the latter compound was proposed to be the major cell-toxic agent under ... A similar conclusion has been described for the facultative methylobacter *Methylobacterium extorquens* AM1 metabolizing C 1 ... Alter the cell yield on methanol, as well as to reduce methanol toxicity ...
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Isolation of an unidentified pink-pigmented bacterium in a clinical specimen.
... The patient appeared very ill and toxic, with a dry cough and tachypnea. Epiglottitis was diagnosed. ...
... Gilardi and Faur (1) described 7 strains of an unnamed taxon that constituted their cluster 2; these 14 strains in their cluster 1 were similar to *Methylobacterium extorquens*. ...
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Selection maintains apparently degenerate metabolic pathways due to tradeoffs in using methylamine for carbon versus nitrogen
DD Nayak, D Agashe, MC Lee, CJ Marx - Current Biology, 2018 - Elsevier
... Tradeoffs between cellular localization and ammonium toxicity lead to selection for this apparent degeneracy as it is ... Methylamine Metabolism in *Methylobacterium extorquens* Strains. ... (B) Methylamine growth mediated by the NMG pathway (blue) in other M. extorquens strains. ...
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Biodegradation of high concentrations of formaldehyde by lyophilized cells of *Methylobacterium* sp. FD1
H Yonemitsu, E Shiozaki, F Hitotsu... - Bioscience, ..., 2016 - Taylor & Francis
... Formaldehyde is frequently discarded in wastes and causes environmental pollution; therefore, because of its high toxicity, it should be degraded before discarding. ... 16–29) These strains include *Methylobacterium* sp. MF1,16( M. extorquens,17,18) Methylobacterium sp. ...
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https://scholar.google.com/scholar?start=60&q=methylobacterium+extorquens+toxicity+-plant&hl=en&as_sdt=0,22
Fluoride Riboswitch
G Riddiough - Science Signaling, 2012 - stke.sciencemag.org
... The bacterium Methylobacterium extorquens DM4, which can use halogenated hydrocarbons as an energy source, was found to encode at ... JL Baker, N. Sudarsan, Z. Weinberg, A. Roth, RB Stockbridge, RR Breaker, Widespread genetic switches and toxicity resistance proteins ...
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Characterization and heterologous gene expression of a novel esterase from Lactobacillus casei CL96
YJ Choi, CB Miguez, BH Lee - Applied and environmental ..., 2004 - Am Soc Microbiol
... of recombinant esterase in methylotrophic yeast (Pichia pastoris) and bacteria (Methylobacterium extorquens), since the ... has many advantages, such as high solubility in water and low toxicity. ... profile of the esterase in the methylotrophic bacterium M. extorquens ATCC 55366 ...
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Genetics of methane and methanol oxidation in Gram-negative methylotrophic bacteria
TM Barta, RS Hanson - Antonie van Leeuwenhoek, 1993 - Springer
... in the production of useful metabolites, and in bioremediation of toxic pollutants (see ... for the lack of success in mutagenesis, such as high mutagen toxicity, inappropiate ... Methylobacterium extorquens NR-2 has been success- fully transformed with the plasmid pLA2917 by ...
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Methylophils: genetics and commercial applications
ME Lidstrom, DJ Stirling - Annual Reviews in Microbiology, 1990 - annualreviews.org
... and the vector pLA2917 is useful for constructing overlapping Sau3A genomic banks (1).
Subcloning vectors that include lacZ screening are available, such as pRK404 and pRK310
(30), although pRK404 is unstable in some strains such as Methylobacterium extorquens AM1 ...
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Genomic insights into methanotrophy: the complete genome sequence of Methylococcus capsulatus (Bath)
... We used phylogenomic analysis, gene order information, and comparative analysis with the
partially sequenced methylophor Methylobacterium extorquens to detect genes of unknown
function likely to be involved in methanotrophy and methylophory ...
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A challenge for 21st century molecular biology and biochemistry: what are the causes of
obligate autotrophy and methanotrophy?
AP Wood, JP Aurikko, DP Kelly - FEMS microbiology reviews, 2004 - Wiley Online Library
... on thiosulphate [66,69,112]; (2) that organic nutrients were toxic or inhibited ... probable in evolutionary
terms than organic substrate exclusion or toxicity, and would be ... The facultatively heterotrophic
methylophor, Methylobacterium extorquens, strain AM1 contains a complete Krebs ...
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Formatrophotrophic Production of Poly-β-hydroxybutyric Acid (PHB) from Methylobacterium
sp. using Formate as the Sole Carbon and Energy Source
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A directed approach to the selection of bacteria with enhanced catabolic activity
K Heesche-Wagner, T Schwarz... - Letters in applied ..., 2001 - Wiley Online Library
... metabolism within crude cell extracts of the two methyllobacteria (KH 5 ... and characterization of
hydroxypropylate reductase from the facultative methylophor Methylobacterium extorquens AM1 ...
... & Timmis, KN (1997) Bioprotection of microbial communities from toxic phenol mixtures ...
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c-Type cytochromes and manganese oxidation in Pseudomonas putida MnB1
R Caspi, BM Tebo, MG Haygood - Applied and environmental ..., 1998 - Am Soc Microbiol
... Mn(II) oxidation in the soil (35); biological Mn(II) oxidation can be used for the removal of toxic
contaminants from ... It has been shown that mutants of Methylobacterium extorquens and Paracoccus
denitrificans deficient in c-type cytochrome biogenesis cannot assemble tryptophan ...
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Mercurial-resistance determinants in Pseudomonas strain K-62 plasmid pMR68
Y Sone, Y Mochizuki, K Koizawa... - AMB ..., 2013 - amb-express.springeropen.com
... of organomercurials and the subsequent reduction of the resulting mercuric ions to the less toxic
and more ... more similar (67–84%) to those of a putative mer operon in Methylobacterium extorquens
AM1, which ... 1) Department of Public Health and Molecular Toxicology. School of ...
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MtdC, a Novel Class of Methylene
T Dehydrogenases, JA Vorholt, MG Katuzhnaya - 2005 - pdfs.semanticscholar.org
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The (d) evolution of methanotrophy in the Beijerinckiaceae—a comparative genomics
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I Tamas, AV Smirnova, Z He, PF Dunfield - The ISME journal, 2014 - ncbi.nlm.nih.gov
... SC2, and more distantly with Methylobacterium extorquens (Supplementary Figure 8). Other
Alphaproteobacteria methylotrophs have very different arrangements (for example,
Hyphomicrobium sp. MC1; Vuilleumier et al., 2011), or lack this island entirely ...
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https://scholar.google.com/scholar?start=80&q=methylobacterium+extorquens+toxicity+plant&hl=en&as_sdt=0,22
Functional analysis of the methylmalonyl-CoA epimerase from Caenorhabditis elegans
J Kühni, T Bobik, JB Procter, C Burmeister... - The FEBS Letters, 2005 - Wiley Online Library
... mitochondrial energy metabolism [6] or whether they are caused by "metabolic stroke" due to accumulating toxic organic acids. ... fixation via the 3-hydroxypropionate pathway and in propionate fermentation [8]. In the methylotrophic bacterium Methylobacterium extorquens, MCE is ...
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Some physicochemical properties of the microbial exopolysaccharide (EPS) ethapolan synthesized by Acinetobacter sp. 12S depended on whether the producer was ...
TA Rodionova, YA Nikolaev, TP Pirog, MA Kovalenko... - Microbiology, 2004 - infona.pl
... The paper deals with a comparative study of the growth of free-living and immobilized predatory bacteria of the genus Bdellovibrio in the presence of toxic concentrations of urea and phenol. It was found that the cell wall of bdelloplasts ...
All 2 versions Cite Save More

The role of physiological heterogeneity in microbial population behavior
ME Lidstrom, MC Konopka - Nature Chemical Biology, 2010 - nature.com
... In a methylotrophic bacterium, Methylobacterium extorquens, the expression from a non-growth-rate-regulated promoter involved in methanol metabolism is not correlated with cell-to-cell variations in growth rate 40, 41, either during steady state or during a response to ...
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Systematics of methanol-utilizing bacteria
K Komagata - FEMS Microbiology Letters, 1999 - Elsevier
... seoxidans" and related methanol-utilizing bacteria in the beta subdivision (cluster B reported by Hori and Osawa [32]) differ clearly from Methylobacterium extorquens in the ... Three new Methylobacterium species: M. rhodesianum sp. ... 2013, The Toxicology of Methanol more ...
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Applications of the NanoDSC
MAA Mathews - 2016 XIX ISBC Conference, 1999 - media.biocalorimetry.org
... However, besides being toxic, methanol is highly volatile. ... The calorimetric control strategy is demonstrated exemplarily for growth and polyhydroxybutyrate formation of the methylotrophic bacterium Methylobacterium extorquens on methanol and compared to alternative ...
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Cloning and sequencing of a novel meta-cleavage dioxygenase gene whose product is involved in degradation of y-hexachlorocyclohexane in Sphingomonas ...
K Miyaochi, Y Adachi, Y Nagata... - Journal of bacteriology, 1999 - Am Soc Microbiol
... Because of its toxicity and long persistence in soil, most countries have prohibited the use of y-HCH. ... genes and their protein products, tcpA of Sphingomonas chlorophenolica(41) (recently the sequence of PcpA was revised) and tcpA of Methylobacterium extorquens AM1(37 ...
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Production of Poly (3-hydroxybutyrate-co-3-hydroxyvalerate) from Methylobacterium organophilum by potassium-limited fed-batch culture
SW Kim, P Kim, JH Kim - Enzyme and microbial technology, 1999 - Elsevier
... 3HV) mass production have been rarely reported due to the toxicity of the ... that P(3HB-co-3HV) production from M. organophilum using toxic auxiliary carbon ... methanol and n-amyl alcohol by the methylotrophic bacteria, Paracoccus denitrificans and Methylobacterium extorquens. ...
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Biomaterials approaches to combating oral biofilms and dental disease
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... Tethered or released toxic agent(s). Base material degradable. External toxic challenge. ... In other experiments, tetraglyme was deposited on glass in a pattern using photolithographic methods before exposure to a suspension of Methylobacterium extorquens. ...
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International Space Station (ISS) Internal Active Thermal Control System (IATCS) New Biocide Selection, Qualification and Implementation
ME Wilson, HE Cole, T Rector, J Steele... - 41st International... 2011 - arc.aiaa.org
... of 400 ppm OPA at pH 9.5 against mixed biofilms consisting of 10 bacteria including Methylobacterium extorquens established on ... D. Toxicological Evaluation of OPA Evaluations of the toxicity of OPA were conducted by NASA Johnson Space Center Toxicology Group and ...
All 4 versions Cite Save More
Methylobacterium bacteremia in AIDS
AL Tmant, R Gulati, O Giger... - Clinical microbiology ..., 1999 - Wiley Online Library
... individual [5]. The genus Methylobacterium includes eight species, Methylobacterium extorquens, 
M. fujisawaense, M ... examined for vacuoles, which are present in the methylobacteria but absent 
in ... Empirical therapy for treatment of serious methylobacterium infection consists of ...
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Facultative methanotrophy: false leads, true results, and suggestions for future research
JD Semreau, AA DiSpirito... - FEMS microbiology ..., 2011 - academic.oup.com
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Corynebacterium glutamicum harbours a molybdenum cofactor-dependent formate dehydrogenase which alleviates growth inhibition in the presence of formate
S Witthoff, L Eggeling, M Bott, T Polen - Microbiology, 2012 - mic.microbiologyresearch.org
... However, a high sequence identity of 48% also exists with FDH4 from Methylobacterium extorquens, which has been characterized as a molybdenum-dependent FDH with an important role in methanol metabolism (Chistoserdova et al., 2007). ...
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Soluble methane monoxygenase production and trichloroethylene degradation by a type I methanotroph, Methylomonas methanica 68-1
... Methylobacterium extorquens ATCC 14718 - (+ = AM1) Methylobacterium organophilum ATCC 27868T - (+ = XX) Methylobacterium rhodesianum ATCC 43882T ND ND Methylosinus sporium, Methylobacterium organophilum, and Methylobacterium extorquens ...
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Microflora on the skin of European eel (Anguilla anguilla L., 1758) sampled from Creek Yuvarlakay, Turkey
A Uğur, F Yılmaz, N Sahin - 2002 - evols.library.manoa.hawaii.edu
... Contamination can occur because pathogenic microorganisms form part of the normal flora of the fish. In other cases, toxic substances are introduced through cross-contamination, recontamination or faulty handling and processing. ... Methylobacterium extorquens 3.44 - + ...
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Cloning and characterization of corA, a gene encoding a copper-repressible polypeptide in the type I methanotroph, Methylocrobium albus BG8
O Berson, ME Liddstrom - FEMS microbiology letters, 1997 - academic.oup.com
... copper was added, although in some cases they also grew slowly when copper was added, presumably due to toxicity. ... AY., Chistoserdova, LV, McIntire, WS and Liddstrom, ME (1994.)
Genetic organization of the magA gene cluster in Methylobacterium extorquens AM1: complete ...
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Genetic determination of polyhydroxyalkanoate metabolism in Rhodobacter capsulatus SB1003
P Ulrich, H Stmad, V Hejkalova... - Folia Biologica - ..., 2002 - researchgate.net
... Compared to tradition- el oil-derived plastics, PHAs have better physical properties and are absolutely non-toxic, granule formation (phaI), a granule-associated protein (pha2) and a gene with homology to PHA depolymerases from Methylobacterium extorquens and Ralstonia ...
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DOE: Community Sequencing Program Department of Energy: Community Sequencing Program
L Chistoserdova, B Dreyfus, D Fleischman, P Jourand... - marxlab.org
... involving sequencing of multiple members of the genus Methylobacterium, facultative methylo-trophs that ... contains the best-studied methylo-trophic model organism, M. extorquens AM1, as ... with diverse physiological capacities ranging from degradation of toxic compounds, high ...
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Genomics of a phototrophic nitrite oxidizer: insights into the evolution of photosynthesis and nitrification
J Hemp, S Läcker, J Schott, LA Pace... - ISME ..., 2016 - authors.library.caltech.edu
... couples in blue are not considered likely transitional intermediates because they require either complex multi-electron transfer reactions (N2 + H2 O -> 2 NO + + 10 e- + 12 H+), produce toxic intermediates (NH3 ..., Methylobacterium extorquens AM1, Alphaproteobacteria, 1, 1, 1, 1 ...
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Genetic and phenotypic comparison of facultative methylothrophs between
Methylobacterium extorquens strains PA1 and AM1
DD Naylor, CJ Marx - PloS one, 2014 - journals.plos.org
... or CH3 OH (methanol) as a sole carbon and energy source [1]-[4]. Methylobacterium extorquens AM1 [1] is ... a hypothesis, based on in vitro studies [44], that MDH in M. extorquens strains can ... lacking theH4MPT pathway were sensitive to methanol because of the toxic effects of ...
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https://scholar.google.com/scholar?q=methylobacterium+extorquens+toxicity+-plant&hl=en&as_sdt=0,22
Archaea and their potential role in human disease
... For example, the presence of intestinal sulfate-reducing bacteria and an increase in potentially toxic levels of hydrogen ... the discovery of archaean genes that encode C1-transfer and methanogenic coenzymes in the aerobic bacterium Methylobacterium extorquens (27). Evidence ...
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Microbial mobilization of rare earth elements (REE) from mineral solids—A mini review
F Barmettler, C Castelberg, C Fabbri, H Brandl - AIMS Microbiology, 2016 - aimspress.com
... Mutant strains of Methylobacterium extorquens showed a REE-dependent growth behavior [28]. ... was also observed when treating CRT powder suggesting either a certain toxicity of the ... lamps is already mandatory in many different countries, mainly to remove toxic mercury form ...
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Isolation and properties of methanesulfonate-degrading Afipia felis from Antarctica and comparison with other strains of A. felis
SA Moosvi, CC Pacheco, IR McDonald... - Environmental... 2005 - Wiley Online Library
... Nitrobacter hamburgensis, L35502; N. winogradskyi, L11661; Bradyrhizobium japonicum, D11346; Rhodopseudomonas palustris, D14435; Methylobacterium extorquens, D32224; Rhizobium ... 500 μM and dimethylsulfide (tested only at 1–10 μM because of its toxicity) were not ...
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Isolation and characterization of naphthalene biodegrading Methylobacterium radiotolerans bacterium from the eastern coastline of the Kingdom of Saudi Arabia
A Nzia, A Thukair, S Sankara, B Chambasha... - Archives of... 2016 - degruyter.com
... Molecular interaction between Methylobacterium extorquens and seedslings: growth promotion, methanol consumption ... corrig... and Methylobacterium mesophilicum (Austin and Goodfellow 1979) comb. ... of Environmental Science and Health, Part A, Toxic/Hazardous Substances ...
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The microbiology of metal working fluids
IP Thompson, CJ van der Gast - Handbook of Hydrocarbon and Lipid... 2010 - Springer
... However, the inclusion of such toxic constituents is under legislative pressure from the EU. ...
Flavobacterium mizutaii. 2. A. S. Myroides odoratus. 2. A. S. Alphaproteobacteria. Methylobacterium extorquens. 1. A. S. Methylobacterium mesophilicum. 1. A. S. Methylobacterium ...
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Structural biology of the lanthanides—mining rare earths in the Protein Data Bank
K Djinovic-Carugo, O Carugo - Journal of Inorganic Biochemistry, 2015 - Elsevier
... species [3]. The large majority of the other metals are not only not essential for life but also extremely toxic, even at ... been proposed that this is due to a lanthanide-dependent methanol dehydrogenase [15], like the recently reported XoxF1 of Methylobacterium extorquens AM1 [16 ... Cited by 7 Related articles All 3 versions Cite Save

Relations and functions of dye-linked formaldehyde dehydrogenase from Hyphomicrobium zavarzini revealed by sequence determination and analysis
AC Schwartz, G Gockel, J Groß, B Moritz... - Archives of... 2004 - Springer
... in these bacteria, (2) how serious the danger of toxic side effects of ... Mutants of Methylobacterium extorquens deficient in the formaldehyde-activating enzyme that catalyzes condensation of ... This suggests that the question of formaldehyde toxicity deserves special attention, when ...
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Identification and characterization of the AgmR regulator of Pseudomonas putida: role in alcohol utilization
H Vrionis, A Daugulis, A Kropinski - Applied Microbiology and... 2002 - Springer
... growth and a solvent phase containing high concentrations of inhibitory or toxic substrates that ...
citic(s) to the bacterial catalys(s) to prevent substrate limitation or toxicity to the ... a putative sensor-regulator pair required for oxidation of methanol in Methylobacterium extorquens AM1 ...
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Mutagenesis of the C1 oxidation pathway in Methanosarcina barkeri: new insights into the Mtr/Mer bypass pathway
... In Methylocbacterium extorquens AM1 this problem is solved by the presence of the formaldehyde-activating ... Intermediate in this bypass pathway, one could imagine that formaldehyde toxicity may play ... that the accumulation of this highly reactive compound could be toxic for the ...
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High-throughput phenomics: experimental methods for mapping fluxomes
U Sauer - Current opinion in Biotechnology, 2004 - Elsevier
... for the interpretation of labeling patterns from isotopic tracer experiments can be distinguished: comparative, analytical and integrated (Figure 2). Comparative multivariate statistics may be used to discriminate strains or conditions (eg the presence of toxic chemicals) in massive ...
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Marker Exchange Mutagenesis of mxaF, encoding the large subunit of the Mxa methanol dehydrogenase, in Methylosinus trichosporium OB3b
MFU Haque, W Gu, AA DiSpirito... - Applied and ..., 2016 - Am Soc Microbiol
... dehydrogenase or reduced to methylene tetrahydrofolate. It is speculated that such redundancy for the conversion of formaldehyde exists to control the buildup of this toxic intermediate (1–9). What is less readily discerned from ...
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Repeated, selection-driven genome reduction of accessory genes in experimental populations
MC Lee, CJ Marx - PLoS Genetics, 2012 - journals.plos.org
... increased growth at the upper end of the temperature range of M. extorquens AM1 (Figure ... switches, starvation, and the toxic effects of an antibiotic and a toxic metal. ... likely that they would impart tradeoffs in components of the natural environment inhabited by Methylobacterium ...
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A review of bacterial methyl halide degradation: biochemistry, genetics and molecular ecology
IR McDonald, KL Warner, C McAnulla... - Environmental ..., 2002 - Wiley Online Library
... increases the yield and quality of crops without leaving behind toxic residues characteristic ... This may reflect the greater toxicity of either methyl bromide or the bromide ... were obtained with DNA from the negative controls (Escherichia coli, Methylobacterium extorquens AM1 and ...
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Bioinformatics classification and functional analysis of PhoH homologs
AE Kazakov, O Vassieva, MS Gelfand... - In silico ..., 2003 - content.iopress.com
... Magnetospirillum magnetotacticum + Methylobacterium extorquens + Methylococcus flagellatus + + + Rhodobacter sphaeroides* + + + + + Magnetospirillum magnetotacticum + + + + + Methylobacterium extorquens* + Methylococcus flagellatus + + + + + Burkholderia cepacia + + + + +...
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... These functions may be damaged by toxic substances, medicines, alcohols, radiation and virus ... liver disease inhibitor very low in general toxicity and specific toxicity to kidney. ... Methylobacterium extorquens DSM 1337 (=JCM 2802=NCIB 9396), JCM 2803 (=NCIB 10409), ATCC ...
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Respiration Rate Determination by Phosphorescence-Based Sensors
TJ Strovas, ME Lidstrom - Handbook of Hydrocarbon and Lipid ..., 2010 - Springer
... This focus stems in part from our work with the facultative methylotroph Methylobacterium extorquens AM1, ... in the MLSC, heat-sealed test tubes were used to analyze cultures of M. extorquens AM1 (Strovas et al). However, the toxicity should be tested before employing these paints. ...
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Microbial characterization of the Mars Odyssey spacecraft and its encapsulation facility
MT La Duc, W Nicholson, R Kern... - Environmental ..., 2003 - Wiley Online Library
... Gene sequences of Methylococcus sp., Streptococcus gordonii and chloroplasts of Nicotiana tabacum were retrieved only from the spacecraft samples, while Methylobacterium extorquens rDNAs were retrieved only from the SAEF-II samples (Table 2). The non-overlapping ...
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JJ Feng, TL Yu, L Liu, LXie, YY Xing, CY Min... - ... and Intelligent Laboratory ..., 2013 - Elsevier
... Cover image Cover image. Mass spectrum selectivity-based chromatogram baseline-shift elimination and its application in metabolomics of liver toxicity ... Baseline-shift has an effect on metabolomics model and evaluation of drug toxicity. Abstract. ...
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Metabolic engineering of Corynebacterium glutamicum for methanol metabolism
S Wirthoff, K Schmitz, S Niedenfuhr, K Noh... - Applied and ..., 2015 - American Society for Microbiology
... Whereas Gram-negative methylotrophic bacteria such as Methylobacterium extorquens employ pyrroloquinoline quinone (PQQ)-dependent and periplasmatic methanol ... also serves as "safety valve" in case of an intracellular accumulation of formaldehyde to toxic amounts. ...
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... These functions may be damaged by toxic substances, medicines, alcohols, radiation and virus ... liver disease inhibitor very low in general toxicity and specific toxicity to kidney. ... Methylobacterium extorquens DSM 1337 (=JCM 2802=NCIB 9396), JCM 2803 (=NCIB 10409), ATCC ...
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Metabolism of dimethylsulphoniopropanoate by Ruegeria pomeroyi DSS-3
CR Reisch, VM Crab, SM Gifford, Q Teng... - Molecular ..., 2013 - Wiley Online Library
... The enzyme that catalyzes the reduction of acryloy-CoA in R. pomeroyi was recently identified by its ability to confer resistance to acrylate toxicity (Todd et al., 2012a), ... It is also implicated in increased resistance to acrylate toxicity and acrylate degradation by resting cells. ...
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Complete sequence and organization of the Sphingobium chungbukense DJ77 pSY2 plasmid
SM Yeon, YC Kim - The Journal of Microbiology, 2011 - Springer
... Strain DJ77 has been further studied for its ability to degrade or transform recalcitrant toxic compounds, such as toluene, benzoate, biphenyl ... 14.2 8485 7634 - 282 Universal stress protein Uspa [Methylobacterium extorquens DM4] YP_003088177.1 5-853 1-282 (282) 73 ...
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Regulation of methanol and methylamine dehydrogenases in Methylophilus methylotrophus
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... termined enzymically using a crude extract of methylamine-grown Methylobacterium extorquens AM1, prepared according to the method of Tatra and ... state concentration of methanol is high, thus minimising the potential for the overproduction of formaldehyde, the toxic product of ...
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... phaC and phaCAB did not increase the biopolymer level in Methylobacterium extorquens G10, despite an ... absent in a wide and phylogenetically divergent group of methylotrophs. In order to prevent toxicity of products of methanotrophic genes, low copy number ...
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... We used phylogenomic analysis, gene order information, and comparative analysis with the partially sequenced methylotroph Methylobacterium extorquens to detect ... environmental roles include degradation of chitin in marine systems, and the breakdown of toxic algal blooms ...
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A glutathione-dependent formaldehyde-activating enzyme (Gfa) from Paracoccus denitrificans detected and purified via two-dimensional proton exchange NMR ...
M Goenrich, S Bartoschek, CH Hagemeyer... - Journal of biological ..., 2002 - ASBMB
... Formaldehyde is a highly toxic compound due to nonspecific reactivity with proteins and nucleic acids (1). It is liberated as a result of demethylation ...
Methylobacterium extorquens AM1 were cultivated as described previously (4, 10). ...
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Metabolic and physiological interdependencies in the Bathymodiola azoricus symbiosis
R Ponnudurai, M Kleiner, L Sayavedra... - The ISME ..., 2017 - ncbi.nlm.nih.gov
... Also, since accumulation of formaldehyde is toxic to the cells, the two formaldehyde oxidation pathways may operate as ... in the facultative methylotroph Methylobacterium extorquens AM1, odh expression is repressed during growth on C1-compounds (Chistoserdova et al., 2003) ...
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... It is speculated that such redundancy for the conversion of formaldehyde exists to control the buildup of this toxic intermediate (1-9). ... Formate as the main branch point for methylotrophic metabolism in Methylobacterium extorquens AM1. J Bacteriol 190:5057-5062 ...
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ND Maluta, P Schwarzentuber, CS Dow - Applied microbiology and ..., 2011 - Springer
... have also been noted to exhibit biocide potential or even toxicity towards bacteria. In general, heavy metal ions are more toxic than the other classes of ... WMD cultures of Pseudomonas putida (CCOS 31) and facultative methylotrophic Methylobacterium extorquens (CCOS 32) ...
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Evidence for the presence of a CmuA methyltransferase pathway in novel marine methyl halide-oxidizing bacteria
H Schäfer, IR McDonald... - Environmental..., 2005 - Wiley Online Library
... avoid inhibition resulting from adverse effects of methyl bromide and methyl chloride, which were found to be relatively toxic, only small... but there were also hits with the beta chain of malate-CoA synthetase (=malate thick kinase) from Methylobacterium extorquens AM1, another...
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Formaldehyde dehydrogenase preparations from Methylococcus capsulatus (Bath) comprise methanol dehydrogenase and methylene tetrahydromethanopterin...
EK Adeosun, TJ Smith, AM Hoberg... - ..., 2004 - mic.microbiologyresearch.org
... In methylotrophic bacteria, formaldehyde is an important but potentially toxic metabolic intermediate that can be assimilated into biomass or oxidized to... In M. extorquens, in which this pathway is well characterized, the formation of methylene H4MPT is catalysed by a specific...
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Microbial synthesis of poly (3-hydroxybutyrate-co-4-hydroxybutyrate) copolymer by Cupriavidus sp. USMAA2-4 through a two step cultivation process
H Chai, R Ahmad, A Yahya, M Majid... - African Journal of..., 2009 - ajol.info
... than the simple carbon sources, and more importantly it is often also toxic... fermentation was prohibited in our study in order to avoid toxicity occurrence in... factors influence the molecular mass of polyhydroxybutyrate accumulated by Methylobacterium extorquens and Alcaligenes...
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Influence of erythromycin A on the microbial populations in aquaculture sediment microcosms
YH Kim, CE Cerniglia - Aquatic toxicology, 2005 - Elsevier
... Aquatic Toxicology. ... Methylobacterium extorquens DSM 1338, Pseudomonas fluorescens DSM 6506, P. pseudoalcaligenes POB310, P. putida DSM 8368, Ralstonia eutropha JMP134, Sphingomonas paucimobilis DSM 7526 and S. yanoikuyae DSM 6900 were included as ...
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C1 metabolism in Corynebacterium glutamicum: an endogenous pathway for oxidation of methanol to carbon dioxide
S Withhoff, A Mühlroth, J Marienhagen... - Applied and ..., 2013 - Am Soc Microbiol
... fungi (3), Gram-negative methylo trophic bacteria, such as Methylobacterium extorquens, use pyrroloquinoline. The toxicity of formaldehyde arises from nonenzymatic reactions with biological macromolecules ... since virtually all organisms have to cope with toxic formaldehyde as ...
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OA Karlsson, Ø Larsen, HB Jensen - FEMS microbiology letters, 2011 - academic.oup.com
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Y Pomerleau, D Bourque... - Control Applications, 1993 ..., 1993 - ieeexplore.ieee.org
... This control strategy for methanol concentration is essential because methanol, as shown in Figure 2, is toxic or inhibitory at saturation j ... This was done to avoid toxic effects caused by the high salts concentrations needed to obtain high cell density fermentations ...
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Recombinant microorganisms comprising stereospecific diol dehydratase enzyme and methods related thereto
... including higher specificity, higher yields, lower energy costs and greater resistance to poisoning ...
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Pseudomonas putida, Lactobacillus plantarum, Methylobacterium extorquens ...
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Engineering Escherichia coli for methanol conversion
JEN Müller, F Meyer, B Litsanov, P Kiefer, E Potthoff... - Metabolic ..., 2015 - Elsevier
... Moreover, as mentioned above, methylophory involves a toxic intermediate and thus any ... number of required proteins, their dependency on co-factors and toxicity of produced ...
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Guidance for engineering of synthetic methylophory based on methanol metabolism in methylophory
W Zhang, T Zhang, S Wu, M Wu, F Xin, W Dong, J Ma... - RSC Advances, 2017 - pubs.rsc.org
... 11 in Methylobacterium extorquens AM1, 15 genes participate in methanol oxidation, and 14 of them ... Although HCHO is an important intermediate in methylophoric metabolism, it is highly toxic. The toxicity arises from the high level of nonspecific reactivity of HCHO with proteins ...
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A cytochrome c peroxidase from Pseudomonas nautica 617 active at high ionic strength: expression, purification and characterization
T Alves, S Besson, LC Duarte, GW Pettigrew... - ... et Biophysica Acta (BBA ..., 1999 - Elsevier
... Hydrogen peroxide is often produced in living cells and its toxicity calls for the existence of particular protection mechanisms. ... Me, MG-Mm, MG-Mf and MG-Pd: methylamine utilization protein MauG precursors from respectively Methylobacterium extorquens [37], Methylophilus ...
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Analyzing bacterial physiology at the single-cell level
TJ Strovas, ME Lidstrom - MICROBE-AMERICAN SOCIETY FOR ..., 2008 - researchgate.net
... It seems likely that these faster-growing cells experience greater initial starvation after the switch and also may temporarily accumulate formaldehyde, the toxic first product of ethanol. Cell to cell heterogeneity in growth rate and gene expression in Methylobacterium extorquens AM1 ...
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JA DUNNE, A HACISALIHOGLU - Biological Electron Transfer ..., 2012 - books.google.com
... LOCALIZATION In view of the toxicity of the products of the amine conversion, it is not unexpected that conversion of methyamine appears to be a special case since formaldehyde is extremely toxic to the cell. ...
2) for that purpose [13] and the Gram-negative Methylobacterium extorquens THF [14 ...
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Production of Poly-α-hydroxybutyrate (PHB) from Sago Starch by The Native Isolate Bacillus megaterium PSA10
NA Yanti, L Sembiring, S Margino - Indonesian Journal of ... , 2009 - journal.ugm.ac.id
... PHB is biodegradable, water insoluble, non-toxic, bio-compatable and thermoplastic and therefore it is suitable for polymer production by PHB producer such as Alcaligenes eutrophus MTCC 1954, Pseudomonas citronellolis 1191 and Methylobacterium extorquens MTCC 298 ...
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JA D'urne, A Hacisalihoglu - ... - Chains: Genetics, Composition and Mode of ..., 1998 - Springer
... In view of the toxicity of the products of the amine conversion, it is not unexpected that Conversion of methyamine appears to be a special case since formaldehyde is extremely toxic to the cell. ...
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... However, hemin can produce reactive oxygen molecules that are potentially toxic (12). ... The involvement of the ECF15-associated response regulator in the alphaproteobacterial GSR was first described in 2006, for Methylobacterium extorquens (30). ...
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Methylotrophic bacteria in trimethylaminuria and bacterial vaginosis
... These are all ultimately channeled to formaldehyde, which although potentially toxic, is a key al., 1992; Sanders et al., 2000), but other species (including M. extorquens) are also ... rates may be underestimated because of the difficulty of identifying Methylobacterium which grows ...
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XJ Zhai, YL Zhang - Medicine and Biopharmaceutical: Proceedings ..., 2016 - World Scientific
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Expression and Simple Purification Strategy for the Generation of Anti-microbial Active Enterocin P from Enterococcus faecium Expressed in Escherichia coli
TN Le, TH Da, TN Nguyen, NT Tran - Iranian Journal of ..., 2014 - ijbitech.com
... formation of a well-designed construct that is stably expressed and are non-toxic to host ... expressed in its active form in E. coli was believed to indicate toxicity to the ... EntIP has been expressed in different host strains, such as E. coli, Methylobacterium extorquens ATCC 55366, L ...
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FW Koopman, JH de Wind, HJ Ruijsenaars - Detail: - biomedsearch.com
... wash-out of the culture, underlining the acute and low-threshold nature of formaldehyde toxicity. ...
methanol is the preferred auxiliary substrate as it is less toxic, easier to ... Methylotrophy in Methylobacterium extorquens AM1 from a genomic point of viewJ Bacteriol 2003;185:2980 ...
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Removal of by-products from crosslinkable preparations
... to claim 1, wherein the by-product is a toxic, strongly smelling... Methanosphaera stadtmannae,
Methylobacillus glycogenes, Methylobacillus methanotivorus sp., Methylobacterium aminovorans,
Methylobacterium extorquens, Methylobacterium fujisawaense, Methylobacterium...
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... The method is based on the utilization of toxic components by group of isolates: five bacteria
related to Methylobacterium extorquens, Pseudomonas Sp, Flavobacterium indologenes,
Acinetobacter sp., Arthrobacter aureascens and one fungus Coniochaeta igniz'arz'a. These...
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E Muller - 2011 - theses.fr
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Formaldehyde fixation contributes to detoxification for growth of a nonmethylotroph, Burkholderia cepacia TM1, on vanillic acid

R Mitsui, Y Usanoe, H Yurimoto, Y Sakai... - Applied and environmental microbiology, 2003 - American Society for Microbiology

... formaldehyde is a highly reactive compound that has a toxic effect on ... Apparently, the overexpressed enzymes contribute to the suppression of formaldehyde toxicity. Novel formaldehyde-activating enzyme in Methylobacterium extorquens AM1 required for growth on

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METALS IN BIOLOGY: THE INORGANIC CHEMISTRY OF LIFE; BIOINORGANIC CHEMISTRY GRS
J Mayer - 2015 -osti.gov
... 7:30 pm - 8:00 pm Jeffrey Granliick (University of Minnesota) "Anaerobic Fe(II) Toxicity in a Dissimilatory Metal Reducing ... 9:20 pm Elizabeth Skovran (San Jose State University) "The Role of Lanthanides During Methanol-Dependent Growth in Methylobacterium Extorquens AM1" ...
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Core pathways operating during methylotrophy of Bacillus methanolicus MGA3 and induction of a bacillithiol-dependent detoxification pathway upon ...
JEN Müller, F Meyer, B Litsanov, P Kiefer ... - Molecular ..., 2015 - Wiley Online Library
... the assimilatory and dissimilatory ribulose monophosphate (RuMP) cycles for conversion of the central but toxic intermediate formaldehyde. ... A closed TCA cycle is not essential during methylotrophic growth for other methylotrophs such as Methylobacterium extorquens AM1 and ...
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Metabolic regulation of “Ca. Methylacidiphilum fumariliicum” SoilV cells grown under different nitrogen and oxygen limitations
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Method for enhancing oxidation of methyl bromide with strain IMB-1 (ATCC 202197) during agricultural fumigations
... is added to soils in conjunction with chloropicrin (“tear gas”) to enhance toxicity and to ...
... microorganisms which are not indigenous to the environment and (2) a non-toxic analog of ... and Methylobacterium extorquens have been isolated which can grow on methyl chloride (6, 7), but ...
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Proteomic examination of Ralstonia eutropha in cellular responses to formic acid
SE Lee, QX Li, J Yu - Proteomics, 2006 - Wiley Online Library
... This fact implies that the toxicity of formic acid is related to the proteins involved in formate utilization in ... 4.1 Down-regulated routes of toxic effects of formic acid in R. eutropha ... affected by formic acid treatment (Table 1). Therefore, formic acid has shown its potent toxicities to a ...
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Pentanol and benzyl alcohol attack bacterial surface structures differently
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... However, although CiaABC, a resistance-nodulation-cell division (RND) transporter which is responsible for efflux of many chemotherapeutic agents in Methylobacterium extorquens DM1, has been reported (32), the functions of membrane proteins are poorly understood in M ...
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The evolution of RecD outside of the RecBCD complex
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... In six of those (Mycoplasma mobile, Mycoplasma mycoides, Acaryochloris marina, Methylobacterium extorquens, Acidiphilium cryptum, and Methylobacterium 4-46), the duplicate genes cluster with the other gene of the same organism. ...
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Role of Metabolic Engineering in Enhancing Hydrogen Yields
C Carere, DB Levinli - State of the Art and Progress in Production ..., 2012 - books.google.com
... catabolic activities for the detoxification, degradation and mineralization of toxic chemicals has ...
... unfavorable energetics, and generally low substrate concentrations and toxicity effects. ... hosts (glucose: E. coli and C. acetobutylicum; methanol: Methylobacterium extorquens)[73] ...
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Inducible/regulated gene expression system in E coli
... recombinant proteins, mainly due to the high cost and potential toxicity of IPTG ... elements from Pseudomonas putida to enable inducible regulation of gene expression in Methylobacterium extorquens. ... of the exogenous inducer, eg p-cumate, which is non-toxic, inexpensive and ...
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Tungsten Cofactors, Binding Proteins, and Transporters in Biological Systems
B Mukherjee, S Ghosh, SR Chowdhury... - Encyclopedia of..., 2013 - Springer
... Heterodimeric enzymes with two subunits (α 2 β 2) of 107 kDa and 61 kDa, respectively, are obtained from the α-proteobacterium Methylobacterium extorquens. Sodium tungstate has less toxic effect on earthworms, but it completely inhibits their reproductive ability...
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C1 compounds as auxiliary substrate for engineered Pseudomonas putida S12
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Characterization and cloning of a 37.6-kb plasmid carried by Legionella pneumophila recovered from patients and hospital water over a 12-year period
SD Mansfield, GS Bezanson... - Canadian journal of..., 1997 - NRC Research Press
... of Legionella-specific translation products may have resulted in some sort of "toxic" effect on... for electroporation of the methylothrophic bacteria Hyphomicrobiuim facilis, Hyphomicrobiuim denitrificans, Methylobacillus glycogenes, Methylobacterium extorquens, and Methylophilus...
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On the control of molecular weight distribution of polyhydroxybutyrate in Azohydromonas lata cultures
G Penioglu, E Kretza, C Chatzidoukas... - Biochemical..., 2012 - Elsevier
... Polyhydroxyalkanoates (PHAs) is a class of biodegradable polymers that are produced intracellularly by various bacterial species as energy and carbon reserves [3] and [4]. PHAs exhibit excellent biodegradability, biocompatibility and zero-toxicity characteristics [5].
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Changes of chlorine isotope composition characterize bacterial dehalogenation of dichloromethane
AM Zyakun, YE Firosova, ML Torgonskaya... - Applied Biochemistry..., 2007 - Springer
... Dichloromethane (CH2Cl2, DCM) is a highly toxic persistent solvent, broadly used... molecules with different chlorine isotopes by aerobic methylobacteria Methylobacterium dichloromethanicum
DM4... extract of strain DM4; and transconjugant lethylbacterium extorquens AM1/pME...
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Methylobacterium spp. from a patient with multiple sclerosis
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... provi... a strong rationale for the use of IVIG as adjunctive therapy in... M. extorquens and M. mesophilicum may be variants of the same species and were probably the... The differentiation of the eight extant species of Methylobacterium requires a variety of tests...
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Fenton process-driven decolorization of Allura Red AC in wastewater using apolaccase-modified or native nanomagnetite immobilized on silica fume
A Alayli Gungor, H Naderoglu, E Kalkan... - Desalination and Water..., 2016 - Taylor & Francis
... These experiments also showed the adsorbent to be reusable, cheap, bio-compatible, easy to prepare, non-toxic (nanomagnetite nanoparticles, H 2, O 2, and silica fume), and capable of generating Fenton reaction conditions with or without additional treatment with apolaccase...
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Isolation of Methylophaga spp. from marine dimethylsulfide-degrading enrichment cultures and identification of polypeptides induced during growth on dimethylsulfide
... This was done to avoid potential toxicity of higher DMS concentrations. Previously, mRNA knockout mutants of Methylobacterium extorquens (similar to xoxF) were not affected in their ability to grow on methanol or methylamine, and a phenotype associated with this gene has...
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A molecular basis for uranium toxicity
KA Burbank - 2014 - scholarworks.montana.edu
... Consequently, the recent discovery of uranium toxicity at submicromolar levels in bacteria provides relevance to serious environmental and public health issues in the light of current EPA ... interest because of its application to nuclear power and military weapons. 1 It is a toxic ...
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... 1982) found that the pink facultative methylotrph Pseudomonas extorquens grew at ... The toxicity of alcohols towards most bacteria increases sharply with increasing size and hydrophobicity ... al., 1983), methanol appeared to enter the cell by passive diffusion in Methylobacterium ...
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... The DNAs in each lane were obtained from bacteria grown on the following carbon sources: Lane 1. Methylobacterium extorquens AM1 grown with methanol. Lane 2, M. trichosporium OB3b grown on methane; Lane 3, M. organophilum XX grown in nutrient broth; Lane 4: M ...
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... Though the concept of “formaldehyde stress” has been mentioned in studies on Methylobacterium extorquens AM1 (Miller, 2009) and tuberculosis ... dysfunction of this gene is related to abnormal metabolism of FA and causes severe toxicity (Duister et ... Toxicology, Vol.75, No.1, pp. ...
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... insert of the λ clone into pGEM3ZF(+) failed, indicating that the expression of MopB in E. coli is toxic to the ... bacter agile A20, Methylobacter capsulatus Y, Methylo- cystis strain M, Methylosinus sporium 5] and four methyl- trophs (Methylobacterium extorquens AM1, Methylobac ...
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Chloromethane utilization gene cluster from Hyphomicrobium chloromethanicum strain CM2T and development of functional gene probes to detect halomethane- ...
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... No growth was observed with bromomethane as the sole carbon and energy source, presumably due to the greater toxicity of this ... from CM2 T, CM4 T, and IMB-1 and with DNA from several non-chloromethane-utilizing bacteria (E. coli, Methylobacterium extorquens AM1, and ...
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S V Кулеверман - 2016 - osti.gov
... energy sources, some (eg carbon dioxide and methane) are potent greenhouse gases, and others (eg chlorinated methanes, carbon monoxide, and methanethiol) are toxic chemicals, produced ...
*Methanol-Based Biotechnology - Engineering Methylobacterium extorquens fo ...
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... The side chains of Leu556 or Leu547 in MDH from Methylobacterium extorquens AM1 or Methylophilus methylophilus, respectively, and Trp557 in qEDH, form a lid-like cover (Fig. 4) to shield the substrate from bulk solvent ...
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https://scholar.google.com/scholar?start=180&q=methylobacterium+extorquens+toxicity+plant&hl=en&as_sdt=0.22
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...to be a faster and more efficient way of methanol (formaldehyde) removal than oxidation, therefore efficiently converting the toxic metabolic intermediate into... is also supported by the fact that there are no EPS synthesis genes found in Methylobacterium extorquens AM1, another...
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...Formaldehyde is also highly toxic to microbes and it has widespread application as a disinfectant for sterilization... FIGURE 1 FIGURE 1. Mechanisms of formaldehyde toxicity...
In methanotrophs and methylotrophs such as Methylobacterium sp. ...
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...These enzymes may remove toxic byproducts of competitive ammonia oxidation by pMMO...
Although we found no homologues to formaldehyde dehydrogenases from Methylococcus capsulatus or Methylobacterium extorquens, there were homologues to alcohol...
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...gdh, pqg Klebsiella pneumoniae gdh, pqg Escherichia coli gdh, pqg TTQ M. extorquens AM1 mau P... 7-10 For the MEDH system, a positive selection method exists for Methylobacterium strains...
MEDH activity will convert the allyl alcohol to allyl aldehyde, which is toxic, and those...
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...This is because formaldehyde is strongly toxic for organisms and therefore cells must rapidly utilize it as a primary source or energy source or dispose it by detoxification...
Specifically, MDH of Methylobacterium extorquens AM1 strain (Biochim. Biophys. ...
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... transporter (Island et al., 1992), and pqqL, a gene that shows homology to a family of endopeptidases and can complement a defect in pyrroloquinoline quinone synthesis in Methylobacterium organophilum (45 and 49). The two other ... Cited by 451 Related articles All 13 versions Cite Save

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... ramosum, X72909; Escherichia coli, M24828; Magnetospirillum gryphiswaldense, Y10109; Mesorhizobium loti, D17291; Methylobacterium extorquens, D32224; Paracoccus... the overall growth yield by providing protection against various harmful agents (eg, toxic oxygen ... Cited by 92 Related articles All 14 versions Cite Save

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... Molecular structure of an unusual cytochrome c2 determined at 2.0 Å; the cytochrome cH from Methylobacterium extorquens ... 5232 S233 S234 S235 S236 S237 S23a S239 Page 8, n 0 Suspect Proteins in Neurodegeneration P-Amyloid toxicity in rat brain re-aggregate cultures ...
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... pathways. Several instances of such applications are available in the literature. For example, Van Dien and co-workers have reconstructed the carotenoid biosynthesis pathway in Methylobacterium extorquens AM1. Protein ...
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Methyl chloride utilising bacteria are ubiquitous in the natural environment
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... However, 16S rRNA sequencing showed that only two distinct strains, recently designated Hyphomicrobiurn chloromethanicum CM2 T and Methylobacterium chloromethanicum CM4... No growth was observed with CH3 Br, presumably due to the greater toxicity of this compound ...
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生產聚羥基酯類發酵策略應用於廢水處理之可行性研究
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Process for bacterial stabilizing of aqueous ground natural calcium carbonate and/or precipitated calcium carbonate and/or dolomite and/or surface-reacted calcium ...
... sp., Methylosinus sp., Hyphomicrobiurn sp., Methylosulfomonas sp., Methylobacterium sp.,
Pseudomonas ... Pseudomonas pseudoalcaligenes, Pseudomonas entomophila, Pseudomonas
syringae, Methylobacterium extorquens, Methylobacterium radiotolerants, Methylobacterium ...
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TP Towrova, BB Kuznetsov, NV Doronina... - Microbiology, 2001 - Springer
... marina VKM B-2159T, Ami- nobacter aminovorans NCIB 9059T, Methylobacterium organophilum
ATCC ... aligned with the respective sequences of bacteria (including methylobacteria) of various ...
Ius glycoproteins ATCC 29475T (M95652), Methylobac- terium extorquens JCM 2802 ...
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... of chain transfer agent than the currently preferred PEG, as they achieve the same effect with reduced toxicity and are ... D, Effect of carbon source and concentration on the molecular mass of poly(3-hydroxybutyrate) produced by Methylobacterium extorquens and Alcaligenes ... 
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L Eggeling - Amino Acid Biosynthesis - Pathways, Regulation and ... , 2007 - Springer
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NJ Silman - 1990 - Ira.iae.ac.uk
... The usefulness of this enzyme resides in its ability to hydrolyse acrylamide to the less toxic products ammonia and acrylic acid. ... methylotrophs is the pink facultative methylotrophs typified by Methylobacterium extorquens strain AM1 (formerly Pseudomonas AM1). ... 
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A comparison of the microbial production and combustion characteristics of three alcohol biofuels: ethanol, 1-butanol, and 1-octanol
F Kremmer, LM Blank, PR Jones... - ... in bioengineering and ..., 2015 - ncbi.nlm.nih.gov
... pathway to alternative host organisms, such as yeast, cyanobacteria, and methylobacteria, all with ... Aside from metabolic modifications, extrinsic factors, such as biological toxicity, will also ... Metabolic engineering of Methylobacterium extorquens AM1 for 1-butanol production. ... 
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... Metabolisms of methanogenesis, osmoregulation, sulfur, and heavy metal toxicity are still being exceptionally ... oxidative tetrahydrodricotoperin-methanofuran-dependent proteins in a methylotrophic bacterial species, Methylobacterium extorquens AM1[34]. ... 
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Proteins secreted by filamentous fungi play key roles in different aspects of their biology.
The fungus Penicillium purpureogenum, used as a model organism, is able to ...
TK Antal, TE Krendeleva, AB Rubin - Applied Microbiology and ..., 2011 - infona.pl
... The ethylmalonyl-CoA pathway is central to the carbon metabolism of many ... α-proteobacteria, like Rhodobacter sphaeroides and Methylobacterium extorquens as well as actinomycetes, like Streptomyces spp. Its function is ... 
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Multi-enzyme Whole-Cell In Situ Biocatalysis for the Production of Flaviolin in Permeabilized Cells of Escherichia coli
S Krauser, P Kiefer, E Heinze - ChemCatChem, 2012 - Wiley Online Library
... Alternative precursor molecules not available in living organisms might be applicable, possibly even at conditions that would be toxic for living cells ... method was applied for quantification according to Wu et al.23 by using a cell extract of Methylobacterium extorquens AM1 grown ... 
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Development of phylogenetic oligonucleotide probes for screening foodborne bacteria

M Ikeda, N Yamaguchi, K Tani, M Nasu - Journal of health science, 2005 - jstage.jst.go.jp
... United States of America (USA), for example, around 75 million cases of foodborne diseases, resulting in 325000 hospitalizations and 5000 deaths, are estimated to occur each year. 1) In Japan, 699–1850 cases of food poisoning occurred from ... Methylobacterium extorquens ...
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Identification, cloning, and sequence analysis of the poly (3-hydroxyalkanoic acid) synthase gene of the Gram-positive bacterium Rhodococcus ruber

U Pieper, A Steinbüchel - FEMS microbiology letters, 1992 - Elsevier
... It employs a mutant of A. eutrophus altered in the amino acid metabolism, thus avoiding the feeding with toxic and more expensive propionic acid. Rhodococcus ruber is a naturally occurring bacterium which synthesizes poly(3HB-co-3HV) from various single substrates [11,12]. ...
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Method for producing target substance

... This is because formaldehyde is strongly toxic for organisms and therefore cells must rapidly utilize it as a carbon source or energy source or dispose it by detoxification. ... Specifically, MDH of Methylobacterium extorquens AM1 strain (Biochim. Biophys. ...
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Analysis of stable isotope assisted metabolomics data acquired by GC-MS

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... Key words: PQQ; Physiological importance; Side effect and toxicity; Mechanism ...
和热稳定性，见光易分解(8)。图1 PQQ的化学结构式 PQQ广泛存在于革兰氏阳性菌中，如图B（梭菌属（Methylobacterium extorquens）的甲醇脱氢酶、...
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Pyrroloquinoline–quinone synthase in Escherichia coli by pyrroloquinoline–quinone synthase of Deinococcus radiodurans plays a role beyond mineral phosphate ...

NP Khairnar, HS Misra, SK Apte - Biochemical and biophysical research ..., 2003 - Elsevier
... Growth characteristics and Rose Bengal mediated cellular toxicity studies. ... Optimum concentration of PQQ showed decrease in lipid peroxidation and protein carbonylation in isolated mitochondria and protecting the cells from hydrogen peroxide toxicity. ...
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Escherichia coli PQQ-containing quinoprotein glucose dehydrogenase: its structure comparison with other quinoproteins

M Yamada, MD Elias, K Matsushita, CT Migit... - et Biophysica Acta (BBA ..., 2003 - Elsevier
... Such a periplasmic oxidation would be crucial in respect to generating membrane potential without importing substrates into cells, and appears to mostly make toxic products. ... c, P 16027, Methylobacterium extorquens. Quinohaemoproteins. Membrane-bound enzyme,...
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Heterogeneity of intracellular replication of bacterial pathogens

S Helaine, DW Holden - Current opinion in microbiology, 2013 - Elsevier
... Thus, heterogeneity is due at least in part to differential exposure or sensitivity to nutritional deprivation or more toxic host processes, and the efficiency with which virulence molecules function to avoid, subvert or tolerate host defences. ...
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Process for bacterial stabilizing of aqueous ground natural calcium carbonate and/or precipitated calcium carbonate and/or dolomite and/or surface-reacted calcium ...

... sp., Methylosinus sp., Hyphomicrobiurn sp., Methylosulphonomonas sp., Methylobacteria sp., Pseudomonas ... Pseudomonas pseudoalcaligenes, Pseudomonas entomophila, Pseudomonas syringae, Methylobacterium extorquens, Methylobacterium radiotolerants, Methylobacterium ...
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https://scholar.google.com/scholar?start=220&q=methylobacterium+extorquens+toxicity+plant&hl=en&as_sdt=0,22
Bioconversion of Methane to Methanol with Methylomonas sp. dh-1 as Biocatalyst
KIM Yujin, JH HAN, KIM Hyeonsoo, P Soohyun... - 한국생물공학회 학술... 2017 - dbpia.co.kr
... 190. Utilization and toxicity analysis of formic acid in gram-negative and gram-positive microorganisms Hyeonsoo... 195. Inhibition of poly 3-hydroxybutyrate (PHB) synthesis by phaR deletion in Methylobacterium extorquens AM1 Yujin ...
Cite Save

Methanotrophs
IR McDonald, JC Murrell - Encyclopedia of Bioprocess Technology - Wiley Online Library
... plates, (2) adding excess methanol with DCM to inhibit possible sMOM-mediated activation of DCM to toxic products in any ... and cloning of a number of genes involved in methanol oxidation from the Gram-negative methanotrophs Methylobacterium extorquens and Paracoccus ...
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Functional analysis of the genome fragment involved in aerobic dichloromethane degradation by Methylobacterium dichloromethanicum DM4
YE Firsova, DN Fedorov, YA Trotsenko - Applied biochemistry and ..., 2012 - Springer
... chloromethanicum CM4 (YP_002421379) Methylobacterium extorquens PA1 (YP_001639788)
Methylobacterium extorquens AM1 (YP_002863395) ... degradation by methylobacteria has not been studied in detail. ... the adaptation of bacterial strains tolerant to toxic organic solvents ...
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Metabolic construction strategies for direct methanol utilization in Saccharomyces cerevisiae
Z Dai, H Gu, S Zhang, F Xin, W Zhang, W Dong... - Bioresource ..., 2017 - Elsevier
... Due to its high toxicity, formaldehyde has to be simultaneously converted to CO2 or some central metabolites catalyzed by hexulose 6-phosphate synthase (HPS) and 6-phospho-3 ... Then the toxic H2O2 are converted to oxygen and water by catalase (CAT) (Saha et al., 2010). ...
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Влияние нормального компонентного состава рубцовой жидкости на уровень свечения биосенсора
ЕА Дроздова, ИФ Каримов - Вестник Оренбургского ..., 2014 - cyberleninka.ru
... considered. Revealed similar toxic effects studied biological fluids, developing in the first minutes of contact. ... Александровская. Читайте также. Генетическая модификация синтеза полиэдеросибутирата у Methylobacterium extorquens ...
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Session II. Regulation of gene expression in Prokaryotes
H Bogusz, R Plocińska, J Dziadek - actabpp.pl
... Several bacterial species, for instance Methylobacterium extorquens AM1 and Methylobacterium extorquens DM4, also contain Mesh-1 homologs. ... Typically, C protein-mediated timing delays expression of the toxic REase activity while DNA modification occurs in a new host ...
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Establishment and validation of new complementing cells for production of E1-deleted adenovirus vectors in serum-free suspension culture
R Gilbert, C Guilbaud, D Gagnon, A Berrier... - Journal of virological ..., 2014 - Elsevier
... E1-deleted AdV, also known as first generation AdV, carry viral genes that are expressed at low level after transduction. Leaky viral gene expression induces an immune response that can be toxic and that prevents stable long-term transgene expression ...
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Building consensus in science: Resources for intertextual dialog in biology research articles
Methanol-induced chain termination in poly (3-hydroxybutyrate) biopolymers: molecular weight control
RD Ashby, DKY Soleiman, GD Strahan - International journal of ..., 2015 - Elsevier
... as a primary feedstock in the synthesis of the co-polymeric poly(3-hydroxybutyrate)-co-(3-hydroxyvalerate) (PHBV) when *Methylobacterium extorquens* AM1 was ... Although MeOH can be toxic to certain bacterial cells, some strains have the capability to survive in the presence of ...
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Replacement of enzyme-bound calcium with strontium alters the kinetic properties of methanol dehydrogenase
TK Harris, VL Davidson - Biochemical Journal, 1994 - biochemj.org
... *extorquens*, Methylophilus methylotrophus, Hyphomicrobiurn X (Richardson and Anthony, 1992), *Methylobacterium* glycogenes (Adachi ..., it has been shown that mutant strains of *M. extorquens* synthesized an ... of cells occurred during growth, presumably due to the toxic effect of ...
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A real-time control system of gene expression using ligand-bound nucleic acid aptamer for metabolic engineering
J Wang, X Cui, L Yang, Z Zhang, L Lv, H Wang - Metabolic ..., 2017 - Elsevier
... eg fatty acid-based products in Escherichia coli via a dynamic protein sensor-regulator system (Zhang et al., 2012); unsaturated fatty acids and triglycerides by utilizing Ubxd8 as a sensor (Lee et al., 2010); methanol for mevalonate production in *M. extorquens* AM1 through a ...
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Aging and immortality in unicellular species
M Florea - Mechanisms of Ageing and Development, 2017 - Elsevier
... of aging is not universally agreed upon (see Do symmetrically dividing species age?), this process is more similar to a stress response than to the process of mandatory aging seen in animals, as the growth arrest is caused by high cell density, starvation or toxic metabolites and ...
All 2 versions Cite Save

Biodegradation of formaldehyde under saline conditions by a moderately halophilic bacterial consortium
K VEENAGAYATHRI, N VASUDEVAN - Current World Environment, 2010 - cwejournal.org
... It is a highly reactive toxic compound which can cause severe action on ... Aerobic biodegradation of formaldehyde, methanol and methanolamine by immobilized *Methylobacterium extorquens* cells ...
Lu, Z. and Hegemann, W., Anaerobic toxicity and biodegradation of formaldehyde in ...
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Metabolism and biology of tryptophan
RR Brown - Recent Advances in Tryptophan Research, 1996 - Springer
... Tryptophan auxotroph associated with Staphylococcus aureus that produce toxic-shock-syndrome toxin. ... Mutants of *Methylobacterium extorquens* and Paracoccus denitrificans deficient in o-type cytochrome biogenesis synthesize the methyamine-dehydrogenase polypeptides ...
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Polyhydroxyalkanoates (PHAs), their Blends, Composites and Nanocomposites: State of the Art, New Challenges and Opportunities
PM Visakh - 2014 - pubs.rsc.org
... 1–3 PHAs containing double bonds can also be produced by recombinant *Methylobacterium extorquens* strains when containing double bonds are cheaper and generally exhibit less toxicity compared to ... most often they have to contend with the drawback of toxic impurities that ...
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Chloride-associated adaptive response in aerobic methylotrophic dichloromethane-utilising bacteria
ML Torgonskaya, NV Doronina - Journal of basic ..., 2011 - Wiley Online Library
... *extorquens* DM4 (a–c), Mp. ... Effects of DNA-damaging agents on aerobic *methylobacteria* capable and incapable of utilizing dichloromethane. Appl. Biochem. ... DNA polymerase I is essential for growth of *Methylobacterium* dichloromethanicum DM4 with dichloromethane. ...
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Evidence of a microbial community associated with rock varnish at Yungay, Atacama Desert, Chile
KR Kuhlman, P Venkat, MT La Duc... - Journal of ..., 2008 - Wiley Online Library
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L-Serine and Glycine Lothar Eggeling
VF Wendisch - Amino Acid Biosynthesis—Pathways, Regulation ..., 2007 - books.google.com
... Due to limiting precursor conversion and toxicity of C-1 substrates in fermentative I-serine production, another development assayed enzymatic... M. Rossignol M, Borderies G, Volker U, Vorholt JA (2004) Comparison of the proteome of Methylo bacterium extorquens AM1 grown ...
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Biosynthesis of poly-3-hydroxybutyrate with a high molecular weight by methanotroph from methane and methanol
Y Zhang, J Xin, L Chen, H Song, C Xia - Journal of Natural Gas Chemistry, 2008 - Elsevier
... The cultivation of cells was carried out at 30 C for about 726 h [8]. Culture with methanol: direct addition of methanol at a concentration of 0.1% (v/v) was found to be toxic for the growth... 14]
reported that the molecular weight, when using Methylo bacterium extorquens depends on ...
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Proteogenomic tools and approaches to explore protein coding landscapes of eukaryotic genomes
D Kumar, D Dash - Proteogenomics, 2016 - Springer
... Discovery of rare protein-coding genes in model methylo troph Methylo bacterium extorquens AM1. Proteomics, 14(23–24), 2790–2794. ... Editors: Ákos Végvári (1). Editor Affiliations: 1.
Department of Pharmacology & Toxicology, University of Texas Medical Branch. Authors: ...
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Screening and isolation of PHB-producing bacteria in a polluted marine microbial mat
A López-Cortés, A Lanz-Landázuri... - Microbial ecology, 2008 - Springer
... High concentrations of ammonia and organic matter, including lipids, produce toxic effects on bacteria communities. ... N. Chistoserdova, L. Lidstrom, ME (2002) Poly-β-hydroxybutyrate biosynthesis in the facultative methylotroph Methylobacterium extorquens AM1: identification ... Cited by 65 Related articles All 14 versions Cite Save

Metabolism of Organosulfur Compounds in Rigeria Pomeroyi DSS-3
W Crabb - 2013 - getd.lib.uga.edu
Page 1. METABOLISM OF ORGANOAROMATIC COMPOUNDS IN RUGERIA POMEROYI DSS-3 by WARNER CRABB (Under the Direction of William B. Whitman) ABSTRACT Dimethylsulfoxonipropionate (DMS) accounts for up to 10% of the carbon fixed by ... Related articles All 2 versions Cite Save More

Physiological characterization of carbazole degrading bacteria isolated from a former gasworks site
G Pasternak, B Kolwzan... - Environment ..., 2012 - researchgate.net
... Indole is another chemical compound highly toxic for aquatic organisms, a source of irritation and damages ... The metabolic profile of GPE1 strain was compared with other Methylobacterium species presented in ... M. extorquens + [7] – [7, 8] – [7, 10] – [7, 10] – [9] NA – [7, 8] V [10] ... Cited by 1 Related articles All 6 versions Cite Save More

Comparison of expression and regulation of the high-density lipoprotein receptor SR-BI and the low-density lipoprotein receptor in human adrenocortical ...
G Martin, A Pillon, C Albert, M Vallé, DW Hum... - The FEBS ..., 1999 - Wiley Online Library
... The FEBS Journal: Previous article in issue: A methenyl tetrahydroxylmethanopterin cyclohydrolase and a methenyl tetrahydrofolic acid cyclodrolase in Methylobacterium extorquens AM1 Previous article in issue: A methenyl tetrahydroxylmethanopterin ... Cited by 62 Related articles All 5 versions Cite Save

Rapid identification of Bacillus cereus based on the detection of a 28.5-kilodalton cell surface antigen
CH Chen, HC Ding, TC Chang - Journal of food protection, 2001 - jfoodprotection.org
... For both types of food poisoning, the food involved has usually been heat treated, and surviving spores germinate to produce ... Enterobacter cloacae Methylobacterium extorquens Microbacterium ammoniophilum Micrococcus luteus M. pyogenes M. varians Proteus mirabilis ... Cited by 18 Related articles All 7 versions Cite Save More

Labrys methylaminophilus sp. nov., a novel facultatively methylotrophic bacterium from a freshwater lake sediment
JA Miller, MG Kalyuzhnyaya... - ... of systematic and..., 2005 - ijs.microbiologyresearch.org
... Concentration of methylamine for growth of JLW107 was 0.705 % and concentrations above 0.75 % were toxic. ... a-subclass, at least 12 genera are classified that include well-characterized methylotrophic species: Hyphomicrobium, Methylobacterium, Aminobacter, Methylophagus ... Cited by 26 Related articles All 12 versions Cite Save

Biosynthesis of PQQ.
CJ Unkefer - Principles and Applications of Quinoproteins, 1993 - books.google.com
... In addition, these results seem to be in partial conflict with mutant studies carried out in M. extorquens AM1 by Lidstrom and coworkers [8] and in Methylobacterium organophilum DSM ... Allyl alcohol is oxidized by methanol dehydrogenase to yield acrolein, which is very toxic. ... Cited by 1 Related articles Cite Save

https://scholar.google.com/scholar?start=260&q=methylobacterium+extorquens+toxicity+-plant&hl=en&as_sdt=0,22
Preliminary characterization of the normal microbiota of the human vulva using cultivation-independent methods
CJ Brown, M Wong, CC Davis... - Journal of ..., 2007 - jmm.microbiologyresearch.org
... 0.9, 0.0 %, Eubacterium desmolans (0.9, 10.6 %), Lactococcus lactis (0.9, 0.0 %), Legionella pneumophila (0.9, 6.6 %). Methylobacterium extorquens (0.9, 1.5 ... Prevalence of toxic shock syndrome toxin 1-producing Staphylococcus aureus and the presence of antibodies ...
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JR Andreeksen, K Madsen - Annals of the New York Academy ..., 2008 - Wiley Online Library
... a lack of discrimination by biological systems and, thus, to the toxicity of tungstate ... chemical elements, being close to the ions of the heaviest toxic heavy metals ... 96 The alphaproteobacterium Methylobacterium extorquens AM1 has a tungsten-containing NAD-dependent FDH that ...
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VN Khmelenina, NE Suzina, YA Trotsenko - Microbiology, 2013 - Springer
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S Puehringer, M Metzler-Zebeli - BMC ..., 2006 - bmcbiochem.biomedcentral.com
... peptide is 23 amino acids in K. pneumoniae [18], 29 amino acids in Methylobacterium extorquens [16], 24 ... at a reduced rate, ie, 10–20% of that for the corresponding M. extorquens wild type ... that PQQ readily reacts with oxygen to generate free radicals [25], which are toxic to the ...
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K Kowalska, E Feliú - Acta Biochimica Polonica, 2015 - actab.pl
... bacterial strains Strain Identification Similarity, % NCBI accession number 1_01 Methylobacterium extorquens 99 NC_012988 ... Pillard DA, Cornell JS, Dufresne DL, Hernandez MT (2001) Toxicity of ... X. Chou N, Lusher D, Davis LC (1998) Benzotriazoles: toxicity and degradation. ... Related articles All 8 versions Cite Save More

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... also showed similarity, although to a lesser extent, to catalases from Drosophila melanogaster, Streptomyces coelicolor, P. aeruginosa, and Methylobacterium extorquens. ... This protective effect is carried out by nullifying toxic derivatives of oxygen produced by the respiratory burst ...
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uTS butyrate) impact occurred at an initial MeOH concentration of 0.10%(w/v) where the number average molecular
RD Ashby, DKY Solaimani, GD Strahan... - Journal of Biological ..., 2015 - naldc.nal.usda.gov
... as a primary feedstock in the synthesis of the co-polymeric poly(3-hydroxybutyrate)-co-(3-hydroxyvalerate)(PHBV) when Methylobacterium extorquens AM1 was ... Although MeOH can be toxic to certain bacterial cells, some strains have the capability to survive in the presence of ...
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Expression of Pseudomonas putrefaciens Zobell cytochrome c-551 and its H47A variant in Escherichia coli
GT Miller, DQ Mackay, MS Standley, SL Fields... - Protein expression and ..., 2003 - Elsevier
... Studies indicating these proteins are not expressed in E. coli due to host-toxicity [3] oppose reports where the cytochromes have been expressed as mature ... to believe that we had reached a point where c-551 levels had increased to a point where they had become toxic to the ...
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Plasmid analysis and cloning of the dichloromethane-utilization genes of Methylobacterium sp. DM4
R Gall, T Leisinger - Microbiology, 1988 - mic.microbiologyresearch.org
... The minimal medium used and the cultivation on the toxic and volatile substrate DCM have been described elsewhere (Kohler-Staub et al., 1986). Methylamine agar contained (1-L) 0.68 g Page 3. ... M27, Methylobacterium sp. AM 1 and Pseudomonas extorquens. ...
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Biochemistry and applications of alcohol oxidase from methylo trophic yeasts
JR Woodward - Autotrophic microbiology and one-carbon metabolism, 1990 - Springer
... Thus the yeasts contain a vast excess of catalase activity, usually 1000 units per unit of alcohol oxidase activity, and a very effective formaldehyde assimilation pathway (Veenhuis et al. 1983; Large & Bamforth 1988) to avoid the toxic effects of the activity of alcohol oxidase. ...
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Regulation of methanol oxidation genes in Methylobacterium extorquens AM1
M Zhang - 2004 - 202.28.199.34
... The model methylo troph: Methylobacterium extorquens AM1 The work described in this thesis was performed with Methylobacterium extorquens AM1. ... It is known that the metabolism in this organism is through formaldehyde, a toxic intermediate, so it is of interest to study how ...
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Stabilisation of aqueous mineral preparations by reuterin
... as Citrobacter freundii, Bacilli, such as Bacillus firmus and Bacillus subtilis, Desulfovibrio desulfuricans, Methylobacteria, such as Methylobacterium extorquens. ... making, paints, detergents and cosmetics, and especially in the fields requiring non-toxic microbicides, such as ...
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Development and validation of promoter-probe vectors for the study of methane monoxygenase gene expression in Methylococcus capsulatus Bath
H Ali, JC Murrell - Microbiology, 2009 - mic.microbiologyresearch.org
... since the MUG assay is performed on fully grown cells in the absence of DMSO, any such toxicity is avoided. ... terminator (trmB) located upstream of the promoter region and the effectiveness of this terminator was demonstrated in Methylobacterium extorquens AM1 (Marx & ...
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... likely to play a role in the removal of ammonia produced by the methylamine dehydrogenase reaction to prevent its accumulation to toxic levels ... Comprehensive proteomics of Methylobacterium extorquens AM1 metabolism under single carbon and non-methylotrophic conditions ...
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A Pieja, A Schauer-Gimenez... - ..., A Practical Viewpoint, 2016 - books.google.com
... In addition to legislation restricting the use of nonbiodegradable or toxic plastics, some regulations now promote the use of ... have been identified. [31] There is one pathway that has been identified in many species, including the methylotroph Methylobacterium extorquens. ...
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... For optimization of poly(3HB-co-3HHx) accumulation in recombinant R. eutropha, the influence of fatty acid concentration and nitrogen source was investigated (Table 3). Octanoic acid concentrations higher than 0.4% were found to be toxic to the cells. ...
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WFM Rønning, S Ortega-Lucach... - Journal of applied ..., 2006 - Wiley Online Library
... most closely related to acidophilic micro-organisms belonging to the genera Acidocella, Acidosphera and Acidiphilium were most frequently encountered in the clone libraries along with the sequences from organisms most closely related to Methylobacterium extorquens. ...
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NB Idupulpati, DS Mainardi - Theory and Experiment in Electro catalysis, 2010 - Springer
... able to improve the performance characteristics of chemical fuel cells since their use avoids the problem of poisoning the fuel ... Amino acids labels denote their location in the sequence obtained from the entry 1W6S (Methylobacterium Extorquens W3A136) of the Protein Data ...
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L Chistoserdova, C Jenkins... - Molecular biology ..., 2004 - academic.oup.com
... Preliminary sequence data for Methylococcus capsulatus were assessed at http://www.tigr.org/, the draft sequence of Burkholderia fungorum was assessed at http://www.jgi.doe.gov/, and the draft sequence of Methylobacterium extorquens was assessed at http://www ...
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TV Galuzina, VA Gerasin, NV Doronina... - Polymer Science Series..., 2015 - Springer

...tyrate and 3 hydroxyvalerate synthesized with the use of the methylobacteria Methylobacterium extorquens G10 and ... the most eff cient cosubstrate for methylobacteria is pentanol [8]. Pentanol was added to ... The cultivation time of M. extorquens G10 was 92 h. The amount of dry ...

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JEN Müller, TMB Heggeset, VF Wendisch... - Applied microbiology..., 2015 - Springer

... heat production may cause increased cooling requirements, and careful substrate feeding is needed to avoid toxic formaldehyde accumulation in ... While the metabolism and potential of Methylobacterium extorquens as another potential platform organism will be presented in a ...

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C1 metabolism in Paracoccus denitrificans: Genetics of Paracoccus denitrificans

N Harms, RJM Van Spanning - Journal of bioenergetics and..., 1991 - Springer

... Analysis of genes involved in methanol oxidation from Methylobacterium extorquens AM 1 revealed ... of the cytochrome catalysed by MDH in Methylophilus methylotrophus, M. extorquens AM1, and ... expression of MDH leading to accumulation of the toxic compound formaldehyde ...

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XY Chan, KO Chua, KY How, WF Yin... - The Scientific World..., 2014 - hindawi.com

... View at Scopus; T. Kreil, J. Lactal, ME Guazzaroni et al., "Responses of Pseudomonas putida to toxic aromatic carbon ... N. Korotkova, L. Christoserdova, V. Kuksa, and ME Lidstrom, "Glyoxylate regeneration pathway in the methylotroph Methylobacterium extorquens AM1," Journal ...

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Aliphatic compounds


... Christoserdova, L. 1995. Metabolism of formaldehyde in Methylobacterium extorquens AM 1.
In: Speaker abstracts of the 8th International Symposium on microbial growth on C 1 compounds, San Diego, California, USA. ... Bacterial toxicity and metabolism of hydrazine fuels. ...

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N Kato, H Yurimoto, RK Thauer - Bioscience, biotechnology, and..., 2006 - Taylor & Francis

... C1 compounds are found at a variety of redox levels in marine hydrothermal vents (eg, methane, CO, and CO2): 31–33) If the original habitat of the archaean is rich in formaldehyde, an enzyme system capable of fixing this toxic compound is essential for survival of the organism ...

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J Myung Choi, TP Cao, S Wook Kim... - Proteins: Structure, ..., 2017 - Wiley Online Library

... of bacteria has drawn industrial and environmental attention for the bio-conversion of useful commercial metabolites and toxic chemicals. Anthony C. The molecular structure of an unusual cytochrome c2 determined at 2.0 A; the cytochrome cH from Methylobacterium extorquens. ...

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HxIR, a member of the DUF24 protein family, is a DNA-binding protein that acts as a positive regulator of the formaldehyde-inducible hxiA operon in Bacillus ...  
H Yurimoto, R Hirai, N Matsuno... - Molecular ...; 2005 - Wiley Online Library  
... Because formaldehyde is toxic to all organisms, metabolic pathways for formaldehyde detoxification are found in a wide variety of organisms. For example, many prokaryotes and eukaryotes possess glutathione-dependent formaldehyde dehydrogenase (Harms et al., 1996). ...  
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Degradation pathway of 2-chloroethanol in Pseudomonas stutzeri strain JJ under denitrifying conditions  
JA Dijk, J Gerritse, G Schraa, AJM Stams - Archives of microbiology, 2004 - Springer  
... However, since halogenated aldehydes are considered to be very toxic (Johnson 1967; McCann et al. ... Toyama H, Chistoserdova L, Lidstrom ME (1997) Sequence analysis of pqq genes required for biosynthesis of pyrroloquinoline in Methylobacterium extorquens AM1 and the ...  
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WJ Hunter, DK Manter - Bioresource technology, 2014 - Elsevier  
... Organisms that have been studied include Acinetobacter sp., Arthrobacter aurescens, Flavobacterium indologenes, Methylobacterium extorquens, Pseudomonas sp., Ureibacillus ... This is a desirable transformation as the aldehyde group is more toxic than is the alcohol group. ...  
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DW Begley, DR Davies, R Hartley... - Methods in ...; 2011 - ncbi.nlm.nih.gov  
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The MoxR ATPase RavA and its cofactor ViaA interact with the NADH:ubiquinone oxidoreductase I in Escherichia coli
KS Wong, JD Snider, C Graham, JF Greenblatt, A Emili... - PloS one, 2014 - journals.plos.org
... For example, MoxR of the MRP subfamily in Paracoccus denitrificans and Methylobacterium extorquens is important for the activation of methanol dehydrogenase (MDH) [3], [4]. NirQ/NorQ, which belong to the CGN subfamily, are necessary for the activity of nitric oxide ...
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... mediated DCM turnover in Methylobacterium in vivo. Methylobacterium dichloromethanicum DM4 ...
Indeed, preliminary experiments suggest that Methylobacterium extorquens AM1, the genome of ...
Vuilleumier S. (1999) Enzyme-mediated dichloromethane toxicity and mutagenicity ...
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Molecular ecology of marine methanotrophs
JC Murrell, AJ Holmes - Molecular Ecology of Aquatic Microbes, 1995 - Springer
... This is based on the ability of MMO to co-oxidise DCM to carbon monoxide which becomes toxic to the ...
... The genes encoding methanol dehydrogenase from the methanol-utilisers Methylobacterium extorquens and Paracoccus denitrificans have been extensively studied in the ...
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Investigation of plasmid-induced growth defect in Pseudomonas putida
J Mi, A Sydow, F Schampa, D Becher, H Schewe... - Journal of ..., 2016 - Elsevier
... putida, for instance, an interesting microbe for the bioconversion of otherwise toxic monoterpenes such ...
... Using metabolomics, a plasmid-induced growth defect in Methylobacterium extorquens could be shown to be ... As we suggested the lack of plasmid toxicity of pMIS4 to be the ...
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Heterogeneity between and within Strains of Lactobacillus brevis Exposed to Beer Compounds
... membrane fluidity (Asai et al., 2000; Behr, 2008). It is conceivable that this can reduce the intrusion of hop compounds into the membrane, thereby making the extraction of hop compounds ...
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Создание плазмиды pRAD для оценки амплифицирующего повреждения ксенобиотиками генома клетки
ИА Лавриненко - Сибирский научный медицинский журнал, 2007 - cyberleninka.ru
... Now the problem of rocket fuel toxic influence on an environment is actual for USA, Russia, France, China and other countries using 1,1-dimethylhydrazine (hydrazine) at start heavy ... А. Генетическая модификация синтеза полигоналхиноната у Methylobacterium extorquens ...
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Compositions and methods for biological production of lactate from C1 compounds using lactate dehydrogenase transformants
... In other embodiments, the C 1 metabolizing microorganism of the present invention is a methylothroph which is a genetically modified cell from one or more of the species Methylobacterium extorquens, Methylobacterium radiotolerans, Methylobacterium populi, ...
Cited by 3  Related articles  All 2 versions  Cite  Save

Real-time detection of actively metabolizing microbes by redox sensing as applied to methylothroph populations in Lake Washington
MG Kalyuzhnaya, ME Lidstrom... - The ISME ..., 2008 - search.proquest.com
... cytometric analysis of cells of Methylococcus capsulatus, Methylococcus flagellatus and Methylobacterium extorquens stained with ... range of the organisms tested: M. flagellatus and M. extorquens can oxidize ... Toxic effects on bacterial metabolism of the Redox Dye 6-cyano-2,3 ...
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https://scholar.google.com/scholar?start=300&q=methylobacterium+extorquens+toxicity+-+plant&hl=en&as_sdt=0,22
Methanol oxidation mutants in *Methylobacterium extorquens* AM1: identification of new genetic complementation groups

AL Springer, HH Chou, WH Fan, E Lee... ... 1995 - mic.microbiologyresearch.org

... Two-hundred-and-eight new *Methylobacterium extorquens* AM1 methanol oxidation (Mox) mutants were isolated... methanol oxidation in the facultative methanol-utilizing bacterium *Methylobacterium extorquens* AM1. ... oxidized by MDH but the product, allyl aldehyde, is toxic to the ...

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Biosynthesis and characterization of poly (3-hydroxybutyrate-co-3-hydroxyvalerate) copolymer from wild-type Comamonas sp. EB172

MR Zakaria, H Ariffin, NAM Johar, S Abd-Aziz... ... 2010 - Elsevier

... A study using sodium valerate as precursor for P(3HB-co-3HV) copolymer production was also carried out. Sodium valerate was used in this study due to the fact that valerate in the salt form is less toxic in comparison to acidic form [16]. Despite the ability of Comamonas sp. ...

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Including metabolite concentrations into flux balance analysis: thermodynamic realizability as a constraint on flux distributions in metabolic networks

A Hoppe, S Hoffmann... ... 2007 - bmcgenetics.biomedcentral.com

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METABOLISM AND BIOLOGY OF

RR Brown - ... Advances in Tryptophan Research: Tryptophan and..., 2012 - books.google.com

... Tryptophan auxotrophy associated with Staphylococcus aureus that produce toxic-shock-syndrome toxin... *Methylobacterium extorquens* and Paracoccus denitrificans deficient in c-type cytochrome biogenesis synthesize the methylamine-dehydrogenase polypeptides but ...

Related articles Cite Save

Synonymous mutations as a cause of human genetic disease

ZE Sauna, C Kimchi-Sarfaty - eLS, 2013 - Wiley Online Library

... role in the so-called absorption, distribution, metabolism, excretion and toxicity system which ... associated with the expression of misfolded proteins which can be toxic (Gusella and ... two extreme variants of the key enzyme-coding gene in *Methylobacterium extorquens* (Agashe et ... Cited by 6 Related articles Cite Save More

Cytochrome c peroxidase from Methylococcus capsulatus Bath

JA Zahn, DM Arciero, AB Hooper, JR Coats... ... 2008 - Archives of..., 1997 - Springer

... 294-6019 e-mail: aland@iastate.edu JA Zahn - JR Coats - AA DiSpirito Graduate Program in Toxicology, Iowa State ... of the muG open reading frame from the methylamine dehydrogenase operon in the methylotrophic bacte- ria, *Methylobacterium extorquens* (Chistoserdov et al ...

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代谢物生物传感器: 微生物细胞工厂构建中的合成生物学工具

周益康，吴亦瑶，王天民，郑翔，邢新会，张军 - 生物技术通报. 2017 - html.rzhz.net

... TAL) [21, 22] 和四氨喹啉 [23] 为基于转录因子的代谢物生物传感器的构建提供了更多的潜力。此外，通过对传感器元件的改造，还可实现传感器的跨种属应用。例如，来源于 E.coli 的甲羟戊酸传感器通过改造已经成功应用于脱甲基甲苯 (Methylobacterium extorquens, M. extorquens) AM1 ...

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An integrated proteomics/transcriptomics approach points to oxygen as the main electron sink for methanol metabolism in *Methylotherma mobilis*

DAC Beck, EL Hendrickson, A Vorobe... ... 2011 - Am Soc Microbiol

... involved in nitrogen species interconversions was NO dioxygenase (Mmio_1063), a detoxification enzyme that converts the toxic NO into ... 2008. Comprehensive proteomics of *Methylobacterium extorquens* AM1 metabolism under single carbon and nonmethylotrophic conditions ...

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Engineering Pseudomonas putida S12 for efficient utilization of D-xylose and L-arabinose

JP Meijnen, JH de Winde... ... - Applied and ..., 2008 - Am Soc Microbiol

... P. putida S12 is exceptionally tolerant to organic solvents (1), which makes this strain an excellent host for the production of chemicals that are generally toxic to other bacterial ... A rapid method for the purification of methanol dehydrogenase from *Methylobacterium extorquens* ...

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Investigation of mutants of Methylophilus methylotrophus which are defective in methanol oxidation
A Dawson, PM Goodwin - Microbiology, 1990 - mic.microbiologyresearch.org
... been isolated using the suicide substrate allyl alcohol, which is oxidized by methanol dehydrogenase to the highly toxic compound acrolein. In Methylobacterium extorquens AM1 at least fourteen genes are required for the production of a functional methanol oxidation system ...
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Method Validation for Progesterone Determination in Poly (methyl methacrylate) Nanoparticles Synthesized via Miniemulsion Polymerization
O Fogolari, AC Felippe, FV Leimann... - International Journal of ... 2017 - hindawi.com
... al. [28] when evaluating in vivo toxicity in albino rats. Authors did ... biochemical parameters. PMMA nanoparticles have also demonstrated lower toxicity in vitro assays with human cell cultures (KS62 [29], TPH1 e A549 [28]). Techniques ...
All 4 versions  Cite  Save  More

The Multiple Scientific Disciplines Served by EcoCyc
PD Karp - Systems Biology and Biotechnology of Escherichia coli, 2009 - Springer
... production of bioproducts such as amino acids and vitamins, to produce pharmaceuticals, and to degrade toxic pollutants (Bailey ... SJ, Strovas T, Lidstrom ME (2003) Quantification of central metabolic fluxes in the facultative methylotroph Methylobacterium extorquens AM1 using ...
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Investigation of Methanol and Formaldehyde Metabolism in Bacillus methanolicus
A Bozdag - 2013 - search.proquest.com
... Bacillus sp. Acetobacter methanolicus MB58. Serine Pathway. Methylosinus sp. Methylobacterium extorquens AM1. Hyphomicrobiurn. 5. ... 8. Putative genes encoding for these enzymes were also identified in the M. extorquens AM1 genome (Vuilleumier et al. ... Formaldehyde toxicity. ...
Cited by 1 Related articles All 3 versions Cite Save More

Metabolite profiling uncovers plasmid-induced cobalt limitation under methylotrophic growth conditions
P Kiefer, M Buchhaupt, P Christen, B Kaup... - PLoS ..., 2009 - journals.plos.org
... One example of toxic effects of an antibiotic resistance protein is Serratia marcescens lactamase bla SME-1, whose signal sequence ... Methylobacterium extorquens AM1 is a model methylotrophic bacterium that is able to grow in the presence of methanol and methylamine. ...
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The ribulose monophosphate pathway substitutes for the missing pentose phosphate pathway in the archaean Thermococcus kodakaraensis
... The R1P can then be converted into R5P by phosphopentomutase (13) and then flow into the general pathway for nucleotide synthesis. As HPS and PHI have been found to function in Ru5P synthesis, this also results in the generation of toxic formaldehyde. ...
Cited by 100 Related articles All 13 versions Cite Save

Overexpression of the methanol dehydrogenase gene mxaF in Methylobacterium sp. MB200 enhances L-serine production
H Chao, B Wu, P Shen - Letters in applied microbiology, 2015 - Wiley Online Library
... FJ973617), which shares 99% identity to the large alpha subunit of methanol dehydrogenase of Methylobacterium extorquens AM1 (Vuilleumier et al. ... step in the catabolism of a compound is often the rate-limiting step, which can avoid the accumulation of toxic substances (Berg ...
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Crystal structures of SULT1A2 and SULT1A1 - 3: Insights into the substrate inhibition and the role of Tyr149 in SULT1A2
J Lu, H Li, J Zhang, M Li, MY Liu, X An, MC Liu... - Biochemical and ..., 2010 - Elsevier
... In some cases, however, the sulfonic esters derived from benzylic and allylic alcohols or aromatic hydroxylamines may be chemically reactive toward nucleophilic sites on DNA, RNA, and proteins, inducing toxic effects or mutations thereby leading to carcinogenic response [4], [5 ... Cited by 15 Related articles All 9 versions Cite Save

Evolution of Escherichia coli to 42 C and subsequent genetic engineering reveals adaptive mechanisms and novel mutations
TE Sandberg, M Pedersen, RA LeCroix... - Molecular biology ..., 2014 - academic.oup.com
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Metabolism of methyl bromide and dimethyl sulfide by marine bacteria isolated from coastal and open waters
SE Hoefs, DR Rogers, PT Visscher - Aquatic Microbial Ecology, 2000 - int-res.com
... In addition, trimethyl-lamine (TMA) enrichments were carried out, because DMS enrichments are often unsuccessful due to toxicitiy of this volatile organosulfur compound. Methylobacterium extorquens AM1 (kindly provided by Dr Mary Lidstrom) was used as a positive control. ...
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Dégradation du dichlorométhane et adaptaction à la production intracellulaire d'acide chez Methylobacterium
... 16 Figure I.3 Observation de la souche DM4 sous microscope à phase inverse et inclusions de poly-β-hydroxybutyrate chez DM4 21 Figure I.4 Métabolisme méthylotrophe chez Methylobacterium extorquens AM1 24 Figure I.5 Représentation schématique du mécanisme ...
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Automated quantification of DNA demethylation effects in cells via 3D mapping of nuclear signatures and population homogeneity assessment

A Gertych, KA Wawrowsky, E Lindsey ... - Cytometry Part B, 2009 - Wiley Online Library

... texture. For example Strovas et al. normalized the intensity of a variant of green fluorescent protein from methylotroph promoter (P mxAF) of single cells to their size, in *Methyllobacterium extorquens* AM1 culture. This served ...

Identifying conditions for inducible protein production in E. coli: combining a fed-batch and multiple induction approach

MG Aucoin ... - Microbial cell factories.biomedcentral ... 

... the start of protein production can be distinctively separated from the growth phase [3]. This also helps if the protein is toxic or detrimental ... However, its use in large-scale production is scarce because of its high cost and its toxicity towards humans [5]. Lactose is also used as an ...

Elements of P1B-type ATPase structure and function

M Traverso - 2010 - search.proquest.com

... cells will still be unable to neither transfer copper into essential enzymes in the Golgi apparatus nor to recover from copper toxicity. ... When ATP7B is deactivated, copper builds to toxic levels in the liver while also spreading unchaperoned throughout the blood stream, in both ...

Design and Statistical Analysis of Multidrug Combinations in Preclinical Studies and Phase I Clinical Trials

MT Tan, HB Fang, H Huang, Y Yang ... - Selected Papers from the 2015 ICSA ..., 2016 - Springer 

... 2008, 2015, 2016; Calzolari et al. 2008) as well as adaptive phase I clinical trial designs that attempt to identify the best possible maximum tolerated doses through modeling of the joint dose-toxicity relationship (see, eg, Yuan and Yin 2008; Yin and Yuan 2009a, b; Yang et al. ...

The ATPases CopA and CopB both contribute to copper resistance of the thermoacidophilic archaean Sulfolobus solfataricus 

C Völlmecke, SL Drees, J Reimann ... - ... - 2012 - mic.microbiologyresearch.org

... organism has developed effective mechanisms to withstand toxic concentrations of ... thermophilus Acidiphilium multivorum Nitrobacter hamburgensis Oligotropha carboxidovorans

*Methyllobacterium extorquens* Afipia sp. The high toxicity of copper to the DcopA mutant is obvious ...

Stealth adaptation of viruses: Review and updated molecular analysis on a stealth adapted African green monkey simian cytomegalovirus (SCMV)


... Recovery from the CPE in Cultures of Stealth Adapted Viruses Under routine virus culture conditions, the early CPE caused by cultured stealth adapted viruses can be mistaken for non-specific toxicity, especially since it tends not to progress and commonly disappears in ...

... OF THE TETRAHYDROMETHANOPTERIN-DEPENDENT FORMALDEHYDE-ACTIVATING ENZYME (Fae) FROM METHYLOBACTERIUM EXTORQUENS AM1

P Acharya, M Goenrich, CH Hagemeyer ... - Journal of Biological ..., 2005 - ASBMB

... we describe the structure of the formaldehyde-activating enzyme Fae from *Methyllobacterium extorquens* AM1 with ... rather than with the shorter H 4 MPT from M. extorquens AM1 (7 ... but it also provides insights into the mechanism of how the highly toxic intermediate formaldehyde ...

Molecular characterization of Pseudomonas sp. LDC-5 involved in accumulation of poly 3-hydroxybutyrate and medium-chain-length poly 3-hydroxyalkanoates

K Sujatha, A Mahalakshmi, R Shenbagarathai - Archives of microbiology, 2007 - Springer 

... used for generating multiple sequence alignment: P50176-PHA synthase of Rhizobium melliloti; Q52728-PHA synthase of Rhizobium melliloti; O66382-PHA synthase of Azorhizobium caulinodans; P52070-PHA synthase of *Methyllobacterium extorquens*; P23608-PHA synthase ...
An efficient design strategy for a whole-cell biosensor based on engineered ribosome binding sequences
Q Yu, Y Li, A Ma, W Liu, H Wang, G Zhuang - Analytical and bioanalytical ..., 2011 - Springer
... widely as simple and practical approaches to the detection of a variety of agents, including heavy metals, toxic cellular organics ... D, Morel L, Grojeau D, Miguez CB (2006) Multicopy Integration and Expression of Heterologous Genes in Methylobacterium extorquens ATCC 55366. ...
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Jonas EN Müller, Tonje MB Heggeset, Volker F. Wendisch
JA Vorholt, T Brautaset - academia.edu
... heat production may cause increased cooling requirements, and careful substrate feeding is needed to avoid toxic formaldehyde accumulation in ... While the metabolism and potential of Methylobacterium extorquens as another potential platform organism will be presented in a ...
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Respiration Rate Determined by Phosphorescence-Based Sensors
M Konopka - ... and Lipid Microbiology Protocols: Activities and ..., 2017 - Springer
... The toxicity of potential oxygen sensors, including any compounds they may be in solution with, is an important consideration. ... Dragavon JM, Hankins TJ, Callis JB, Burgess LW, Lidstrom ME (2006) Measurement of respiration rates of Methylobacterium extorquens AM1 cultures ...
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Distribution of abundant prokaryotic organisms in the water column of the central Baltic Sea with an oxic–anoxic interface
M Labrenz, G Jost, K Jürgens - Aquatic microbial ecology, 2007 - int-res.com
... Methylobacterium extorquens DSM13060 (AF267912) Methylobacterium sp. GK101 (D25305) FD 37 Uncultured marine proteobacterium BY-75 (AJ298361) FD 20 Sulfate-reducing bacterium strain mXyS1(AJ008853) Uncultured bacterium clone:12ws (AB154443) FD 33 ...
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Genome sequence analysis of the emerging human pathogenic acetic acid bacterium
Granulibacter bethesdensis
DE Greenberg, SF Porcella, AM Zelazny... - Journal of ..., 2007 - Am Soc Microbiol
... CGD is a rare genetic disease of the phagocyte NADPH oxidase system characterized by defective
production of toxic oxygen metabolites... has several methanol dehydrogenase genes that appear
to have been acquired recently from Methylobacterium extorquens, an organism...
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Comparative proteomic analysis reveals insights into anoxic growth of Methyloversatilis
universalis FAM5 on methanol and ethanol
H Lu, M Kalyuzhnaya... - Environmental..., 2012 - Wiley Online Library
... et al., 2012) and are also required for the expression of the methanol dehydrogenase (mxaFl)
genes in Methylobacterium extorquens AM1 (Skovran et al. ... The product of methanol oxidation,
formaldehyde, is a toxic intermediate The genome of M. universalis FAM5 predicts three...
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Cloning and genetic analysis of six pyrroloquinoline quinone biosynthesis genes in
Methylobacterium organophorum DSM 760
F Biville, E Turfin, F Gasser - Microbiology. 1989 - mic.microbiologyresearch.org
... In some facultative methylotrophic bacteria such as M. extorquens strain AM1, the ability to ... In
a previous paper, we showed that methylamine utilization in Methylobacterium organophorum
is ... expression of active MDH (MDH oxidizes allyl alcohol to the toxic compound acrolein...
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Photomixotrophic growth of Rhodobacter capsulatus SB1003 on ferrous iron
SH Kopf, DK Newman - Geobiology, 2012 - Wiley Online Library
... It could reflect a requirement for ligand-bound Fe(II) to be recognized for efficient uptake into
the cell, and/or result from a toxic effect of the free metal ion, as suggested by Poulain and
Newman (2009). ... In Methylobacterium extorquens AM1 from a genomic point of view ...
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The microbial degradation of azimsulfuron and its effect on the soil bacterial community
A Valle, G Boschin, M Negri... - Journal of applied ..., 2006 - Wiley Online Library
... Introduction. Sulfonylureas are widely used herbicides, as they are characterized by high crop
selectivity, low application rates and very low acute and chronic animal toxicity (Beyer et al. ... (III),
Sphingomonas sp. (IV), Methylobacterium extorquens (V), Corynebacterium sp. ...
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Metabolomics in molecular microbiology
ML Reaves - 2013 - search.proquest.com
... Figure 2. Elucidation of the methanol assimilation pathway in Methylobacterium extorquens ... both
to optimize long-term fluxes and to avoid immediate toxicity due to ... lacking the ability to inactivate
glutamine synthetase by covalent modification suffer toxic metabolic derangements ...
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A new modified ortho cleavage pathway of 3-chlorocatechol degradation by Rhodococcus
opacus 1CP: genetic and biochemical evidence
OV Moiseeva, IP Solyanikova... - Journal of ..., 2002 - Am Soc Microbiol
... 1). In this case, the enzymes had to evolve the ability to avoid formation of the toxic protoanemonin
which is generated ... For panel D, ORF2 from Methylobacterium extorquens AM1 (U72662) and
Usf from Aquifex pyrophilus Ko15a (U17570), both with unknown function, were ...
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Purification of the formate-tetrahydrofolate ligase from Methylobacterium extorquens
AM1 and demonstration of its requirement for methylotrophic growth
... In the facultative methylotroph Methylobacterium extorquens AM1, the formaldehyde produced
from the primary ... be other aldehyde dehydrogenases that are present in M. extorquens AM1 (17 ...,
however, indicated that the intracellular concentration of this toxic intermediate would ...
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https://scholar.google.com/scholar?start=340&q=methylobacterium+extorquens+toxicity+plant&hl=en&as_sdt=0,22
Rapid bacteria identification from environmental mining samples using MALDI-TOF MS analysis
IR Avanzi, LH Gracioso, MPG Baltazar... - ... Science and Pollution .... 2017 - Springer
... are as follows: Burkhodella cepacia DDS97-2, Escherichia coli ATCC8739, Methylobacterium extorquens ATCC23326, Pseudomonas ... Despite the toxicity of copper, some microbial species are known to resist and to ... Scholar. Baby J, Raj J, Biby E et al (2011) Toxic effect of ...
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An experimental study on molecular weight of poly-3-hydroxybutyrate (PHB) accumulated in Methylosinus trichosporum IMV 3011
... Direct addition of methanol at a concentration of 0.10 % (w/v) was found to be toxic for the growth of strain IMV 3011 ... From the study in the Mw of PHB produced by M. extorquens in shake-flask culture (Taidi et al., 1994), it has been found that the Mw of PHB was dependent on the ...
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Characterization of the genes encoding the three-component membrane-bound alcohol dehydrogenase from Gluconobacter suboxydans and their expression in ...
K Kondo, S Horinouchi - Applied and environmental microbiology, 1997 - Am Soc Microbiol
... alcohol, showing that, due to the lack of ADH activity in the transformants, allyl alcohol was not converted to the corre-sponding aldehyde, which is toxic to the ... Nucleotide sequence of the Methylobacterium extorquens AM1 mxaF and mxaJ genes involved in methanol oxidation. ...
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Prospects of bacterial poly [(R)-3-hydroxyalkanoates]
GJM de Koning - 1993 - pure.tue.nl
... Generally, synthetic polymers are relatively inert and hardly pose any toxic danger to the environment. Being xenobiotic materials, however, they do not degrade easily and therefore accumulate as 'visual pollution'. ... 12, Pseudomonas extorquens, Methylobacterium sp. 17 ...
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Metagenomic analyses of the autotrophic Fe (II)-oxidizing, nitrate-reducing enrichment culture KS
S He, C Tominski, A Kappler, S Behrens... - Applied and ..., 2016 - Am Soc Microbiol
... lacks nitric oxide and nitrous oxide reductase genes and may partner with flanking populations capable of complete denitrification to avoid toxic metabolite accumulation, which may explain its resistance to growth in pure culture. ...
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On the unfounded enthusiasm for soft selective sweeps
JD Jensen - Nature Communications, 2014 - search.proquest.com
... producing plants, Zhen et al.45 also noted repeated bouts of parallel evolution for dealing with this toxicity not only ... replicated populations of Methylobacterium extorquens Identifying as many as 17 simultaneous beneficial mutations existing in a population which may rise in ...
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Chloromethane-induced genes define a third C1 utilization pathway in Methylobacterium chloromethanicum CM4
A Studer, C McAnulla, R Bachele... - Journal of ..., 2002 - Am Soc Microbiol
... of M. dichloromethanicum (14); P mxaF (AM1), methanol dehydrogenase promoter of M. extorquens AM1 (2); P mxaF (XX), methanol dehydrogenase promoter of Methylobacterium organophillum XX ... This suggested a toxic effect of chloromethane dehalogenation in this mutant ...
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Characterization of the general stress response in Bartonella henselae
N Tu, A Lima, Z Bendealii, B Anderson - Microbial pathogenesis, 2016 - Elsevier
... to determine the transcription of badA and hbs when the bacteria are assaulted with a toxic concentration of ... Bh), Bartonella quintana (Bq), Brucella abortus (Ba), Bradyrhizobium diazoefficiens (Bd), Caulobacter crescentus (Cc), Methylobacterium extorquens (Me), Rhizobium ...
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Expression of a novel bacteriocin—the plantaricin Pln1—in Escherichia coli and its functional analysis
F Meng, H Zhao, C Zhang, F Lu, X Bie, Z Lu - Protein expression and ..., 2016 - Elsevier
... In addition, a number of other bacteriocins were expressed in lactic acid bacteria [31], [32] and [33], Methylobacterium extorquens [34], Saccharomyces cerevisiae [35], Leuconostoc mesenteroides [36], and Carnobacterium piscicola [15]. ...
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Genome-guided insight into the methylothrophy of Paracoccus aminophilus JCM 7686
... Moreover, their ability to utilize pesticides and insecticides, including the highly toxic chlorpyrifos, 3,5,6-trichloro-2-pyridinol, methyl ... In many methylothrophs (eg, Methylobacterium extorquens) the reduction process is performed by the sequential action of two enzymes: CH 2 ...
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Qing Yu, Yan Li, Anzhou Ma, Weifeng
... widely as simple and practical approaches to the detection of a variety of agents, including heavy metals, toxic cellular organics ... D, Morel L, Groieau D, Miguez CB (2006) Multipropy Integration and Expression of Heterologous Genes in Methylobacterium extorquens ATCC 55386. ...
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A new methanol-feeding strategy for the improved production of β-galactosidase in high cell-density fed-batch cultures of Pichia pastoris Mut+ strains
A Maghsoudi, S Hosseini, SA Shojaosadati... - Biotechnology and ..., 2012 - Springer
... The accumulation of formaldehyde, as a toxic metabolite, may also result in the decrease of β-gal production rate ... and A. Heidarzadeh-Vezifehkoran (2009) Effect of feed composition on PHB production from methanol by HCDC of Methylobacterium extorquens (DSMZ 1340). ...
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Purification and properties of the formate dehydrogenase and characterization of the fdhA gene of Sulfitrospirillum multivorans
RPH Schmitz, G Diekert - Archives of microbiology, 2003 - Springer
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РАЗНООБРАЗИЕ ГЕНОВ ПОЛНОКИТЕДИНТАЗ (PKS) В МЕТАГЕНЕМНОМ СООБЩЕСТВЕ ПРЕСНОВОДНОЙ ГУБКИ Lubomirskia baikalensis
ОВ Калюжная, НВ Кулакова, ВБ Ицкович - Молекулярная биология, 2012 - elibrary.ru
... 74 1d KSLb (JQ771598) Methylobacterium extorquens DSM 13060 (EHP94300) 66 ... 26. Fewer DP, Österholm J., Rouhainen L., Jokela J., Wehlsten M., Svonen K. 2011. Nostocysin biosyn thesis is directed by a hybrid PKS NRPS in the toxic cyanobacterium Nostoc sp. 152. ...
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Transfer of a Catabolic Pathway for Chloromethane in Methylobacterium Strains
Highlights Different Limitations for Growth with Chloromethane or with ...
... a level that gives the appearance of essentiality or lead to increased accumulation of one or more toxic intermediates ... also explain our inability to productively transfer the cmu operon from its best-studied host, M. extorquens CM4, into closely related Methylobacterium strains ...
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Poly-3-hydroxybutyrate metabolism in the type II methanotroph Methylocystis parvus
OBBP
AJ Pieja, ER Sundstrom, CS Cridde - Applied and environmental ..., 2011 - Am Soc Microbiol
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1. Methane-production pathways
L Nazaries, JC Murrell, P Millard, L Baggs, BK Singh - researchgate.net
... due to its Cu-chelating properties: 1) Cu shuttle; 2) regulation of MMO activity; and 3) reduction of Cu toxicity (Choi et al., Korotkova, N., Chistoserdova, L., Kuksa, V., and Lidstrom, ME (2002) Glyoxylate regeneration pathway in the methylophry Methylobacterium extorquens AM1. ...
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Formaldehyde as a carbon and electron shuttle between autotroph and heterotroph populations in acidic hydrothermal vents of Norris Geyser Basin, Yellowstone ...
JJ Moran, LM Whitmore, NG Isen, MF Romine. - Extremophiles, 2016 - Springer
... The reverse RuMP pathway can produce relatively high concentrations of formaldehyde which, due to its inherent toxicity, must be removed to ... These heterotrophs, by consuming the formaldehyde as a carbon and energy source, reduce any toxic effects of its production on the ...
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Unfamiliar metabolic links in the central carbon metabolism
The central carbon metabolism of all organisms is considered to follow a well established fixed scheme. However, recent studies of autotrophic carbon fixation i.
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АНАЛИЗ 3-ОБЛАСТИ ГЕНА ДИХЛОРМЕТАНДЕГАЛОГЕНАЗЫ DCMA
METHYLOBACTERIUM DICHLOROMETHANICUM DM4
ЮЕ Фирсова, ДН Федоров, ЮА Троценко - Микробиология, 2011 - elibrary.ru
... штамма M. dichloromethanicum DM4 и деструкторов ДХМ Methylobabbus multivorans DM15 и Methylobacterium extorquens DM17, в ... М: ПЦР с ге номной ДК штаммов M. dichloromethanicum DM4 (1), M. extorquens DM17 (2 ... 4. Dhillon S., Von Burg RJ Toxicology update. ...
Cited by 1 Related articles Cite Save
Immobilization of Acetobacter sp. CGMCC 8142 for efficient biocatalysis of 1, 3-propanediol to 3-hydroxypropionic acid
J Li, H Zong, B Zhuge, X Liu, H Fang, J Sun  - Biotechnology and bioprocess ..., 2016 - Springer
... Beyond that range, however, substrate would bring negative factors such as osmotic pressure and toxicity of 3-HP so ... Structure of the quinoprotein glucose dehydrogenase of Escherichia coli modelled on that of methanol dehydrogenase from Methylobacterium extorquens. ... Related articles All 4 versions Cite Save

Carbon monoxide-dependent energy metabolism in anaerobic bacteria and archaea
E Oelgeschläger, M Rother  - Archives of microbiology, 2008 - Springer
... However, the concentration of CO is held below toxic levels by microorganisms utilizing it. Also, the requirement for more elaborate laboratory equipment due to the toxicity of CO and long adaptation periods often prevents assessment of carboxidotrophic capabilities of laboratory ... Cited by 130 Related articles All 11 versions Cite Save

Challenges Associated to the Multi-Scale Modeling of Fuel Electro-Oxidation for Fuel Cell Applications
KK Fung, P Kharidehal, DS Mainardi  - Design and Applications of ..., 2014 - Springer
... frac{1}{2}(O_[2]+2(e^-)+2(H^+)+2H^+)+leftarrow2(H_[2]+O$_2$). Although pure hydrogen gas is highly desired as fuel to avoid catalyst poisoning with carbon monoxide, it is not readily available and typically undergoes a reforming step. ... Related articles All 4 versions Cite Save More

Profiling of cytosolic and peroxisomal acetyl-CoA metabolism in Saccharomyces cerevisiae
... biomass was observed. Although MLS1 was deleted, isocitrate lyase was still active in these cells producing glyoxylate, which has been reported to be a toxic intermediate for mammalian cells [25] and bacteria [26]. To test the ... Cited by 52 Related articles All 13 versions Cite Save More

Cobalt: its role in health and disease
K Yamada  - Interrelations between Essential Metal Ions and Human ..., 2013 - Springer
... group. Crystal structures of the MeaB protein from Methylobacterium extorquens AM1 [50] and the human MMAA protein [51] have been reported. The toxicity of high doses of CoCl$_2$ has been recently reviewed [125]. Moreover ... Cited by 39 Related articles All 4 versions Cite Save More

Biosynthesis and lipase-catalysed hydrolysis of 4-hydroxybutyrate-containing polyhydroxyalkanoates from Delftia acidovorans
DHE Ch'ng, WH Lee, K Sudesh  - Mal J Microbiol, 2012 - mjm.usm.my
... this study, it was not possible to use sodium propionate as 3HV precursors since it displayed toxicity to the bacterial cells and contributed to subsequent reduction of terpolymer production (results not shown). Previous reports ... Cited by 9 Related articles All 4 versions Cite Save More

Thermoplastic Biopolymer Production (PHB, Poly 3-Hydroxybutyric acid) using Secondary Carbon Source Bioreactor Based on Nitrogen Fixation Biotechnology
M Sadeghi Pour Marvi  - 2011 - bioresonline.org
... They are ubiquitously present contaminants which are toxic, mutagenic and carcinogenic. ... agilis, AZ. insigne, macrocytogenes, AZ. beijerinckii, Chromobacterium violaceum, Methylobacterium organophilum, Pseudomonas extorquens, Pseudomonas oleovorans ... Related articles Cite Save More

A mutational hotspot and strong selection contribute to the order of mutations selected for during Escherichia coli adaptation to the gut
M Lourengo, RS Ramiro, D Güleresi  - PLoS ..., 2016 - journals.plos.org
Author Summary The relative contribution of random loss and migration versus de novo mutation to the overall diversity of the gut microbiota is far from understood. Population sizes of bacterial communities inhabiting the gut can be very large and therefore, both weak and strong ... Cited by 5 Related articles All 11 versions Cite Save More

https://scholar.google.com/scholar?start=30&hl=en&as_sdt=0,22
Recovering from a bad start: rapid adaptation and tradeoffs to growth below a threshold density
CJ Marx - BMC evolutionary biology, 2012 - bmcevolbiol.biomedcentral.com
... an unwavering exponential process fully captured by an internal capacity for expansion, such
as accumulation of toxic products, changes ... involves the fortuitous discovery of a density threshold
for growth for a metabolically engineered strain of Methylobacterium extorquens AM1 ...
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Methods for treating bacterial infections
... drugs such as colistin with narrow spectrum and considerable potential for toxic side-effects. ... wolffii;
Leptospira yanagawae.—Leptotrichiaceae.—Leptotrichia buccalis; Streptococcus moniliformis.—Methylobacteriaceae.—Methylobacterium extorquens group; Methylobacterium ...
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Effect of agave fiber content in the thermal and mechanical properties of green composites
based on polyhydroxybutyrate or poly (hydroxybutyrate-co-hydroxyvalerate ...
EV Torres-Tello, JR Robledo-Ortiz... - Industrial Crops and ..., 2017 - Elsevier
... Natural fibers like flax, hemp, jute, kenaf, abaca, sisal and agave as reinforcements offer some
advantages compared to synthetic fibers such as low density, renewability, biodegradability and
low cost; in addition they are non-toxic and have good physical and mechanical ...
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Experimental Study to Remediate Acid Fuchsin Dye Using Laccase-Modified Zeolite from
Aqueous Solutions.
E Kalkan, H Nadaroglu, N Celebi, H Celik... - Polish Journal of ..., 2015 - pjoes.com
Page 1. Introduction The release of colored effluents to the aquatic environ- ment
without adequate treatment causes public concern, legislative problems, and is a
serious challenge to environ- mental scientists. Synthetic origin ...
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Use of the yeast Pichia pastoris as an expression host for secretion of enterocin L50, a leaderless two-peptide (L50A and L50B) bacteriocin from Enterococcus...
A Basanta, B Gómez-Sala, J Sánchez... - Applied and..., 2010 - Am Soc Microbiol
... organization of at least four genes, which are closely associated in one or two operon-like structures: (i) the structural gene encoding the prebacteriocin; (ii) a gene encoding the dedicated protein, which confers producer self-protection (immunity) against the toxicity of the...
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The genetics and molecular biology of methanol-utilizing bacteria
ME Lidstrom - Methane and methanol utilizers, 1992 - Springer
... alcohol, to the corresponding aldehyde (Anthony, 1986). The product of allyl alcohol oxidation, allyl aldehyde (acrolein), is toxic and kills the cells. ... Two Mox systems have been studied in detail, in M. extorquens AM1 and Methylobacterium organophilum XX; in addition, the...
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Predicting Multi-Drug Inhibition Interactions based on Signaling Networks and Single Drug Dose-Response Information
HB Fang, H Huang, R Clarke, M Tan - J Comp Sys Bio, 2016 - researchgate.net
... Synergistic drug combinations, which are more effective than predicted from summing the effects of individual drugs, often achieve increased efficacy with lower doses and have reduced toxicity [2]. Since many molecularly-targeted agents exhibit synergy when used in...
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Methanotrophs and copper
JD Semrau AA Díspinto S Yoon - FEMS microbiology reviews, 2010 - academic.oup.com
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Microfabricated platforms to quantitatively investigate cellular behavior under the influence of chemical gradients
M Eltis S Sadeghi H Karamahmutoglu D Gozuacik... - 2017 - iopscience.iop.org
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Bioreactor comprising immobilized enzyme, method for improving activity of immobilized enzyme, and biofuel cell
... of the imidazole compound is above such range, the imidazole compound might become toxic to the... of PQQ dehydrogenases that can be used include: PQQ alcohol dehydrogenases from Acetobacter pasteurianus, Methylobacterium extorquens, Paracoccus denitrificans ...
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... target. False negatives typically occur in assays that use concentrations of test compounds that are either too high (resulting in toxicity) or too low relative to the binding or dissociation constant of the compound to the target. Another ...
Cited by 37 Related articles All 2 versions Cite Save

Sequence and functional analysis of an Escherichia coli DNA fragment able to complement pqqE and pqqF mutants from Methylobacterium organophilum
E Turlin F Gassner F Biville - Biochimie, 1996 - Elsevier
... can be drawn with regard to PQQ biosynthesis since disruption of this ORF is apparently toxic for the... Isolation, phenotypic characterization, and complementation analysis of mutants of Methylobacterium extorquens AM1 unable to synthesize pyrroloquinoline quinone and...
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Methods for treating bacterial infections
... for multidrug resistant (MDR) bacterial infections, forcing clinicians to consider older generation drugs such as colistin with narrow spectrum and considerable potential for toxic side-effects. ...
Methylobacteriaceae—Methylobacterium extorquens group; Methylobacterium ...
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1/3
Pathways of carbon assimilation and ammonia oxidation suggested by environmental genomic
SJ Hallam, TJ Mincer, C Schleper, CM Preston... - 2006 - openwetware.org
... 6.4.1.3 accB b ZP_00148271 Methanococcoides burtonii 1.00 3 10A 128 AACY01042731 0
acct b AAC24624 Methylobacterium extorquens 9.00 3 10A 9 AACY01150397 8.00 3 10A 40
accB b AAC24624 Halobacterium salinarum 1.00 3 10A 166 AACY01042731 0 2,3 ... Related articles All 6 versions Cite Save More

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МЛ Торжонская, СК Лауринашвили... - Известия Тульского..., 2013 - cyberleninka.ru
... vitro ассоциированные аэробными метаболическими бактериями Methylobacterium extorquens
D10, образующими ... на деклорирование синтетических Methylobacterium dichloromethane DM4 ...
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Interactions of TolB with the translocation domain of colicin E9 require an extended TolB box
SL Hands, LE Holland, M Vankemmelbeke... - Journal of..., 2005 - Am Soc Microbiol
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Respiration in methylotrophic bacteria
IJ Higgins - Diversity of bacterial respiratory systems, 1980 - Florida, USA: CRC Press
Cited by 9 Related articles All 9 versions Cite Save

The histidine kinase PdhS controls cell cycle progression of the pathogenic alphaproteobacterium Brucella abortus
C Van der Henst, F Beauffay, J Mignollet... - Journal of..., 2012 - Am Soc Microbiol
... n = 93 and a deletion probability of 7/106). The low frequency of pdhS deletion in the presence of pBPR1MC-pdhS is probably due to the toxicity of pdhS overexpression. The absence of deletants for the strain harboring the ...
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Metabolic modelling in the development of cell factories by synthetic biology
P Jouhten - Computational and structural biotechnology journal, 2012 - Elsevier
... like high tolerance (L-valine tolerant uncommon E. coli engineered to a platform strain [29]; solvent tolerant Pseudomonas putida S12 engineered to an L-tyrosine producing platform strain [30]; Bacillus subtilis able to modify the cell wall in response to toxicity [31]), ability to ...
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Improvement of RNA-SIP by pyrosequencing to identify putative 4-n-nonylphenol degraders in activated sludge
O Zemb, M Lee, ML Gutierrez-Zamora, J Hamelin... - Water research, 2012 - Elsevier
Nonylphenols (NP) have estrogenic potential because of their phenolic ring, but the organisms involved in the degradation of this alkylated phenol remain unident.
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Degradation of Acetaldehyde and Its Precursors by Pelobacter carbinolicus and P. acetylenicus
A Schmidt, M Fresch, D Schleheck, B Schink... - PLoS one, 2014 - journals.plos.org
Pelobacter carbinolicus and P. acetylenicus oxidize ethanol in syntrophic cooperation with methanogens. Cocultures with Methanospiillum hungatei served as model systems for the elucidation of syntrophic ethanol oxidation previously done with the lost "Methanobacillus ..."
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Prokaryotic Systems Biology
A Schmid, N Baliga - Systems Biology, 2007 - Springer
... 27 Using a similar strategy, metabolic models have been constructed for several other organ-
isms, including Methylobacterium extorquens AM1, 31 ... nearly 500 microarray experiments were conducted in response to UV and gamma irrad- ation, 56, 57 metal toxicity, 59 and ...
Archaea-like genes for C1-transfer enzymes in Planctomycetes: phylogenetic implications of their unexpected presence in this phylum
M Bauer, T Lombardot, H Teeling, NL Ward... - Journal of molecular..., 2004 - Springer
... In Methylobacterium extorquens, fae and the genes encoding the H 4 MPT-dependent enzymes have been... the product of one of the genes present in the M. extorquens cluster, orf4... that produces energy from C1-substrates and/or detoxifies the toxic intermediate formaldehyde...
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Dimethylsulfone as a growth substrate for novel methylotrophic species of Hyphomicrobium and Arthrobacter
E Borodina, DP Kelly, FA Rainey... - Archives of..., 2000 - Springer
... Potentially toxic substrates (formaldehyde, dimethylsulfoxide and dimethylsulfide) were added in sequential 0.5, 1, or 2 mM... DSM 11073, DSM 11104, Paracoccus versutus strain DSM 582, Xanthobacter tagetidis strain DSM 11105, or Methylobacterium thiocyanatum strain...
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Mapping the fitness landscape of gene expression uncovers the cause of antagonism and sign epistasis between adaptive mutations
HH Chou, NF Delaney, JA Draghi, CJ Marx - PLoS genetics, 2014 - journals.plos.org
...mutations that altered enzyme levels in the central metabolism of Methylobacterium extorquens to uncover...relationship between s and c for previous datasets from M. extorquens and E...of formaldehyde production, this threshold phenomenon may be explained by toxic effects of...
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Identification of a methanol-inducible promoter from Rhodococcus erythropolis PR4 and its use as an expression vector
Y Kagawa, Y Mitani, HY Yun, N Nakashima... - Journal of bioscience..., 2012 - Elsevier
...10, 11, and 14. Although Escherichia coli is not particularly tolerant to solvents, it has been used for whole-cell bioconversion in the presence of toxic solvents because of its ease of handling (15). Nevertheless, rhodococci...
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Genome Sequence Analysis of the
EHPA Acid - J. Bacteriol, 2007 - Citeseer
...GbCDDN1H1_0344 shows a best BLAST hit to the methanol dehydrogenase gene of another methylotrophic bacterium, Methylobacterium extorquens AM1, and shares a locational context identical to that of orthologous clusters in both M. extorquens AM1 and Paracoccus...
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Engineering the biological conversion of methanol to specialty chemicals in Escherichia coli
WB Whitaker, JA Jones, RK Bennett, JE Gonzalez... - Metabolic..., 2017 - Elsevier
...In both cases, oxidation of methanol yields the toxic product formaldehyde, which must then be assimilated into central...Recently, the serine pathway methylotroph, Methylobacterium extorquens, has been engineered to produce butanol from ethylamine, but not from methanol...
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Probing the active site tryptophan of Staphylococcus aureus thioredoxin with an analog
M Engiert, A Nakamura, YS Wang, D Eller... - Nucleic acids..., 2015 - academic.oup.com
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Protein Engineering of POO Glucose Dehydrogenase
S Igarashi, K Sode - Enzyme Functionality: Design; Engineering..., 2003 - books.google.com
...4.2 Application of POODH for DNA Sensors DNA sensing has become very important since it is a powerful tool for detection of the toxic microorganisms in food (or the environment) and may also be used for fundamental studies in molecular biology (94)... Cited by 2 Related articles All 10 versions Cite Save

Optimization of gene expression through divergent mutational paths
HH Chou, CJ Marx - Cell Reports, 2012 - Elsevier
...enzyme production decelerates flux, which may lead to a build-up of toxic metabolites and...optimization during adaptation of an engineered strain of Methylobacterium extorquens AM1 (EM...In order to grow on methanol, Methylobacterium must oxidize formaldehyde into formate...
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Current trends in polyhydroxyalkanoates (PHAs) biosynthesis: insights from the recombinant Escherichia coli
YK Leong, PL Show, CW Ooi, TC Ling, JCW Lan - Journal of biotechnology, 2014 - Elsevier
...is biocompatible and complete biodegradable, enantiomerically pure, non-toxic, exhibit piezoelectricity...scale production, which are C. necator, Methylobacterium organophilum, Pseudomonas oleovorans, A. latus, Protomonas extorquens, Azotobacter vinelandii...
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Comprehensive genomic analyses of the OM43 clade, including a novel species from the Red Sea, indicate ecotype differentiation among marine methylotrophs
F Jimenez-Infante, DK Ngugi, M Vinu... - Applied and..., 2016 - Am Soc Microbiol
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https://scholar.google.com/scholar?start=400&q=methylobacterium%20extorquens%20toxicity%3A%20plant&hl=en&as_sdt=0,22
Characterization and population dynamics of Toluene-degrading bacteria in a contaminated freshwater stream

Parallellism and Epistasis in the de novo Evolution of Cooperation between Two Species

Prevention Strategy of Urogenital Infections by Using Lactobacilli with Probiotic Properties

Protein and nucleic acid expression systems

Nucleic acids and vectors for use with methanotrophic bacteria

Paracoccus denitrificans CcmG is a periplasmic protein−disulphide oxidoreductase required for c-and aa3-type cytochrome biogenesis; evidence for a reductase role

Identification of Staphylococcus aureus proteins recognized by the antibody-mediated immune response to a biofilm infection
The Ribulose Monophosphate Pathway
H Atomi, T Imanaka, Y Sakai, I Orita, T Sato, H Yurimoto... - J. Bacteriol, 2006 - Citeseer
... The R1P can then be converted into R5P by phosphopentomutase (13) and then flow into the
general pathway for nucleotide synthesis. As HPS and PHI have been found to function in Ru5P
synthesis, this also results in the generation of toxic formaldehyde. ...
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Biodegradation of low-molecular-weight halogenated hydrocarbons by methanotrophic bacteria
RS Hanson, HC Tsien, K Tsuji, GA Brusseau... - FEMS Microbiology ..., 1990 - Elsevier
... eubacteria [19], while the pink-pigmented facultative methylotrophs "Methylo bacterium
extorquens" strain AM1", "Methylo bacterium strain DM4" and Methylobacterium organophilum
strain ... Furthermore, they are non-toxic, unlike toluene that induces toluene oxygenases. ...
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Microorganism modified for the production of 1, 3-propanediol
T Walthier, JM Francois - US Patent 9,605,283, 2017 - Google Patents
... However, comparatively low product yields, harsh reaction conditions, and the production of toxic waste streams ... most preferentially Escherichia coli, Bacillus subtilis, Corynebacterium glutamicum, Clostridium acetobutylicum, Methylobacterium extorquens, or Lactococcus lactis ...
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Structure-function studies of the methanopterin biosynthesis enzymes MJ1099, DmrB, and DmrX
EJ Morales - 2015 - search.proquest.com
... that when M. extorquens lacks the means to synthesize H4MPT, the metabolic intermediate formaldehyde accumulates and is toxic to the cell ... In Methylobacterium extorquens, insertion or deletion mutagenesis studies of genes in an archaeal-like gene cluster found six genes (orf ...
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Metabolic and stress responses of Acinetobacter oleivorans DR1 during long-chain alkane degradation
C Park, B Shin, J Jung, Y Lee... - Microbial ... 2017 - Wiley Online Library
... Staphylococcus aureus (Togashi et al., 2007) and Mycobacteria (Mukherjee et al., 2013), although the toxicity mechanism remains ... pathways to the glyoxylate shunt during alkane metabolism as seen in Rhodobacter sphaeroides and Methylobacterium extorquens AM1 (Ensign ...
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Production of carbon-13-labeled cadaverine by engineered Corynebacterium glutamicum using carbon-13-labeled methanol as co-substrate
L Leßmeier, J Pfeiferschneider, M Carnicer... - Applied microbiology ..., 2015 - Springer
... 2008) as in the Gram-negative methylotrophs like Methylobacterium extorquens. ... Formaldehyde produced in the oxidation of methanol may be dissimilated by oxidation to CO₂ in order to regenerate reducing equivalents and to regulate toxic formaldehyde levels (Guthiel et al. ...
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Genetics in methylotrophic bacteria: Appendix. Final report
ME Lidstrom - 1998 -osti.gov
... We have concentrated our effort on studying promoters in M. extorquens AM1. ... Isolation of a RecA strain of Methylobacterium AM1 will be extremely useful for future genetic ... and industrial sectors, as TCE contamination of groundwater, terrestrial sites and toxic waste dumps is ...
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Processes and Rates of Bacterial Evolution
N Delaney - 2013 - search.proquest.com
... The MP medium, similar to other media used for Methylobacterium species [36,40,41], is unusually rich. ... The higher metal concentrations in MP medium are not toxic to M. extorquens however, as we found no advantage on either succinate or methyamine to increasing ...
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Cultivation optimization of Methylosinus trichosporium OB3b for methanobactin recovery:
Structural effects of dissolved oxygen and cell density on the ...
I Chavarri - 2015 - search.proquest.com
... methanol oxidation to formaldehyde reactions, which may cause formaldehyde to accumulate poisoning the cells. ... or consumed by these organisms by binding to them and reducing their toxicity. ... Methylochory in Methylobacterium extorquens AM1 from a genomic point of view. ...
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Methods for rapid identification of bacillus cereus
... BACKGROUND OF THE INVENTION Bacillus cereus is gram-positive, spore-forming, motile, aerobic rod which inhibits in soil and has been recognized as an opportunistic food poisoning pathogen. ... cloacae. Methylobacterium, 11048, 12234, 2, 0, 2. extorquens. ...
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Structure, mechanism and physiological roles of bacterial cytochrome c peroxidases
JM Atack, DJ Kelly - Advances in microbial physiology, 2006 - Elsevier
... Oxidative stress results from the formation of toxic oxygen intermediates formed by incomplete reduction of oxygen. Reduction of oxygen ... Imay, 1999). Superoxide and H₂O₂ interact to form the highly toxic hydroxyl radical. Build ...
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Experimental horizontal gene transfer of methylamine dehydrogenase mimics prevalent exchange in nature and overcomes the methylamine growth ...
DD Nayak, CJ Marx - Microorganisms, 2015 - mdpi.com
... In contrast, when three replicate populations of wild type M. extorquens PA1 were ... Keywords: Methylotrophy; Methylamine; Experimental Evolution; Methylobacterium; Horizontal Gene Transfer (HGT). ... amine, mono-methylamine (CH₃ NH₂; MA) is a toxic, inflammable organic ...
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Assembly and catalysis of molybdenum or tungsten-containing formate dehydrogenases from bacteria
T Hartmann, N Schwanhold, S Leimkühler - Biochimica et Biophysica Acta ( ..... , 2015 - Elsevier
... has the advantage of safe portability as compared to liquid fuels such as methanol, which is toxic and highly ... Table 1, Mo/W-containing FDHs were isolated and characterized from several prokaryotes, including methylotrophs (Methylobacterium extorquens, Methylobacterium sp ... Cited by 17 Related articles All 7 versions Cite Save

Molecular Biology of Methanol-Utilizing Bacteria
ME LIDSTROM - Methane and Methanol Utilizers, 2013 - books.google.com
... The product of allyl alcohol oxidation, allyl aldehyde (acrolein), is toxic and kills the cells .... organoniphilium XX: moxF Met Ser Arg Phe Val Thr Ser Val Ser Ala Leu Ala Met Leu Ala Leu Ala Pro Ala Ala Leu Ser Ser Val Ala Tyr Ala Methylobacterium extorquens AM1: moxF Met Ser ...
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VA Herrera - The McNair Scholars Journal of the University of .... , 2013 - depts.washington.edu
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Whole genome comparison of 1,803 bacteria: An analysis of genetic relatedness and species-specific antibiotic target identification.
A Bissell - 2013 - repository.library.northeastern.edu
... computational methods has been demonstrated (Kitchen, 2004; McInnes, 2007, Schneider, 2010), candidate drugs have failed to make it to market for lack of penetration and human cell toxicity, among other reasons. Combining the search for ...
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FJ Bruggeman, B Teusink - pdfs.semanticscholar.org
... that increases CheB activity. Chemotaxis allows bacterial cells to swim in the direction of favoured chemical attractants (such as food) or away from repellents (such as toxic compounds) by changing the frequency of tumbling (Larsen et al, 1974; Berg and Tedesco, 1975). ...
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Oxidation Pathways in Methylotrophs
I Goldberg - Biology of Methylotrophs, 2013 - books.google.com
... can only autoreduce the homologous cytochrome c₁l, whereas the MDH of Methylobacterium extor- quens ... Mutants of M. extorquens AM1 and Hyphomicrobium X lacking MDH grow unimpaired on meth ... concentration must be kept very low since this compound is toxic to the cells. ...
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... The vast majority of colicins exert their lethality by a C-terminal cyto- toxic domain that either causes membrane depolarization of the cytoplasmic membrane (the pore-forming colicins) or deg- radation of RNA or DNA (the enzymatic colicins). ...
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Methylotrophic producers of bioplastics
SA Zamakhaeva, DN Fedorov, YA Trotsenko - Applied Biochemistry and ..., 2017 - Springer
... The data from enzymological analysis and isotopic experiments were the foundation to propose a regula- tory model for the biosynthesis of PHB and its copo- lymer PHB/V in Methylobacterium extorquens, which is a typical representative of serine methylobacteria [17, 18]. ...
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Stable isotopes have been used to trace atoms through metabolism and quantify metabolic fluxes for several decades. Only recently non-targeted stable isotope la.
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CHD Williamson, LA Jain, B Mishra, DL Olson... - Applied microbiology ..., 2015 - Springer
... 2011; Pollock 2012). At high concentrations, ethanol is thought to be toxic to microbes due to negative impacts on cell membranes (Taylor et al. 2012). ... 2012). The Alphaproteobacteria in the pyrosequencing library from sample EXT.1 included Methylobacterium spp. ...
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Essential functions in bacteria
T Bergmiller - 2011 - e-collection.library.ethz.ch
... Katz C, Cohen-Or I, Gophna U, Ron EZ. The ubiquitous conserved glycopeptidase gcp prevents accumulation of toxic glycosylated proteins. ... Laukel M, Rossignol M, Borderies G, Volker U, Vorholt JA: Comparison of the proteome of Methylobacterium extorquens AM1 grown under ...
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R Hedderich, WB Whitman - The prokaryotes, 2006 - Springer
... Therefore, microorganisms that catalyze these reactions cannot grow, and toxic levels of the
VFAs accumulate. However, if the methanoarchaea are present, H 2 is rapidly metabolized,
and its partial pressure is maintained below 10 -3 - 10 -4 atmospheres. ...
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Propionate metabolism in Mycobacterium tuberculosis: characterization of the vitamin
B12-dependent methylmalonyl pathway
SA Savvi - 2009 - wiresharce,wits.ac.za
... source.....106 5.11 Propionyl-CoA incorporation into virulence lipids relieves toxicity on valerate
.....110 5.11.1 Maintaining methylmalonyl-CoA homeostasis in MTB.....112 5.12 ...
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Genetically modified bacteria and methods for genetic modification of bacteria
... In some embodiments a pathogenic molecule is a toxic molecule (eg, a toxin). In certain
embodiments a gene encoding a pathogenic molecule and/or a toxic molecule is
knocked out. In certain embodiments a bacteria is genetically ...
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Evolution after introduction of a novel metabolic pathway consistently leads to restoration
of wild-type physiology
SM Carroll, CJ Marx - PLoS genetics, 2013 - journals.plos.org
... and evolutionary responses to a novel, sub-optimal central metabolism in Methylobacterium
extorquens AM1 ... As a facultative methylotroph, M. extorquens AM1 is capable of utilizing
one-carbon (C ... are oxidized first to formaldehyde, and in wild-type (WT), this toxic intermediate ...
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Draft genomes of Nautella italica strains CECT 7645 T and CECT 7321: Two roseobacters
with potential pathogenic and biotechnological traits
L Rodrigo-Torres, MJ Pujalte, DR Araghal - Marine genomics, 2016 - Elsevier
Nautella italica is a member of the family Rhodobacteraceae described in 2009. Strain
LMG 24365T (= CECT 7645T, = DSM 26436T, = CCUG 55857T) was.
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The modifier protein of formaldehyde dehydrogenase from Methylococcus capsulatus
(Bath)
SA Tate - 1996 - wrap.warwick.ac.uk
... From the data presented it is proposed that the function of mFDH may be to aid in reducing
toxic formaldehyde concentrations in the organism and the role of the nFDH ... 1970). The MDH
isolated from Methylobacterium extorquens AM1 is composed of two ...
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Bacterial genome evolution within a clonal population: from in vitro investigations to in vivo
observations
M Beaume, N Monina, J Schrenzel... - Future microbiology, 2013 - Future Medicine
... was notably highlighted in two other studies: one with long-term laboratory evolution of E. coli
[10], and one with an engineered strain of Methylobacterium extorquens [11]. ... The species E. coli
is partly defined by its inability to metabolize citrate (Cit -) under toxic conditions. ...
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https://scholar.google.com/scholar?q=methylobacterium+extorquens+toxicity+plant&hl=en&start=440&as_sdt=0,22
Life in extreme environments: approaches to study life-environment co-evolutionary strategies
X Xiao, Y Zhang - Science China Earth Sciences, 2014 - Springer
... oxygen species (ROS) increases significantly at low temperature, and ROS are toxic to the ... to this process is that O2, which may cause addi- tional toxicity, is not ... Towards kinetic modeling of global metabolic networks: Methylobacterium extorquens Am1 growth as Validation...
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... Another object of the invention is to provide a novel, highly specific, recombinase system for site-specific genetic recombination with preferably low toxicity. ... 21, SEQ ID No. 22.
Methylobacterium extorquens DM4. YP_003280820.1, SEQ ID No. 23, SEQ ID No. 24...
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Protein with recombinase activity for site-specific DNA-recombination
... Another object of the invention is to provide a novel, highly specific, recombinase system for site-specific genetic recombination with preferably low toxicity. ... 21, SEQ ID No. 22.
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Minimal effect of gene clustering on expression in Escherichia coli
LW Liang, R Hussein, DHS Block, HN Lim - Genetics, 2013 - Genetics Soc America
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Performance, Microbial Ecology, and Life Cycle Assessment of an Activated Carbon Biofilter for Methanol Removal
CW Babhike - 2007 - researchgate.net
... requirements of the PCO biofilter system. However, the operating impacts to global warming and human toxicity for the PCO-biofilter system were higher than for the RTO, because of the replacement requirements of packing for the...
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Quinoproteins as Biosensors
Y Kilagawa - Principles and Applications of Quinoproteins, 1992 - books.google.com
Page 445. 20 Quinoproteins as Biosensors Issa Karube and Kenji Yokoyama University of Tokyo, Tokyo, Japan Yasushi Kitagawa Asahi Breweries, Ltd., Tokyo, Japan I.
INTRODUCTION Many biosensors using biocatalysts, such ...
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Modularity of methylotrophy, revisited
L Chistoserdova - Environmental Microbiology, 2011 - Wiley Online Library
... A MDH first characterized in Methylobacterium extorquens (Anthony, 1982; 2004) and later detected in most of the model methylotrophs was a heterotetramer ... in terms of energy generation but also in terms of keeping the intracellular levels of formaldehyde at non-toxic levels. ...
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Metabolic network analysis of the marine bacterium Dinoroseobacter shibaei
AF Bartsch - 2016 - scidok.subb.uni-saarland.de
... Roseobacter clade, a subgroup of the Alphaproteobacteria. The Gram-negative small oval rod bacterium has first been isolated from the toxic marine algae Prorocentrum lima occurring in sand and sediment (Pradella et al. 2004, Wagner-Dobler et al. 2010, Biebl et al. 2005). ...
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S Mukherjee, A Bandyopadhyay - Clinical ..., 2016 - clinicalproteomicsjournal ...
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The effectors and sensory sites of formaldehyde-responsive regulator FrmR and metal-sensing variant
D Osman, C Piergentili, J Chen, LN Sayer... - Journal of Biological..., 2016 - ASBMB

Promiscuous anaerobes
LL Grochowski, RH White - Annals of the New York Academy of..., 2008 - Wiley Online Library

... Life arose and first evolved on earth under anaerobic conditions, 1 where the effect of toxic oxygen gas was not able to influence the nature of reactions leading to the first living system(s). It may be thus expected that the most likely place to gain insights into the earliest...
Isotopomer analysis of cellular metabolism in tissue culture: A comparative study between the pathway and network-based methods
TD Vo, SK Lim, VNP Lee, BO Palsson - Metabolomics, 2005 - Springer
... The combination of higher lactate, proton, and urea secretions into media A creates a higher energy demand and is likely to be more toxic to the cells. Media B is thus more advantageous and can be further improved with an increased asparagine addition. ...
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Prospecteço de genes codificadores de enzimas lipolíticas em biblioteca metagenômica de consórcio microbiano degradador de óleo diesel.
MR Pereira - 2011 - teses.usp.br
... Most lipolytic enzymes are derived from microbes, present low toxicity, are easily biodegraded and are notably selective of chemicals, a very positive trait which permits pharmaceutical products made with these enzymes to have few collateral effects. ...
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Chapter Twenty-Four-De Novo Designed Imaging Agents Based on Lanthanide Peptides Complexes
AFA Peacock - Methods in enzymology, 2016 - Elsevier
Herein are discussed a selection of lanthanide peptide/protein complexes in view of their potential applications as imaging agents, both in terms of luminescence.
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Parallel mutations result in a wide range of cooperation and community consequences in a two-species bacterial consortium
SM Douglas, LM Chubiz, WR Harcombe, FM Ytreberg... - PloS one, 2016 - journals.plos.org
... to support community growth failed. We thus turned to a classic route to generating methionine overproduction in S. enterica, selection of resistance to ethionine, a toxic methionine analog [19,20]. Methionine production in S ...
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Constraint-based analysis of metabolic capacity of Salmonella typhimurium during host-pathogen interaction
A Raghunathan, J Reed, S Shin... - BMC systems ..., 2009 - bmcrsstbiol.biomedcentral.com
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Applications of cellular fatty acid analysis.
DF Welch - Clinical Microbiology Reviews, 1991 - Am Soc Microbiol
Page 1. CLINICAL MICROBIOLOGY REVIEWS, Oct. 1991, p. 422-438 Vol. 4, No. 4 0893-8512/91/040422-17502.00/0 Copyright © 1991, American Society for Microbiology Applications of Cellular Fatty Acid Analysis DAVID ...
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Characterization of microbial populations in the subsurface
MP Buttner, P Cruz, KJ Stetzenbach, AJ Smiechnski - 2006 - digitalrepository.unlv.edu
... Barton et al. (1992) compiled a list of bacteria from various sources capable of binding, precipitating, absorbing, depositing, reducing and transforming various toxic elements, including Aeromonas, Bacillus megaterium, Citrobacter, Desulfovibrio, Escherichia coli, Flavobacterium ...
All 2 versions Cite Save

Physiology and biochemistry of the methane-producing archaea
R Hedderich, WB Whitman - The Prokaryotes, 2013 - Springer
... Under standard conditions, when the H2 partial pressure is 1 atm, the fermentations of VFAs and alcohols to acetate and H2 are thermodynamically unfavorable. Therefore, microorganisms that catalyze these reactions cannot grow, and toxic levels of the VFAs accumulate. ...
Cited by 23 Related articles Cite Save More

Newly discovered bacterium in the family acetobacteraceae
SM Holland, DE Greenberg, A Zelazny... - US Patent ..., 2015 - Google Patents
... These costs hinder market expansion for these and other related businesses. It would be useful to manufacture and market a biomass degrading and treatment method capable of converting organic waste materials into non-toxic end-products. ...
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A tricistronic heat shock operon is important for stress tolerance of Pseudomonas putida and conserved in many environmental bacteria
SS Krajewski, M Joswig, M Nagel... - Environmental ..., 2014 - Wiley Online Library
... procedures. Since P. putida has the ability to inhabit environments contaminated with aromatic substances, we asked whether HspX, Y and Z are involved in tolerance against the toxic effects of aromatic compounds. All mutants ...
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Multiple oEcG and NepR Proteins Are Involved in the General Stress Response in Methylobacterium extorquens
A Francez-Charlot, J Frunzke, J Zingg, A Kaczmarczyk... - PloS one, 2016 - journals.plos.org
... However, only the deletion of rsa1 is lethal (being toxic due to the overactivation of ... expansion of regulatory components of the GSR can be more pronounced: Methylobacterium strains genome ... since deletion of ecgG1, one of the six ecgG paralogues of M. extorquens AM1, does ...
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The pyrroloquinoline quinone (PQQ)-containing dehydrogenases
C Anthony - ADVANCES IN PHOTOSYNTHESIS AND ..., 2004 - books.google.com
... role in energy production and (in enteric bacteria) they may also function in the rapid removal of potentially toxic oxygen during ... The X-Ray Structure of Methanol Dehydrogenase The X-ray structure has been determined for the MDH from Methylobacterium extorquens (Blake et ...
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Interaction of the Escherichia coli transporter DctA with the sensor kinase DcuS: presence of functional DctA/DcuS sensor units
J Witam, J Bauer, I Wittig, PA Steinmetz... - Molecular ..., 2012 - Wiley Online Library
... The study was performed with DctA rather than DcuB as the co-sensor, since overexpression of dcuB and many of its variants is toxic to the cell (Klekfeld et al., 2009; Bauer et al., 2011). It was tested whether the DctA and DcuS proteins interact and form functional units. ...
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Method for measuring cells, and reagent for cell measurement
... 11. The method according to claim 1, wherein at least one microbial species selected from the group consisting of Bacillus subtilis, Pseudomonas aeruginosa, Pseudomonas fluorescence, Methylobacterium extorquens, Escherichia coli, Staphylococcus aureus, Clostridium ...
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Pyridine nucleotide transhydrogenases enable redox balance of Pseudomonas putida during biodegradation of aromatic compounds
Pl Nikhil, D Pérez-Pantoja... - Environmental ..., 2016 - Wiley Online Library
... On the other hand, toluene and xylenes are quite toxic for bacteria above a certain threshold concentration, since they can partition into the bacterial cell membrane and disorganize its structure by removing lipids and proteins, which eventually leads to cell death, and also by ...
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Development of a novel prokaryotic two-hybrid system for the detection and analysis of protein-protein interactions in vivo
PA Clarke - 2000 - doras.dcu.ie
Page 1. Development Of A Novel Prokaryotic Two-Hybrid System For The Detection And Analysis Of Protein-Protein Interactions In Vivo. Paul Clarke PhD. 2000 Page 2. Development Of A Novel Prokaryotic Two-Hybrid System For The Detection And ...
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Molecular basis for trimethoprim and sulphonamide resistance in Gram negative pathogens
M Grape - 2006 - openarchive.ki.se
... 1968 [15, 18, 19]. Since the drug has a wide antibacterial spectrum, low toxicity and few side effects, is easy to produce and thus relatively inexpensive, the drug has been widely used for many types of infections. It turned out ...
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Methylo trophs in natural habitats: current insights through metagenomics
L Chistoserdova - Applied microbiology and biotechnology, 2015 - Springer
... A major metabolic challenge for methylo trophs is dealing with formaldehyde, the extremely toxic intermediate of many of the C1 oxidative ... also of a variety of species without an obvious role in methane oxidation such as Methylophilaceae, Methylobacterium, Xanthobacter, and ...
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Biochemische und molekularbiologische Untersuchungen zu Lacton-Hydrolasen des bakteriellen Aromaten-und Halogenaromen-Abbaus
IS Hinner - 1968 - books.google.com
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18 Physiology and Biochemistry of the Methane-Producing Archaea
RHWB Whitman - 2013 - Springer
... Under standard conditions, when the H2 partial pressure is 1 atm., the fermentations of VFAs and alcohols to acetate and H2 are thermodynamically unfavorable. Therefore, microorgan- isms that catalyze these reactions cannot grow, and toxic levels of the VFAs accumulate. ...
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The biosynthesis of methanol dehydrogenase
IW Richardson - 1992 - eprints.soton.ac.uk
... This thesis reports studies on the periplasmic quinoprotein methanol dehydrogenase (MDH), principally from the facultative methylotrroph Methylobacterium extorquens, to investigate which factors are necessary for the formation of active enzyme. ... Methylobacterium extorquens 9 ...
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Expression vectors based on RK2 and TOL plasmids
... This may be particularly useful if the gene product is toxic to the host cell. ... The effects of the cop254D mutation on expression was rather puzzling, but we believe that the results may at least partly be caused by a poisoning effect on the cells mediated by the high copy number of ...
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Page 1. НАЦІОНАЛЬНА АКАДЕМІЯ НАУК УКРАЇНИ МІНІСТЕРСТВО ОСВІТИ I НАУКИ УКРАЇНИ ТОВАРИСТВО МІКРОБІОЛОГІЇ УКРАЇНИ ІМ. С.М. ВІНОГРАДСЬКОГО ІНСТИТУТ МІКРОБІОЛОГІЇ І ВІРУСОЛОГІЇ ІМ. Д.К. ...
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Global trends, seasonal cycles, and European emissions of dichloromethane, trichloroethene, and tetrachloroethene from the AGAGE observations at Mace ...
PG Simmonds, AJ Manning... - Journal of ..., 2006 - Wiley Online Library
... However, they are classed as hazardous air pollutants and toxic volatile organic compounds in regional air quality inventories. [3] About 70% of CH 2 Cl 2 emissions are anthropogenic in origin from foam plastic products, metal cleaning and other solvent uses [Cox et al., 2003]. ...
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Bioreactor cultivation of Bacillus methanolicus expressing green fluorescent protein
B Wong - 2012 - search.proquest.com
... Previous feed strategies in B. methanolicus have been designed to minimize the toxic effects of formaldehyde and formate accumulation in culture [15] and also to utilize direct methods in measuring methanol concentration in bioreactors [5]. Although carbon-limited feeding ...
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... enrichment culture, and then provided for testing. [0003]. For example, a sensitivity of 1 cfu/25 g is required for testing bacteria capable of causing food poisoning, such as Salmonella. Moreover, testing of not only a pyrogen but ...

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Protein


... Furthermore, Bitt (Arch Microbiol (1997) 167:78-88) discloses anaerobic citrate metabolism and its regulation in enterobacteria, and Ars et al. (J Bacteriol, June 1993, 175(2): 3776-83) discloses the genetics of malyl coenzyme A lyase in Methylobacterium extorquens AM1.

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Der mikrobielle Abbau von Ether-Verbindungen unter besonderer Berücksichtigung von Aralkyl- und Alkylethern

YH Kim - 1999 - elib.uni-stuttgart.de

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P Höfer, P Vermette, D Groleau - Bioengineered bugs, 2011 - Taylor & Francis

... A recent example of micro- organism and product development is the use of recombinant Methylobacterium extorquens ATCC 55366 strains in the production of second generation bio- polyesters. Methylobacterium extorquens tuned as a microbial bioplastic factory ...

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P Grunwald - 2009 - books.google.com

... and thus low energy consumption. Amount of byproducts is low. They are biodegradable. Preparation on large scale is possible through fermentation (microbial enzymes). Reuse is possible (immobilization). They can be designed to a certain extent. They are non-toxic if correctly ...

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NB Idupulepali - 2009 - search.proquest.com

... Amino acids labels denote their location in the sequence obtained from the entry 1W6S (Methylobacterium Extorquens W3A132) of the Protein. For catalyst materials, tertiary platinum/ruthenium-based alloys seem to offer the best performance when CO poisoning is of ...

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B Jansen - INFECTIONOUS DISEASE AND THERAPY SERIES, 1997 - books.google.com

... bacteria and C. albicans (96). Among metals with antimicrobial activity, silver has raised the interest of many investigators because of its good antimicrobial action and low toxicity. Sioshansi et al. used ion implantation to deposite ...

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Engineered botulinum neurotoxin

M Dong, L Peng, PEG Steenmark... - US Patent ..., 2017 - Google Patents

... the receptor binding domain of BoNT/A and BoNT/B, as indicated in the table, can significantly change the potency and toxicity of these ... toxin protease domain' means a C. botulinum toxin domain that can execute the enzymatic target modification step of the intoxication process. ...

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... There are few currently registered alternatives for multidrug resistant (MDR) bacterial infections, forcing clinicians to consider older generation drugs such as colistin with narrow spectrum and considerable potential for toxic side-effects. ...

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ВН Хмеленина, НЕ Сузина, ЮА Троценко - Микробиология, 2013 - elibrary.ru
Page 1. МИКРОБИОЛОГИЯ, 2013, том 82, № 5. с. 515–527 515 1 Общим свойством многих прокариот является присутствие на внешней поверхности клеточной стенки (КС) регулярных гликопротеиновых обра зований ...
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KH Nealson, R Bhatia, W Hug - 2016 - dtic.mil
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N-Heterocyclic quinones
RH Thomson - Naturally Occurring Quinones IV, 1997 - Springer
Page 1. 5 N-Heterocyclic quinones In a different context the quinones in this chapter would be regarded as alkaloids. It is a miscellaneous group with no large families of closely related compounds. The pyrrole ring occurs in ...
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MG Maldonado Díaz - 2013 - repositorio.ipicyt.edu.mx
... M3 Módulo 3 Page 12. xi NIOSH National Institute of Occupational Safety and Health (Instituto Nacional de Seguridad Ocupacional y Salud) NTP National Toxicology Program (Programa de Toxicología Nacional, Estados Unidos de América) O2 Oxígeno molecular O3 Ozono ...
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CL Hemme - 2004 - mospace.umsystem.edu
... The sulfate-reducing bacteria are also among a select group of organisms that may be used as tools for the bioremediation of toxic heavy metal contaminants from the bioremediation efforts (15-18). Several Desulfovibrio species have been shown to reduce toxic heavy ...
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Modified Clostridial Toxins Comprising an Integrated Protease Cleavage Site-Binding Domain
... BuNT, 143, M1-R422, K423-J847, K848-K1251. [0016] The binding, translocation and enzymatic activity of these three functional domains are all necessary for toxicity. While all details of this process are not yet precisely known, the overall cellular intoxication mechanism whereby ...
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... it is toxic for denitrifiers too. In fact, a knockout mutation for NO reductase is lethal, but the effect can be suppressed inactivating the NO generator (ie nitrite reductase). During denitrification, the steady state NO concentration is around 0.5-30 nM, while the toxicity of NO is shown ...
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An investigation into carbon flow through the metabolic networks of Rhodobacter sphaeroides
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... CcrR Transcriptional activator of ccr in Methylobacterium extorquens. ... Conversely, a transcriptional activator has been identified in Methylobacterium extorquens, but it is reported to be responsible only for the regulation of ccr expression and is not present in R. sphaeroides (54). ...
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ME Bechard - 2003 - etd.fcla.edu
... 2003). Methylothrophic growth of M. extorquens on one-carbon compounds such as methanol, and methylenes results in the production of the toxic compound formaldehyde. ... 2003.
Methylothrophy in Methylobacterium extorquens AM1 from a genomic point of view. J. Bacteriol. ...
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G Arias, L Yhiset - 2011 - repository.javeriana.edu.co
... negative control, but no with the positive control, showing that the Cry2Aa protein has a toxic activity against this pest. On the other hand, E. coli BL21 pET151-Cry2AAb had no significant differences with the negative control, which in this case, demonstrates the low toxicity of this ...
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DV Miller - 2017 - vtechworks.lib.vt.edu
... 630 0.82% Bacteroides fragilis YCH46 0.73% Methylobacterium extorquens AM1 0.41% Escherichia coli K12 0.44% Saccharomyces cerevisiae (Baker's yeast) 0.05% Table 2. Kinetic parameters of DdD with 5'-dA, MTA, SAH, and Ad Substrate KM (mM) kcat (s-1) kcat/KM (M ...
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LN Merkov - 2006 - digitalcommons.rockefeller.edu
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SP Valappil, AR Boccacini, C Bucke, I Roy - Antonie Van Leeuwenhoek, 2007 - Springer
... They are biodegradable, insoluble in water, non-toxic, biocompatible, piezoelectric, thermoplastic and/or elastomeric. ... are produced on the industrial scale using Gram-negative bacteria exclusively (such as Wautersia eutropha, Methylobacterium organophilum, Pseudomonas ...
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M Koepke, RO Jensen, JBYH Behrendorff... - US Patent ..., 2017 - Google Patents
... lactis, Bacillus subtilis, Bacillus licheniformis, Zymomonas mobilis, Klebsiella oxytoca, Klebsiella pneumonia, Corynebacterium glutamicum, Trichoderma reesei, Cupriavidus necator, Pseudomonas putida, Lactobacillus plantarum, and Methylobacterium extorquens. 10. ...
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Formate metabolism in sulfate reducing bacteria
SIM Silva - 2011 - search.proquest.com
... human large intestine, has also been implicated in inflammatory bowel diseases because of its toxic effects to epithelial colonic cells [19]. Nevertheless, SRO are drawing increased attention because of their... enzymes to cope with oxygen toxicity. It was recently shown that a ...
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Multiple ligand binding and kinetic isotope effects in methanol dehydrogenase
P Hothi - 2004 - Ira.ite.ac.uk
... 2.4.2 Purification of Mutant MDH from Methylotractrum extorquens
AM 1. ... 55 2.4.3 Partial Purification of Anaerobic MDH from M.
methylotrophus W 5 A 1. ... 56 2.5 KINETIC STUDIES. ... 57 ...
All 2 versions Cite Save More

Infections associated with urinary catheters
CE Chenoweth, S Saint - Catheter-Related Infections, 2005 - researchgate.net
... Because this practice allows for flow of organisms colonizing the catheter into the bladder, and in view of the potential for local toxicity and the complexity of this method, antibacterial irrigation cannot currently be recommended. ...
Cited by 2 Related articles All 4 versions Cite Save More

Destoxificação biológica do hidrolisado hemicelulósico de bagaço de cana-de-açúcar para utilização em processos fermentatitivos
LCSR Soares - 2012 - teses.usp.br
... Paulo, 2012. During the acid pretreatment step, required for the disruption of the lignocelluloses matrix and sugars release, several toxic compounds are produced and released in the hemicellulosic hydrolyzates. These compounds ...
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Methods of activating clostridial toxins
... The binding, translocation and enzymatic activity of these three functional domains are all necessary for toxicity. While all details of this process are not yet precisely known, the overall cellular intoxication mechanism whereby Clostridial toxins enter a neuron and inhibit ...
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Genetics and physiology of ammonia catabolism by the methane-oxidizing bacterium, Methylococcus capsulatus Bath
A Pore-Peterson - 2009 - search.proquest.com
... Whether genes involved in both processes are co-regulated remains to be answered, but their NH3-responsiveness has physiological implications and suggests that M. capsulatus Bath has a tiered strategy to cope with potential toxicity from NH3 exposure. ...
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Genomic patterns and phenotypic plasticity in prokaryotes analyzed within an ecological framework
JA Garcia López, J Mas Gordi - 2011 - ddd.uab.cat
... Bioremediation refers to the use of microorganisms to return toxic chemical elements to their natural cycles in nature. It may provide an effective method of environmental cleanup, which is one of the major challenges facing human society today. ...
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Degradable clostridial toxins
LE Steward, EG Fernandez-Salas, MA Gilmore... - US Patent ... - 2011 - Google Patents
... The binding, translocation and enzymatic activity of these three functional domains are all necessary for toxicity. While all details of this process are not yet precisely known, the overall cellular intoxication mechanism whereby Clostridial toxins enter a neuron and inhibit ...
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Staphylococcus aureus osteomyelitis: Characterization of bacterial antigens and utilization as vaccine candidates and imaging targets
R Brady - 2007 - search.proquest.com
... dorsal pedis and posterior tibia pulses, poor capillary refill, and decreased sensation, but fever and systemic toxicity are often absent. ... Several of these are enterotoxins, which cause food poisoning. Another toxin, toxic shock syndrome toxin (TSST), causes toxic shock syndrome. ...
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Conformational Analysis
C Jones - NUCLEAR MAGNETIC RESONANCE-LONDON-, 1993 - books.google.com
Page 395. 10 Conformational Analysis BY C. JONES 1 INTRODUCTION The format of this review is similar to that in the previous volume. There have been an increasing number of studies of biopolymers, particularly oligonucleotides, large peptides and proteins ...
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Produkcja polihydroksykwasów z osadu czynnego
E Klimiuk, T Pokój - Biotechnologia, 2006 - pbf.info.pl
... They are marked by high degree of polymerization, non-toxicity, wide range of application ...
Methyllobacterium organophilum lub Protonomas extorquens syntezują kwas poli-3-
hydroksyaminsowy w obecności metano- lu ... Do tej grupy należą również P. extorquens i P ...
Cited by 1 Related articles All 7 versions Cite Save More

Characterization of mechanisms involved in rickettsia pathogenicity
M Vellaswamy - 2011 - hal.archives-ouvertes.fr
... recognize one epitope and have markedly higher specific activity than polyclonal serum.
Advantages of mAbs formulations are superior in homogeneity, constancy, pathogen specificity, low toxicity, enhancement of immune function. Advances in biotechnology have enabled the ...
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Improving biotechnological processes through automated flow cytometry
AB Gilbert - 2008 - search.proquest.com
Improving biotechnological processes through automated flow cytometry. Abstract.
In the cytostat, an automated flow cytometry system is used to monitor and control a continuous culture. Cytostat technology was applied to measure ...
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Zum Mechanismus der 2-Hydroxyglutaryl-CoA Dehydratase aus Clostridium symbiosum
M Hetzel - 2004 - archiv.ub.uni-marburg.de
Page 1. Zum Mechanismus der 2-Hydroxyglutaryl-CoA-Dehydratase aus Clostridium symbiosum zur Erlangung des Doktorgrades der Naturwissenschaften (Dr. rer. nat.) dem Fachbereich Biologie der Philipps-Universität Marburg vorgelegt von Marc Hetzel aus Darmbach/WW ...
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Probiotic potential of lactic acid bacteria isolated from rainbow trout (Oncorhynchus mykiss, Walbaum) and rearing environment. Importance in the prevention of fish ...
CAD Araújo - 2016 - search.proquest.com
... the ban of antibiotics as prophylactic treatment, the reduction of authorized antibiotics, the control of the veterinary prescription, the establishment and surveillance of maximum residue limits and the prohibition of the use of certain antibiotics for their high toxicity or importance in ...
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Inverse metabolic engineering: a rational approach for efficient and robust microorganism development
CT Trinh - 2008 - search.proquest.com
... et al. 2005 ; Lee, et al. 2003). Efficient and robust microorganisms can also be used for bioremediation to detoxify toxic chemicals such as pesticides and industrial wastes (Wackett and Hershberger 2001). An application that ...
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In silico analysis of microbial biosynthetic capabilities at the genome-scale
M Imieliński - 2007 - search.proquest.com
... 5.3.3DHA or DHAP toxicity may underly the lethality of 3 glycolytic mutants ... disables the production of a pathogenic factor or induces the accumulation of a toxic metabolic intermediate ... flexibility in in the C3-C4 interconversion pathways of the organism M. extorquens and validate ...
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Evaluación y diseño de bacterias lácticas (BAL) de origen alimentario y de otros hospedadores como factores celulares de producción de bacteriocinas
JJJ Martinez - 2015 - eprints.ucm.es
Page 1. UNIVERSIDAD COMPLUTENSE DE MADRID FACULTAD DE VETERINARIA
Departamento de Nutrición, Bromatología y Tecnología de los Alimentos TESIS DOCTORAL Evaluación y diseño de bacterias lácticas (BAL ...
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Modeling molecular mechanisms of mammalian mineralization
JA Horst - 2010 - search.proquest.com
... personal communication, Sam Stupp). Self assembly has been extended to design
peptides comprised by only natural amino acids, thus lowering the chance for adverse
immune responses and toxicity. Beta sheet conformations ...
Related articles All 2 versions Cite Save More

Les modules de" détection/résistance" aux antibiotiques peptidiques chez les firmicutes
S Coumes - 2011 - theses.fr
Page 1. Université de la Méditerranée, Aix-Marseille II Faculté des Sciences de Luminy 163,
Avenue de Luminy 13288 Marseille Cedex 09 THESE DE DOCTORAT Spécialité : Microbiologie
présentée et soutenue publiquement par Stéphanie Coumes Florens ...
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Studies on a new oxalate-decomposing bacterium, Pseudomonas oxalaticus
SR Khambata, JV Bhat - Journal of bacteriology, 1953 - repository.ias.ac.in
... Furthermore, the loss of virulence of strain Ox4 indicates that pathogenicity is an unstable characteristic. ... What is even more significant, two of the strains were observed to be pathogenic to white ... JANOTA, L. 1950 Utilization of oxalic acid by Pseudomonas extorquens, Bassallik. ...

Methylobacterium species: an increasingly important opportunistic pathogen
AL Truant, R Gulati, O Giger... - Laboratory ..... 2015 - academic.oup.com
... classification and to develop an algorithm for the proper identification and treatment of infection with this opportunistic pathogen. ... Pseudomonas extorquens, V extorquens, and Flavobacterium extorquens are now synonymous with M extorquens u'2x The genus Protomonas has ...

Isolation of Protomonas extorquens (the 'Red Phantom') from a patient with AIDS
J Holton, R Miller, V Furst, H Malnick - Journal of Infection, 1990 - Elsevier
... Materials and methods Strains examined Pseudomonas extorquens (NCIB9399). Ps. ... Identification of unusual pathogenic Gram-negative aerobic and facultatively anaerobic bacteria. ... mesophilicum infection: Case report and literature review of an unusual opportunistic pathogen. ...

The role of oxalic acid and bicarbonate in calcium cycling by fungi and bacteria: some possible implications for soil animals
K Cromack Jr, P Sollins, RL Todd, R Fogel, AW Todd... - Ecological Bulletins, 1977 - JSTOR
... The plant pathogen Sclerotium rolfsii Sacc, by excreting oxalic acid, chelates Ca from Ca pectate in ... Pseudomonas extorquens Pseudomonas oxalaticus Streptomyces sp ... production and synergistic action of oxalic acid and polygalacturonase during pathogenesis by Sclerotium ...
Studies on a new oxalate-decomposing bacterium, Pseudomonas oxalaticus
SR Khambata, JV Bhat - Journal of bacteriology, 1953 - repository.ias.ac.in
... Furthermore, the loss of virulence of strain OX4 indicates that pathogenicity is an unstable characteristic. ... What is even more significant, two of the strains were observed to be pathogenic to white ... JANOTA, L. 1950 Utilization of oxalic acid by Pseudomonas extorquens, Bassalik. ...

Methylobacterium species: an increasingly important opportunistic pathogen
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... classification and to develop an algorithm for the proper identification and treatment of infection with this opportunistic pathogen. ... Pseudomonas extorquens, V extorquens, and Flavobacterium extorquens are now synonymous with M extorquens. The genus Pseudomonas has ...

Isolation of Protomonas extorquens (the 'Red Phantom') from a patient with AIDS
... Materials and methods Strains examined Pseudomonas extorquens (NCIB9399), Ps. ... Identification of unusual pathogenic Gram-negative aerobic and facultatively anaerobic bacteria. ... mesophilic infection: Case report and literature review of an unusual opportunistic pathogen. ...

The role of oxalic acid and bicarbonate in calcium cycling by fungi and bacteria: some possible implications for soil animals
K Cromack Jr, P Sollins, RL Todd, R Fogel, AW Todd... - Ecological Bulletins, 1977 - JSTOR
... The plant pathogen Sclerotium rolfsii Sacc, by excreting oxalic acid, chelates Ca from Ca pectate in ...

A contribution to the study of the intestinal microflora of Indian earthworms
SR Khambata, JV Bhat - Archives of Microbiology, 1957 - Springer
... a red, non water-soluble pigment resembled BASSALIK'S (1913 b) Bacillus extorquens--now reisolated and reclassified as Pseudomonas extorquens by LUD ... and perhaps the oxalates present therein, are the factors preventing the growth and survival of pathogenic bacteria. ...

Pseudomonas mesophilica and an unnamed taxon, clinical isolates of pink-pigmented oxidative bacteria.
... 1974. Studies on the production of pink pigment in Pseudomonas extorquens NCIB 9399 growing in continuous culture. J. Appl. Bacteriol. ... 1983. Revised tables from the identification of unusual pathogenic gram negative bacteria. Centers for Disease Control, Atlanta, Ga. VOL. ...

Ecology of the methylotrophic bacteria on living leaf surfaces
WA Corpe, S Rheem - FEMS Microbiology Letters, 1989 - Elsevier
... The predominant type of methylotroph encountered on the surfaces of more than 50 species of plants, were the pink-pigmented, facultatively methylotrophic bacteria (PPFM) of the Pseudomonas extorquens type [1 ... [20] Leben, C. (1974) Survival of plant pathogenic bacteria. ...

Antimicrobial Activities of Different Organic Extracts of Nut Shells of Juglans Regia (walnut)
N Raaman, K Mathiyazhagan, R Jegadeesh, S Divakar... - researchgate.net
... S. aureus and S. mutans), gram negative (E. coli and P. aeruginosa) and pathogenic yeast (C ... cereus, Micrococcus luteus, Salmonella typhimurium, Streptococcus pneumonia, Enterococcus faecalis, Bacillus thurungiensis, Serratiamarcescens, Pseudomonas extorquens, Proteus sp ...
Antimicrobial susceptibility of glucose-nonfermenting gram-negative bacilli (NFGNB)
GL Gilardi - Clinical Microbiology Newsletter, 1984 - Elsevier

... The pathogenic anaerobic bacteria, 2nd ed. Charles C. Thomas Co., Springfield. 13. mendocina (6)
Pseudomonas putrefaciens (72) Pseudomonas maltophilia (527) Pseudomonas diminuta
(42) Pseudomonas vesicularis (32) Pseudomonas extorquens (6) Pseudomonas ...

Phylogenetic affiliation of the pseudomonads based on 16S rRNA sequence.
Y Anzai, H Kim, JY Park... - ... of systematic and ..., 2000 - ijs.mycrobiolegyresearch.org
... (1996) IAM 12691T AB021415‡ Pseudomonas echinoides Sphingomonas rRNA lineage Kersters
et al. (1996) ATCC 14820T AB021370† 'Pseudomonas extorquens' and 'Pseudomonas rosea'
Methylobacterium extorquens Kersters et al. (1996) JCM2802T D32224 ... star Cited by
787 Related articles All 17 versions
Microbial dynamics during shelf-life of industrial Ricotta cheese and identification of a Bacillus strain as a cause of a pink discolouration
E Satin, NA Andreani, L Carraro, L Fasolato, S Balzan… - Food …. 2016 - Elsevier
... The chance of spoilage and pathogenic microorganism growth and survival depends on extrinsic factors associated with production and storage conditions, but also on intrinsic factors such as the composition of the microbial community (Ledenbach and Marshall, 2009).

Antimicrobial activity of the ethanol extracts of some plants natural growing in Aydin, Turkey
H Biyik - African Journal of Microbiology Research, 2010 - academicjournals.org
... susceptibly of the probiotic strains to those of clinical isolates, and their antimicrobial activity against food-bome pathogenic and spoilage ... study examines the antimicrobial efficacy of a phytochemical and a metallic nanoparticle against the top Gram positive resistant pathogen.

Microbiodeterioration of library materials part 1, chapters 1—3
R Kowalik - Restaurator, 1980 - degruyter.com
... Some yeast cells have a volume hundreds of times that of Staphylococcus aurcus, bacteria pathogenic to man. ... Silicates are dissolved by the activity of microorganisms and the highest degradation is caused by Pseudomonas extorquens.1 It evidently can destroy marble, the...
Aspects of Single-Cell Protein Processes
JH LITCHFIELD - Advances in Applied Microbiology, 1978 - books.google.com

... through residues in the substrate such as polyaromatic hydrocarbons and from contamination by pathogenic microorganisms or ... Examples of these organisms include Pseudomonas extorquens (Harrison, 1973; Downs and Harrison, 1974), Hyphomicrobium sp.(Wilkinson and ...
Bioprocess technology


Cited by 5 Related articles All 2 versions Class I.

Alphaproteobacteria class. nov.


Grouping of Pseudomonas species on the basis of cellular fatty acid composition and the quinone system with special reference to the existence of 3-hydroxy fatty …

H OYAIZU, K KOMAGATA - The Journal of General and Applied …. 1983 - jstage.jst.go.jp

… Pseudomonas palero- nii KS 0230 had 3-OH C$;o. "Pseudomonas extorquens" KS 0111, "P. rosea" KS 0312, and Pseudomonas sp. BP-22 had 3-OH C14;o• ... Page 16. 1983

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Mikrobielle Protein-Gewinnung auf Methanol-Basis

M Reuß, H Sahm, F Wagner - Chemie Ingenieur Technik, 1974 - Wiley Online Library

… 1.) Der Organismus darf nicht pathogen sein und darf keine Toxine produzieren. ... Johnson und Quayle [32] konnten ein ähnliches oder gleiches Enzym in Pseudomonas AM 1, Pseudomonas methanica, Pseudomonas extorquens und Protaminobacter ruber nachweisen. ... Cited by 26 Related articles

Microbial biotechnology: principles and applications

LY Kun - 2003 - books.google.com

… Secondary metabolites, particularly from microbial sources, are selective in their actions on pathogenic bacteria and fungi. ... Lactic cultures are also believed to neutralize the effect of enterotoxin from E. coli, which are pathogenic for pigs. ...

Cited by 57 Related articles All 4 versions

Isolation and Characterization of Pink Pigmented Facultative Methylo trophs From Coleus forskohlii and Their Influence on Growth and Tuber Yield

SR Pattanashetti - 2012 - krishikosh.egranth.ac.in

… Figure No. Title 1 Antagonistic activity of the PPFM isolates against different plant pathogenic fungi ... They sequester ferric iron, whose concentration is very low in well aerated soils, in a form that cannot be utilized by the pathogen, thereby reducing its number and/or activity. ...

Related articles All 2 versions

Physiology and biochemistry of amidase production by Methylophilus methylotrophus.

NJ Silman - 1990 - lra.le.ac.uk

… Methylocysts spp. Type II facultative methanotrophs Pink-pigmented facultative methylotrophs Methylobacterium organophium Pseudomonas AM1 Pseudomonas extorquens Pseudomonas TP I Pseudomonas At2 9 10 The Hyphomicrobia ...

Related articles All 2 versions

Myco-protein: A twenty-year overnight success story

APJ Trinci - Mycological Research, 1992 - Elsevier

… subjects (see below) showed the strain to Growth of Fusarium graminearum in continuous flow be non-toxic to animals, non-pathogenic to wheat … 1983), Harrison (1976) described an improvement in yield factor from 0'40 to 0'47 for a strain of Pseudomonas extorquens grown in ...

Cited by 66 Related articles All 6 versions

A taxonomic study of some Gram-negative facultatively methylotrophic bacteria

PN Green, IJ Bousfield - Microbiology, 1982 - mic.microbiologyresearch.org
One hundred and fifty pink-pigmented facultatively methylotrophic bacteria (PPFMs) of the 'Pseudomonas extorquens' type, 28 other facultative methylotrophs and 16 non-methylotrophic marker strains of the genera Pseudomonas, Alcaligenes, Mycoplana and Microcyclus...
Heterologous gene expression in methylotrophic yeast
JF Tschopp, JM Cregg - Biology of Methylotrophs, 1991 - books.google.com
... 305 Page 329. 306 Heterologous Gene Expression in Methylotrophic Yeast timum of most microorganisms, P. pastoris cultures are less susceptible than most to contamination. Studies to date suggest that P. pastoris SCP is non-pathogenic and devoid of toxins and pyrogens. ...

Taxonomic studies on some Gram-negative methylotrophic bacteria
O Jenkins, D Jones - Microbiology, 1987 - mic.microbiologyresearch.org
... Vibrio anguillarum Area I11 Cluster IIIA Subcluster IIIA 1 'Methylobacterium organophilum' 'Pseudomonas extorquens'... NCTC, National Collection of Type Cultures; ATCC, American Type Culture Collection; NCPPB, National Collection of Plant Pathogenic Bacteria; NRRL ...

Expression of antibody or a fragment thereof in lactobacillus
L Hammarström, H Marcotte, MA Alvarez... - US Patent ..., 2014 - Google Patents ...
In one embodiment the microorganism expresses one or more exogenous proteins. In one embodiment the one or more exogenous proteins treats or prevents a pathogenic infection. In one embodiment the pathogen is a virus. ...

Evoluzione della comunità microbica durante la shelf-life della Ricotta Industriale
A Tiengo - 2015 - tesi.cab.unipd.it
Page 1. UNIVERSITÀ DEGLI STUDI DI PADOVA Dipartimento di Biomedicina Comparata ed Alimentazione Corso di Laurea Magistrale in Biotecnologie per l'Alimentazione Evoluzione della comunità microbica durante la shelf-life della Ricotta Industriale ...

Ülkemizde doğal yayılışa sahip karayosunlarından Sphagnum centrale CEO Jensen ve S. Capillifolium (Ehrh.) Hedw'un (Bryophyta) anti-mikrobiyal aktivitesinin ...
F Başer - 2016 - adudspace.adu.edu.tr
... Salmonella thphimurium CCM 5445, Klebsiella pneumoniae UC57, Micrococcus roseus, Micrococcus flavus ATCC 14452, Citrobacter freundii ATCC 8090, Bordatella bronchiseptica ATCC 4617, Erwinia amylovora, Pseudomonas extorquens, Pseudomonas fluorescens ...

16S amplicon Next Generation Sequencing approach evaluation and its application to food microbial communities characterization
E Sattin - 2016 - paduaresearch.cab.unipd.it

Process for the production of fine chemicals
... The term “analogous conditions” means that all conditions such as, for example, culture or growing conditions, assay conditions (such as buffer composition, temperature, substrates, pathogen strain, concentrations and the like) are kept identical between the experiments to be ...

Process for the production of fine chemicals
The present invention relates to a process for the production of fine chemicals in a microorganism, a plant cell, a plant, a plant tissue or in one or more parts thereof. The present invention relates further to a process for the control of the production of fine chemicals in a microorganism...
Process for the production of fine chemicals
... The term “analogous conditions” means that all conditions such as, for example, culture or growing conditions, assay conditions (such as buffer composition, temperature, substrates, pathogen strain, concentrations and the like) are kept identical between the experiments to be ...

Adapting microorganisms for agricultural products
Disclosed herein are methods and compositions to convert a carbonaceous material to produce a fatty acid, biofuel, biodiesel, or other useful end-product. Organisms are evolutionarily modified to utilize carbon and/or nitrogen sources available in a carbonaceous material. Culture ...
"pseudomonas extorquens" pathogenicity - Google Scholar

https://scholar.google.com/scholar?start=30&q=%22pseudomonas+extorquens%22+pathogenicity&hl=en&as_sdt=0,22
Adapting Microorganisms for Agricultural Products
US Patent 20,150,004,672, 2015 - freepatentsonline.com
Disclosed herein are methods and compositions to convert a carbonaceous material to produce a fatty acid, biofuel, biodiesel, or other useful end-product. Organisms are evolutionarily modified to utilize carbon and/or nitrogen sources available in a carbonaceous material. Culture ...

Adapting Microorganisms for Agricultural Products
Disclosed herein are methods and compositions to convert a carbonaceous material to produce a fatty acid, biofuel, biodiesel, or other useful end-product. Organisms are evolutionarily modified to utilize carbon and/or nitrogen sources available in a carbonaceous material. Culture ...

Process for the production of fine chemicals
... The term "analogous conditions" means that all conditions such as, for example, culture or growing conditions, assay conditions (such as buffer composition, temperature, substrates, pathogen strain, concentrations and the like) are kept identical between the experiments to be ...
https://scholar.google.com/scholar?start=40&q=%22pseudomonas+extorquens%22+pathogenicity&hl=en&as_sdt=0,22
August 9, 2018

Louis Carlacci, Ph.D.
Chemist, Ingredient Safety Team
Division of Animal Feeds
Center for Veterinary Medicine
U.S. Food and Drug Administration
7519 Standish Place
Rockville, MD 20855

RE: GRAS Notice No. AGRN 26

Dear Dr. Carlacci:

KnipBio, Inc., would like to thank you and your colleagues at CVM for the very productive conference call on July 12, 2018 regarding the above-referenced GRAS Notice, and for sending us the meeting minutes for that call. The following are KnipBio’s responses to the questions and other issues raised during that call. In the remainder of this letter, CVM’s comments and questions are shown in italics, followed by KnipBio’s response to each. We have marked certain information that we consider a part of the pre-fermentation manufacture information as confidential. Confidential information in the text, figures and tables is enclosed within black boxes or borders. We believe this is consistent with the agency’s policy that manufacturing-related information is considered confidential business information and not released under the freedom of information procedures (21 CFR 20.61(a)). We understand the final determination will be made by the FOI officers of the Center for Veterinary Medicine.

Background

The substance is Methylobacterium extorquens protein (or KBM) derived from genetically engineered Methylobacterium extorquens strain KB203 through fermentation and spray drying the biomass. This notice filed February 7, 2018, informs the FDA of KnipBio’s view that Methylobacterium extorquens protein is GRAS through scientific procedures when used as a protein source in food for aquaculture species and when used at an intended use rate of up to 10% of the diet. The substance is intended to replace soybean or fish meal in the aquaculture diet.
Chemistry, Manufacturing and Controls:

1. **CVM recommended that the notifier explain where the signals for spirilloxanthin would be located in the tunable UV spectra and total ion current MS spectra as this relates to the conclusion that the parent strain does not produce spirilloxanthin, given that *M. extorquens* strain KB203 is genetically engineered to remove the spirilloxanthin production pathway and the physical data on strain KB203 and the parent strain KB200 are the same.**

This finding is supported in the literature. It has been broadly published that certain bacteria, including spirilloxanthin-producing *R. rubrum*, use bacteriochlorophyll systems to utilize light energy for reducing equivalents to improve growth. Such systems use a variety of carotenoids including spirilloxanthin to efficiently transfer energy to bacteriochlorophyll molecules, and many strains have been reported to exhibit different color phenotypes under light and dark conditions ([Yurkov and Beatty, 1998]; [Papagiannakis et al., 2002]; [Niedzwiedzki et al., 2015]; [Siddaramappa et al., 2018]). Indeed, Steifel et al. (2013) identified several species of *Methylobacterium* that express bacteriochlorophyll (as determined by fluorescent phenotype) in light conditions found on the leaves of plants. These strains exhibited varying phenotypes when cultivated on various media with a day/night cycle. Specifically, in data reported in Steifel et al., the reference strain *M. extorquens* PA1 did not exhibit fluorescence when grown on methanol or succinate, suggesting a downregulation of these genes under methanol fermentation (i.e. the conditions of KnipBio’s fermentation).
(b) (4)

(b) (4)

(b) (4)
2. CVM recommended that for all the components in the defoamer, the notifier provide the chemical name, CAS number and either the AAFCO ingredient definition number, the CFR citation or other information (such as citing the FDA letter that contains a list of allowed technical additives, that was sent to the Enzyme Technical Association) justifying its acceptability for use in the manufacture of animal food.

Please refer to the two letters dated July 13, 2018, from Appendix 2, stating that the composition of Foam Control is “polyglycol”, i.e. [alpha]-Hydro-omega-hydroxy-poly (oxyethylene)/poly(oxypropylene)/ poly(oxyethylene) block copolymer (CAS Reg. No.), and that the use of this product complies with 21 CFR Part 173.340, Secondary Direct Food Additives Permitted in Food for Human Consumption, when used as a defoaming agent, and which notes that its ingredients are listed under §173.340(a)(3). The letter further states that “The Center for Veterinary Medicine has used regulatory discretion and not taken action against the use of substances approved for use in human food as antifoaming or defoaming agents in animal feeds (21 CFR Part 173.340) when used according to the existing regulations.”

Please also refer to the letter of September 11, 2003 from FDA CFSAN to Gary Yingling on behalf of the Enzyme Technical Association, shown in Appendix 3, discussing the use of several antifoaming agents, and stating the conclusion that these agents can be used by enzyme manufacturers in accordance with good manufacturing practice. Note that the chemical compound making up , with the CAS number cited above, is the third compound listed in Table 1 of the September 11, 2003 letter.

CVM recommended that the notifier provide a replacement for boric acid that is appropriate for use in animal food production as boric acid is not approved for this use. The notifier stated on the call that a replacement for boric acid would not be used. This should be confirmed in the amendment.

KnipBio confirms that boric acid will not be used in the manufacture of the notified substance.
CVM recommended that the notifier provide an animal food grade specification for methanol, as the specification in the notice does not include tests for the heavy metal lead, and acetone and aldehyde impurities, which are tests listed in the Food Chemicals Codex monograph for methanol.

The specification of the methanol used for manufacture of the notified substances will follow the specification in the Food Chemicals Codex monograph (Food Chemicals Codex, 4th Edition (1996) page 251).

Table 1. Food Chemicals Codex specification for methanol.

<table>
<thead>
<tr>
<th>Methanol specification</th>
<th>Min. 99.85%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetone + aldehydes</td>
<td>Not more than 0.003%</td>
</tr>
<tr>
<td>Acidity (as formic acid)</td>
<td>Not more than 0.0015%</td>
</tr>
<tr>
<td>Alkalinity (as NH₃)</td>
<td>Not more than 3 ppm</td>
</tr>
<tr>
<td>Heavy metals (as Pb)</td>
<td>Not more than 1 ppm</td>
</tr>
<tr>
<td>Non volatiles residues</td>
<td>Not more than 10 ppm</td>
</tr>
<tr>
<td>Water</td>
<td>Not more than 0.1%</td>
</tr>
</tbody>
</table>

As an example of the sourced methanol to be used in commercial manufacture, Table 2 below is a comparison of the Certificate of Analysis of 3 batches of methanol that have been used for large scale fermentation by KnipBio.

Table 2: Example of source of methanol to be used in the KnipBio fermentation.

<table>
<thead>
<tr>
<th>Supplier</th>
<th>(b) (4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Product #</td>
<td>(b)</td>
</tr>
<tr>
<td>Spec</td>
<td>Results</td>
</tr>
<tr>
<td>Methanol spec</td>
<td>Min. 99.85%</td>
</tr>
<tr>
<td>Acetone + aldehydes</td>
<td>Max. 0.003%</td>
</tr>
<tr>
<td>Acidity (as formic acid)</td>
<td>Max. 0.0015%</td>
</tr>
<tr>
<td>Titrable Acid (meq/g)</td>
<td></td>
</tr>
</tbody>
</table>

As an example of the sourced methanol to be used in commercial manufacture, Table 2 below is a comparison of the Certificate of Analysis of 3 batches of methanol that have been used for large scale fermentation by KnipBio.

Table 2: Example of source of methanol to be used in the KnipBio fermentation.

<table>
<thead>
<tr>
<th>Supplier</th>
<th>(b) (4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Product #</td>
<td>(b)</td>
</tr>
<tr>
<td>Spec</td>
<td>Results</td>
</tr>
<tr>
<td>Methanol spec</td>
<td>Min. 99.85%</td>
</tr>
<tr>
<td>Acetone + aldehydes</td>
<td>Max. 0.003%</td>
</tr>
<tr>
<td>Acidity (as formic acid)</td>
<td>Max. 0.0015%</td>
</tr>
<tr>
<td>Titrable Acid (meq/g)</td>
<td></td>
</tr>
</tbody>
</table>
KnipBio Amendment to GRAS Notice AGRN 26

<table>
<thead>
<tr>
<th></th>
<th>Max.</th>
<th>Actual</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alkalinity (as NH₃)</td>
<td>3.0 ppm max.</td>
<td>2.000 ppm</td>
</tr>
<tr>
<td>Titrable Base (meq/g)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heavy metals (as Pb)</td>
<td>Max. 1.0 ppm</td>
<td>0.200 ppm</td>
</tr>
<tr>
<td>Non volatiles residues</td>
<td>Max. 10 ppm</td>
<td>10.000 ppm</td>
</tr>
<tr>
<td>Solubility in Water</td>
<td></td>
<td>Passes test</td>
</tr>
<tr>
<td>Water</td>
<td>Max. 0.1%</td>
<td>0.04%</td>
</tr>
</tbody>
</table>

KnipBio will ensure that the manufacturing of the notified substance will be performed under GMP conditions.

3. **CVM recommended that the notifier provide a specification that includes an analytical test for PHB content, as this is an important identity and safety marker.** CVM recommended that the notifier provide a specification that includes tests for impurities including methanol and heavy metals, such as lead, cadmium, mercury and arsenic or explain why they are not needed. For each test in the specification, CVM recommended that the notifier provide the analytical method citation and acceptance criteria. The acceptance criteria should be supported by batch analysis. Analytical methods should be citations of compendia analytical methods or, in lieu of citations of compendia methods, copies of the validated analytical methods supported with validation summaries.

Then notified substance is a safe and efficacious protein that can be used at a 10% inclusion in aquafeed. The specification of the notified substance is shown in the following Table 3, which also indicates citations for the analytical methods to be used.
KnipBio Amendment to GRAS Notice AGRN 26

Table 3. Specification of the notified substance.

<table>
<thead>
<tr>
<th></th>
<th>Method</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moisture %</td>
<td>AOAC 930.15</td>
<td>&lt;7</td>
</tr>
<tr>
<td>Protein (crude) %</td>
<td>AOAC 990.03</td>
<td>&gt;50</td>
</tr>
<tr>
<td>PHB %</td>
<td>Adapted from Karr et al. (1983) (see Appendix 4)</td>
<td>&lt; 25</td>
</tr>
<tr>
<td>Methanol % (w/v)</td>
<td>Adapted from Anthon et al. (2004) (see Appendix 5)</td>
<td>&lt;0.004</td>
</tr>
<tr>
<td>Total coliform (cfu/g)</td>
<td>MFHPB-34</td>
<td>&lt;5</td>
</tr>
<tr>
<td>Appearance (color)</td>
<td></td>
<td>Light pink to reddish color</td>
</tr>
<tr>
<td>Appearance (form)</td>
<td></td>
<td>Fine powder</td>
</tr>
</tbody>
</table>

KnipBio suggests that a specification for heavy metals such is not needed based on the fact that there is no source of these heavy metals in the growth media. We verified the absence of heavy metals in 3 fermentation batches (table below).

The following Table 4 shows the analysis of heavy metals and other constituents in 3 batches of the notified substance, as performed by (b) (4). The column in the Table entitled “Methods” indicates the methods used by (b) (4), identified by their AOAC reference numbers (http://www.aoac.org/).

Table 4. Heavy metal analysis in three batches of the notified substance.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Moisture %</td>
<td>AOAC 930.15</td>
<td></td>
<td></td>
<td>(b) (4)</td>
</tr>
<tr>
<td>Protein (crude) %</td>
<td>AOAC 990.03</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fat (crude) %</td>
<td>AOAC 920.39</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fiber (crude) %</td>
<td>AOAC 978.10</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ash %</td>
<td>AOAC 942.05</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calcium %</td>
<td>AOAC 985.01/984.27</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phosphorus %</td>
<td>AOAC 985.01/984.27</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sodium %</td>
<td>AOAC 985.01/984.27</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chloride %</td>
<td>AOAC 937.09</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Magnesium %</td>
<td>AOAC 985.01/984.27</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Manganese ppm</td>
<td>AOAC 985.01/984.27</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Iron ppm</td>
<td>AOAC 985.01/984.27</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zinc ppm</td>
<td>AOAC 985.01/984.27</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Copper ppm</td>
<td>AOAC 985.01/984.27</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Potassium %</td>
<td>AOAC 985.01/984.27</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Selenium ppm</td>
<td>AOAC 986.15</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Table 5. Methanol analysis in three batches of the notified substance.

<table>
<thead>
<tr>
<th>Sample</th>
<th>% Methanol (w/v)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Batch from June 2015</td>
<td>(b) (4)</td>
</tr>
<tr>
<td>Batch from May 2016</td>
<td></td>
</tr>
<tr>
<td>Batch from October 2016</td>
<td></td>
</tr>
</tbody>
</table>

LOD: 0.002475 % (w/v)

AOAC methods for measurement of heavy metals are cited above.

5. For the room temperature stability results in Table 2-5, CVM recommended that the notifier provide the acceptance criteria and analytical methods. Analytical methods in the notice should include citations for the compendia analytical methods or, in lieu of citations of compendia methods, copies of the validated analytical methods supported with validation summaries.

The notified substance is a nutritious and efficacious protein flour. Measurement of the protein content as well as PHB over time show that the substance is stable under standard storage conditions (room temperature and ambient humidity): the protein content is very consistent (50-52%) and does not
change within a 15% range (acceptance criteria). These results, along with the citations for the analytical methods used, are shown in Table 6.

Table 6. Analytical results of 3 batches of the notified substance.

<table>
<thead>
<tr>
<th>Analysis date</th>
<th>Moisture (%)</th>
<th>Protein (%)</th>
<th>Fat (%)</th>
<th>Fiber (%)</th>
<th>Ash (%)</th>
<th>PHB (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Method</td>
<td></td>
<td>AOAC 930.15</td>
<td>AOAC 990.03</td>
<td>AOAC 920.39</td>
<td>AOAC 978.10</td>
<td>AOAC 942.05</td>
</tr>
<tr>
<td>Batch June 2015</td>
<td>8/8/2018</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>7/24/2017</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>5/17/2017</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>10/31/2016</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>8/17/2016</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>9/14/2015</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Avg</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>std</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Batch June 2016</td>
<td>8/8/2018</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>7/24/2017</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>5/17/2017</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2/10/2017</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>10/31/2016</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>9/9/2016</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td>6/15/2016</td>
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<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Avg</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>std</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Batch Oct 2016</td>
<td>8/8/2018</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>7/24/2017</td>
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<tr>
<td></td>
<td>5/17/2017</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2/10/2017</td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td>11/9/2016</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>10/31/2016</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Avg</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>std</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CVM noted that the stability information obtained for one batch stored at a higher temperature, 45°C, for period of 3 months, is an appropriate combination of temperature and duration to support stability for up to one year. However, for accelerated stability testing, we typically expect stability for three batches, and for each batch, 3 temperatures and appropriate duration. We allow a stability claim of up to 1 year with a successful accelerated stability study. CVM
recommended that the notifier explain the increase in standard plate count in the stability study at a higher temperature (see Table 2-6 of the notice) and rule out the possibility of pathogenic organisms.

KnipBio will rely on the room temperature stability study, which demonstrates the stability in excess of one year on multiple batches. However, we are answering the questions raised on the standard plate count assessment related to the accelerated storage conditions (see table 2-6), to be thorough.

KnipBio has solicited the comments of the lab supervisor at who said: “Modern microbiological theory for standard plate count is based on the possibility of counting bacterial colonies in plates. Under this theory, 87,000 to 180,000, 57,000 and 120,000 are considered to be very similar numbers as they are in the same magnitude.” This statement strongly suggests that there is no significant difference between the different measurements at week 3 and week 12. Because there were no pathogens such as Staphylococcus aureus, Salmonella or E. coli detected at time zero of this study, KnipBio did not anticipate that any of these bacteria would appear during the accelerated shelf life study. Moreover, none of these microorganisms could be detected in the notified substance after 1 year of storage at room temperature, which is another reason KnipBio did not anticipate the presence of pathogens. As mentioned in the Narrative of the GRAS Notice, containers with samples stored at room temperature were often opened to withdraw samples for protein and PHB QC analysis, and that might explain the increase in standard plate count. Upon manufacturing, such processes are not anticipated as the notified substance is destined to be processed in a timely manner and not subject to long period of storage.

The numerical, but non-statistically relevant increase in CFUs noted suggests a possibility of human handling error. In addition to the single cell protein samples tested in the accelerated stability test described above, the company also tested various batches, from its inventory. In approximately four tests, where samples were stored in a way consistent with product specifications (i.e. stored at room temperature, inside a propylene bag), CFU derived from the product was observed to be very low. Two samples from 2015 and two samples from 2016 yielded 1800, 38000, 2800 and 8600 CFUs respectively at initial testing, suggesting that the residual biological potential remains quite low under proper storage conditions.
6. CVM recommended that the notifier provide information on the verification of the in-house method for the analysis of PHB content in the notified substance, which is based on a comparison with the results of a validated method. This information consists of the standard calibration procedure, the equations used to compute the PHB content, method verification summary, a summary of standard calibration results and the validation summary for the method used for comparison.

KnipBio has developed an in-house method for the analysis of PHB content, that has been adapted from the published method of Karr et al. (Karr, Waters and Emerich, 1983). As shown in Appendix 4, this method has been verified against the Karr method, using the criteria of “Guidelines for the Validation of Chemical Methods for the FDA FVM Program.” 2nd edition. April 2015. US Food & Drug Administration, Office of Foods and Veterinary Medicine. The following is a summary of the experiments that have been carried out: please see Appendix 4 for more detail.

Summary:
KnipBio adapted and verified a method based on a HPLC assay published by Karr et al. 1983 (Karr, Waters and Emerich, 1983) to measure Polyhydroxybutyrate (PHB). PHB is converted by sulfuric acid into crotonic acid. Crotonic acid can be measured in crude reactions by absorbance at 210 nm or more precisely by separation and measurement on an HPLC or UPLC. Following conversion, there are no major peaks other than crotonic acid when measured by absorbance at 210nm.

Appendix 4 describes two methods KnipBio evaluated for assaying PHB content. The chosen method, referred to as “Method 1” in the Appendix, showed excellent repeatability, linearity, low limits of detection and quantitation, and acceptable specificity. Our adaptation to using a UPLC reduced per sample times from 30 minutes in Karr et al. to 3 minutes per sample. The data presented herein supports the use of Method 1 for the analysis of PHB content in KnipBio produced single cell protein (SCP) containing 0.05 to 30% PHB (w/w). Collectively, the results presented here suggest that the largest contributions to error are in measuring dry cell weights and standard preparation.

Table 7: Summary of acceptance criteria and results of PHB assay.

<table>
<thead>
<tr>
<th>Verification</th>
<th>Acceptance Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Repeatability Precision</td>
<td>RSD, &lt; 4 %</td>
</tr>
<tr>
<td>Linearity*</td>
<td>r &gt; 0.995</td>
</tr>
<tr>
<td>LOD†</td>
<td>S/N &gt; 5</td>
</tr>
</tbody>
</table>
The repeatability/ precision of the method was tested by comparing (1) the same sample injected three times, and (2) ten separate dilutions of the same analyte. By using a 500µg PHB standard diluted 50 times, we determined that the Quantitative Method Acceptability Criteria RSD (Guidelines for the Validation of Chemical Methods for the FDA FVM Program) was below the 4-6% values for 100 to 10mg/kg method levels. These results are shown in Section 3 of Appendix 4.

The linearity of the method was determined based on the correlation coefficient for at least six standards generated from purified PHB in amounts between 50 and 3000 µg. The results for four separately prepared standards from three users showed a r²>0.99 fitting a quadratic equation, thus demonstrating the linearity of the method. These results are shown in Section 4 of Appendix 4.

The limits of detection (LOD) and limits of quantitation (LOQ) for the method were determined by (1) quantifying the minimum amount of PHB possible, and (2) the range over which the method can be accurately used. By using standards of 50, 25, 12.5, 5, 2.5 µg PHB injected multiple times, we obtained an acceptable linearity (r > 0.99295, r² > 0.998590) of the method. The LOD is 0.0067 mg/mL or an equivalent amount of 1ug PHB. The LOQ is 0.0167 µg/mL or an equivalent amount of 1.25 ug PHB. The low concentration samples were also compared to their theoretical value. For samples with greater than a 5 ug PHB equivalence (0.0333 µg/mL concentration), the % deviation was less than 10%. Linearity between the theoretical and measured values was acceptable (r² > 0.9992). These results are shown in Section 5 of Appendix 4.

The specificity and accuracy of the method was determined by (1) investigating whether there are other substances in matrix blanks or media lacking PHB that could interfere with determining the PHB content and (2) measuring the accuracy or closeness of the results to a theoretical value of PHB. To determine if other substances in the matrix or media could interfere with PHB measurement, KnipBio analyzed several strains grown in minimal media supplemented with either methanol or succinate as the sole carbon source. We used strains unable to produce PHB (as described in Appendix 4) and also spiked known amounts of PHB in cell extracts prior to analysis by UPLC. Based on specificity and accuracy acceptance criteria, no signal in the matrix blanks should be greater than 2 times the LOQ (<2 .5ug) and spiked samples of 2 matrix blanks with 1mg PHB should be within 10% of their theoretical values. No PHB could be detected in the samples from cells unable to produce this compound, demonstrating that no other substance in the matrix could interfere with the signal. Moreover, all the theoretical PHB added to the sample was measured within a 10 % error, demonstrating the accuracy of the method. These results are shown in Section 6 of Appendix 4.
In summary, through the experiments and data summarized above and presented in Appendix 4, KnipBio has verified that the analytical method developed and used in-house accurately measures PHB in the notified substance.

7. The notice Part 3 section “Concentration of methanol in the notified substance” argues that there is less than 0.00125% MeOH (0.01mg/mL) in the notified substance given that “samples were run [sic] at a 4X concentration compared to the standards, and no signal was found to be more fluorescent than the blank control.” CVM recommended that the notifier explain how the methanol content in the notified substance can be reduced by a factor of 4, as the method determines the methanol content in culture supernatant, and the sample is derived by re-suspending the notified substance in phosphate buffer solution.

We describe with more detail in Appendix 5 how we determined the LOD of methanol with the verified method and how we measured the amount of methanol in the notified substance.

For the validation of the in-house method used to determine the contents of methanol and formaldehyde, CVM recommended that the notifier provide the equations used to compute the results, a method validation summary, and a summary of standard calibration results. The validation summary should demonstrate performance characteristics such as precision, accuracy, sensitivity, selectivity, limit of detection, limit of quantitation, linearity, range, and ruggedness to ensure that results are meaningful and appropriate to make a decision. The method validation should address the completeness of the extraction of methanol from the notified substance.

KnipBio has developed an in-house method for the analysis of methanol and formaldehyde content, that has been adapted from the published method of Anthon and Barrett (2004) (Anthon, Barrett and Arrett, 2004). As shown in Appendix 5, this method has been verified against the published method, using the criteria of “Guidelines for the Validation of Chemical Methods for the FDA FVM Program.” 2nd edition. April 2015. US Food & Drug Administration, Office of Foods and Veterinary Medicine. The following is a summary of the experiments that have been carried out: please see Appendix 5 for more detail.

We sought to test the amounts of formaldehyde and methanol in spray dried batches of biomass by using a colorimetric method commonly used for quantifying methanol in aqueous solutions (Anthon, Barrett and Arrett, 2004). The same method is used for both analytes, with one added step used in the methanol assay. To test for methanol, an alcohol oxidase from Pichia pastoris is first used to convert methanol to formaldehyde prior to adding the Nash reagent. The Nash reagent is a mixture of acetylacetone and ammonia which reacts specifically with formaldehyde to produce a chromophore that can be detected with absorbance or fluorescence. To test for formaldehyde, samples are simply mixed with the Nash reagent without the enzymatic pretreatment.
Formaldehyde and methanol are not expected to be in high concentrations at the end of methanol fermentation of *Methylobacterium extorquens* due to the residual enzyme activities from multiple methanol oxidases and formate activating enzyme ([Marx et al., 2003];[Chistoserdova et al., 2003];[Ochsn et al., 2014]). Furthermore, any residual formaldehyde is expected to react with proteins, lipids, and other compounds in the biomass. Methanol which is much more volatile than water (vapor pressure 13.02 kPa vs 2.34 kPa at 20 °C), would be expected to evaporate during spray drying, drum drying, or lyophilization.

In Appendix 5, we describe several experiments in which we adapt and verify the Anthon and Barrett method to measure methanol and formaldehyde in dried cellular biomass.

| (1) | To extract any cellular methanol or formaldehyde in the dried biomass, we resuspend the biomass in dilute phosphate buffered saline (PBS) and subject the cellular material to freeze thaw cycles that is frequently used to lyse bacterial cells. |
| (2) | To ensure that all methanol or formaldehyde could be detected, we spiked samples with known amounts of methanol or formaldehyde. |
| (3) | To test for specificity of the methanol signal, we extracted methanol from cells grown in absence or presence of methanol. |
| (4) | To test for lower amounts of methanol or formaldehyde, we include higher amounts of the sample in the reaction relative to the standards. |

**Summary of the verification of the method used to detect methanol**

| (1) | We established the linearity of a standard methanol curve with concentration of methanol between (v/v) (r²>0.99). (Experiment 1 in Section 3 of Appendix 5). |
| (2) | Specificity was validated with cell samples grown in absence of methanol (no detectable methanol in the cell pellet or supernatant of the cultures). Taking into account the dilution factors, we show that the methanol detected is specific in spray dried samples when spiked in at 0.05 and 0.005%. Experiment 2 in Section 4 of Appendix 5). |
| (3) | Method accuracy within 10% was established by spiking known amounts of methanol into the measured samples. Experiment 2 in Section 4 of Appendix 5). |
| (4) | Full extraction of the methanol was verified by recovering and measuring known spiked amounts of methanol. The spiked samples, which confirmed that all methanol has been properly extracted and accounted for, had measured values that were on average 5.6% of the expected values. Experiment 3 in Section 5 of Appendix 5). |
| (5) | We determined the limit of methanol detection by increasing sample volumes relative to standards: it is possible to detect methanol as low as 0.002475 % (w/v)). Experiment 1 in Section 3 of Appendix 5). |
| (6) | Based on the data in Appendix 5, the levels of methanol measured in 3 different batches of fermentation) are summarized in the table below. |
Table 8. Assayed levels of methanol in 3 batches of the notified substance.

<table>
<thead>
<tr>
<th>Sample</th>
<th>mg/mL cell susp.</th>
<th>% MeOH (w/v)</th>
</tr>
</thead>
<tbody>
<tr>
<td>P1 (June 2015 sample)</td>
<td>(b) (4)</td>
<td></td>
</tr>
<tr>
<td>P2 (May 2016 sample)</td>
<td></td>
<td>(b) (4)</td>
</tr>
<tr>
<td>P3 (October 2016 sample)</td>
<td></td>
<td>(b) (4)</td>
</tr>
</tbody>
</table>

Summary of verification of the formaldehyde detection method

As described in more detail in Experiment 4 in Section 6 of Appendix 5, the method used has acceptable linearity when using formaldehyde standards of 0.001 to 0.05% (w/v). When linearity is below our acceptance criteria of $r^2 < 0.99$, it is usually due to a pipetting error. Samples outside the acceptable linear range, such as those giving values above 0.05% (w/v) or below 0.001% (w/v) are discarded.

As in the Methanol assay, the amount of formaldehyde measured can be lowered by using more sample than standard. When tested between 0.00004% (w/v) and 0.0001% (w/v) linearity was an acceptable $r^2 > 0.9918$.

None of the extractions from the powders had any response even when sample were 25 times greater than the formaldehyde standard (50μL sample volume).

Target Animal Safety:

1. CVM noted that for certain contaminants/fermentation end products, the notifier cites regulations in the Code of Federal Regulations as demonstrating that the amounts in the biomass do not raise safety concerns. However, these regulations are for specific uses of these substances and/or their contaminants and thus, a simple citation of the regulation is not sufficient; there should be consideration of target species. CVM suggested use of exposure calculations with reference to species and the appropriate scientific literature to support the lack of safety concerns. In addition, when addressing target animal safety, stating and relying on actual animal exposure is preferable to reliance on percent replacement of another dietary ingredient.

The maximum level of methanol in the notified substance is 0.004% (w/v). In 20mg/mL dried biomass no formaldehyde above the LOD could be detected. At a 10% maximum inclusion volume in the final animal feed, the levels would be as indicated in Table 9 below:
Table 9. Maximum levels of methanol and formaldehyde in the notified substance.

<table>
<thead>
<tr>
<th></th>
<th>Maximum amount in KBM (% w/v)</th>
<th>Maximum amount in feed using 10% KBM (Calculated level: % w/v)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methanol</td>
<td>0.004</td>
<td>0.0004</td>
</tr>
<tr>
<td>Formaldehyde</td>
<td>&lt;0.00004</td>
<td>&lt;0.000004</td>
</tr>
</tbody>
</table>

LOD methanol: (b) (4) (w/v)

LOD formaldehyde: (b) (4) (w/v)

The levels of Methanol and Formaldehyde present in the notified substance are insignificant and not a safety concern.

With regard to formaldehyde, as an example, the product Formalin (a 37% solution of formaldehyde containing up to 15% methanol) has been approved by the FDA to control parasites in fin fish and shrimp hatcheries at levels up to 250ppm (0.0005% w/v) in the water (21 CFR 529.1030). As such, a safety assessment has been completed to permit these levels in the water for a short time.

In addition, a paper from 1997 (Tisler and ZagorcKoncan, 1997) found the 48h LC90 to be 87.0 mg/L (87 ppm) in water for juvenile rainbow trout (Oncorhynchus mykiss) which is ~87.0 ppm (0.015% w/v).

As described in the Narrative in KnipBio’s original submission, formaldehyde levels were determined in three 1500L batches of the dried notified substance. Although the sample was concentrated 20X, formaldehyde could not be detected, based on the extrapolation of a standard curve established with known amounts of formaldehyde.

FDA has reviewed the safety of the use of a formaldehyde solution as a Salmonella control agent in animal feeds (all animal feeds) at a level of 5.4 pounds/ton of feed (0.27%) (see 21 CFR 573.460(b)(1)). Based on the fact that this formaldehyde solution contains only 37% formaldehyde, this is an effective level of 0.1% formaldehyde compound in feed (or 1000 ppm in feed).

In the finished commercial product KnipBio will specify on the label of the notified substance either that the levels of formaldehyde in the product are guaranteed to be below 0.00004% w/v (as currently measured) or that the levels of formaldehyde are in compliance with 21 CFR 573.460.

With regard to methanol, a literature search suggests that methanol has low toxicity to aquatic organisms as indicated on the Safety Data Sheet (SDS) below.
A recent research article from Kaviraj et al. (Kaviraj, Bhunia and Saha, 2004) studied the toxicity of methanol in Tilapia and no significant difference in growth parameters could be observed in their 90-day chronic toxicity bioassay for a methanol concentration < 23.75 ppm (0.0000475 % w/v).

One can also note that the notified substance does not contain toxic heavy metals. As a comparison, the table below compares the notified substance with fish meal, one of the most important source of protein in aquaculture feed.

Table 10. Comparison of heavy metal levels in fishmeal and notified substance.

<table>
<thead>
<tr>
<th></th>
<th>Fishmeal*</th>
<th>Notified substance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Selenium ppm</td>
<td>2-5</td>
<td>&lt; 0.1</td>
</tr>
<tr>
<td>Arsenic ppm</td>
<td>10</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Lead ppm</td>
<td>10</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Mercury ppm</td>
<td>0.5</td>
<td>&lt; 0.05</td>
</tr>
</tbody>
</table>

*(Adamse, Van der Fels-Klerx and de Jong, 2017)

2. CVM indicated that the notifier did not address the potential for spillover effects resulting from the genetic engineering of the microbial strain in the notice. Data, such as the spectral analyses, fermentation end product analyses, and other information, may be able to address this point, i.e., that the deleted genetic material was not expressed in the parent strain and thus, there are no metabolic differences between the parent and engineered strains.
There is no reason to believe that the limited genetic modifications KnipBio made to the parental strain had any spillover effects. As reported in the original GRAS Notice, KnipBio performed whole-genome sequencing of the production strain, and a comparison to the parental strain showed that there was no unexpected genetic rearrangement after the genetic manipulations performed in addition, as described above, KnipBio demonstrated that therefore suggesting that did not result in spillover effect. Finally, KnipBio has been using and growing strain KB203 in its laboratories and in fermentors for more than 4 years and has never identified or noticed any adverse traits, certainly none that would affect the safety of the notified substance.

3. CVM noted that the bioengineered organism may be viable when present in animal feed products. The notifier should clarify why the presence of these viable bioengineered cells is not a concern. Potential avenues would be to indicate that labeling will include processing instructions to address viability or again, to compare the engineered strain to its parent and explain how viability is not a concern.

Although there is a possibility that there may be some viable cells in the KBM product, the downstream processing and pelletization will include high-temperature extrusion (process in which the mixed feed ingredients are cooked under high temperature (usually >100°C), moisture and high pressure within a short time) which will further decrease the number of these viable cells to approximately zero. Extrusion is a process in which the mixed feed ingredients are cooked under high temperature (usually >100°C), moisture and high pressure within a short time. In every test we have conducted to measure CFU formation using standard plate assays, we have found this process to be highly effective in eliminating viability. We have tested feed manufactured for shrimp and trout feeding trials and have not been able to recover any Methylobacterium microorganisms from these feeds, therefore KnipBio strongly believes that the notified substance will be depleted of live Methylobacterium.

We do not believe the engineered version of the strain has a competitive advantage as compared to the wild type in any way. Specifically, by eliminating the microbe’s ability to produce bacterial cellulose, fermentations benefit from more thorough mixing and significantly less clumping. However, in nature, bacteria prefer to attach themselves to a surface in many cases. The engineered strain has a significantly lower ability to attach because of this modification and therefore would be expected to be outcompeted in a theoretical head-head match-up.

Additionally, we accept CVM’s recommendation to include a requirement for pelleting the final feed in the directions for use of the final commercial product.
4. CVM reported that the Hardy et al. reference became publicly available in April 2018. The final, published paper should be included in any amendment.


5. The published article authored by Tlusty et al. is considered pivotal for target animal safety. The Tlusty article has inconsistencies/omissions within the section reporting the salmon study, such as actual biomass inclusion rate, test diet composition, references to tables, etc. Given this, the notifier should explain how it can be concluded that the studies in grunt and shrimp were adequate, well-controlled, and thus, suitable to support its conclusion.

The studies discussed in the Tlusty article were independently conducted. The salmon study was restricted to a digestibility study and did not include a growth study. Diets and techniques used in the salmon digestibility study were described in Table 2 of the Tlusty paper and are based on the standard method described (Gaylord et al., 2009). The experimental design of the salmon digestibility study included a 70%-30% diet with chromic oxide used as an inert marker. Experimental diet formulations were consistent with the experimental design in which two experimental diets were used: 1) the control diet and 2) the diets containing 70% control feed and 30% KBM. This is discussed on page 8 of the Tlusty paper (Digestibility of KBM using Atlantic salmon). Table 5 of the Tlusty paper provides the protein digestibility measurements as assessed by the formulas provided on page 9 of the paper. The study demonstrated that there was no significant difference between diet digestibility, protein digestibility or individual amino acid digestibility between the control diet and the diet containing 30% KBM. KnipBio has not discerned the concerns CVM has expressed regarding the quality of the reporting of the salmon study in the Tlusty paper, and wish to discuss this further if CVM continues to have concerns.

The shrimp diets in the growth studies sought to replace 50% and 100% of fishmeal (FM) of a diet considered to be commercially relevant and are described as % FM. These percentages correlate to an inclusion rate of 6.3% and 12.6% respectively. The diet formulation description is found in Table 1 of the Tlusty paper, which describes the inclusion rate as (g kg$^{-1}$).

Grunt diets are described similarly to the shrimp diets (g kg$^{-1}$) and are found in Table 3 of the Tlusty paper. The two experimental diets were 5% and 25% respectively and while there was a numeric increase in growth for grunts fed KBM at the higher inclusion rate, it is not considered statistically significant.

It may be that the difference in the way the Tlusty paper reported the inclusion rate is confusing, but we have full confidence that the studies were well-controlled and suitably designed and conducted in the aquaculture studies. All these trials were conducted by aquaculturists skilled in the science of animal husbandry, aquatic biology and mechanisms were in place to comply with IACUC standards. State of the art facilities at Roger Williams University and USDA-ARS were employed to conduct these trials. Tanks
were randomized appropriately, and diets were fed strictly according to protocol. The studies meet the requirement of an adequate and well-controlled experiment.

6. The proposed NOEL for shrimp, based on the pivotal Tlusty article, is contradicted by the data/information present in the article. Data within the Tlusty article may support a use rate for KBM of 6%. It was discussed that shrimp growth was consistently decreased at higher inclusion rates for the biomass. The notifier stated that the shrimp diet used in the Tlusty study may have encountered a formulation error. CVM commented that if the diet was not formulated correctly, it may call into question the suitability of the study to support safety in shrimp. The notifier will consider how the proposed use rate could be supported with other data and information, potentially corroborative unpublished information.

We note that the thrust of our safety and utility argument is based on the comparison of the composition of Methylobacterium extorquens biomass with conventional feed ingredients and feeds and is based on the compositional analysis. This is a typical approach for major ingredients in the diet. We are corroborating this assessment with live animal studies. Some of this corroborating data is found in the published paper (Tlusty et al., 2017). However, in Appendix 2-11 and Table 2-8 of the original GRAS Notice, KnipBio provided a number of additional studies that can be used to corroborate the safety and utility of the biomass as a protein source.

CVM has specially questioned the support of the Tlusty article for the use of use of up to 10% of the diet with the M. extorquens biomass in shrimp diets. As you note, this paper reported that the shrimp on the high KBM diet (12.6% KBM) had a decreased growth rate; but an increase in feed conversion ratio, indicating that there was not an issue with availability of the nutrition of the M. extorquens biomass diet was observed. The Tlusty paper reported that air bubbles were seen in the pellets prepared for the shrimp diet SHR-KH (100% KBM replacement, which corresponds to a 12.6% inclusion for the total diet) and therefore the pellets likely did not properly sink in the water column while the other two diets (control and 6.3% inclusion) did. Shrimp are bottom feeders and it is very likely that the shrimp that were fed the high inclusion biomass received fewer available pellets in the water column, which may account for the reduced weight gain and SGR.

However, other adequate and well-controlled studies have corroborated the safety and availability of the notified substance for Pacific White Shrimp. In another recently completed study (Appendix 7) the notified substance KBM was fed at 0, 6, 13.3 and 26.6 % of the feed. The study included a growth trial (using the four identified diets) and demonstrated no difference in growth between the 13.3% inclusion and the control group when expressed as biomass, mean weight, weight gain or feed conversion ratio.

Table 2-8 in the submitted GRAS Notice and the companion Appendix 2-11, as well as the published Tlusty study clearly demonstrated that the notified substance is an available and safe protein source when fed at levels up to 10% of the feed. The safety is corroborated by the University of Auburn growth study (2016—see GRAS Notice appendix 2-11) as well as another digestibility study from University of Auburn (2016—see appendix 2-11) at levels up to 12% of the diet.
Based on the totality of the data, the composition of the biomass, the published study, and the corroborative studies there is ample evidence to demonstrate that use of the notified substance at levels up to 10% in shrimp diets is safe.

7. CVM also noted that the European Food Safety Authority’s (EFSA) Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) published two scientific opinions in July, 2017: the publications were subsequently revised to include another author. In their publications, the FEEDAP expressed concerns about the safety of *Escherichia coli* and other gram negative bacterial biomasses intended to be fed to food producing animals. The notifier should explain how the information and conclusions within the FEEDAP documents impact their determination that the proposed use of the notified substance is GRAS. The publications are:


KnipBio thanks FDA for bringing these publications to our attention. We first note that these two publications (“the FEEDAP documents”) are largely positive statements that certain strains of modified *E. coli* can be safely used in the European Union to produce a substance for use in animal feed. Although these documents expressed some uncertainties, there were few or no assertions that the *E. coli* biomass would have adverse effects on animals, or on humans ingesting products derived from such animals. Indeed, the panel’s conclusions in both the FEEDAP documents included the statement “*The recipient strain *E. coli* K-12S B-7 is considered to be safe.*” (emphasis added)

We further note that the FEEDAP documents produce absolutely no evidence to implicate gram-negative organisms other *E. coli* as having any adverse effects – the documents merely assert that products derived from other gram-negative microorganisms may pose similar issues as those considered in the FEEDAP documents, without providing any specifics or rationale in support of such assertions, much less the citation of any literature supporting the assertions.

Although KnipBio respectively contends that the FEEDAP documents do not add any tangible evidence or scientific arguments that are relevant to the safety assessment of the notified substance, we offer the following additional comments to distinguish any plausible concerns raised in the FEEDAP documents from the present safety assessment.

There are biological, physiological and taxonomic differences between *E. coli* and the species used to produce the notified substance, *M. extorquens*. There is no evidence that *M. extorquens* produces harmful endotoxins, lipopolysaccharides (LPS), or any other substance identical or similar to such
substances that are produced by some strains of *E. coli* or other Gram-negative microorganisms that are known to be pathogens. In fact, as KnipBio exhaustively set forth in the Narrative section of the original GRAS Notice, there is no evidence in the literature which implicates *M. extorquens* as having any pathogenic, toxic or other negative characteristics.

Gram-negative microorganisms are used as fish feed or to produce fish feed substances. For example, a species of *Methylococcus capsulatus* has been approved as a fish feed for use in the EU (product name: FeedKind). Although this species does not use methanol as a carbon source, it uses methane (which is converted to methanol by a methane monoxygenase enzyme with high requirement in copper). Another Gram negative alphaproteobacterium species used for aquaculture is *Rhodopseudomonas palustris* (Kim and Lee, 2000). Please also refer to a recently-published review article (Gamboa-Delgado and Márquez-Reyes, 2018) that summarizes the safe use of a variety of microbial species for aquaculture feed.

KnipBio believes that the conclusions of this literature review in the original GRAS Notice are more than sufficient to rebut the unspecific, hypothetical concerns expressed in the FEEDAP documents regarding hypothetical risks of unspecified Gram-negative species.

KnipBio would like to briefly address several specific comments in the FEEDAP documents pertaining to these hypothetical concerns. On page 9 of Document 2017.4935, EFSA says:

> The traits introduced [into the strain of *E. coli*] are well known and do not raise safety concern.

KnipBio’s production organism has no added traits — only gene deletions.

Also on page 9 of Document 2017.4935, EFSA says:

> Southern or PCR analysis confirmed the absence of all full-length antibiotic resistance genes used during the entire genetic modification.

KnipBio has confirmed through whole-genome sequencing of the production organism that there is no antibiotic resistance gene present in the production organism. Similarly, this whole-genome sequencing showed that there was no unexpected genetic rearrangement after the genetic manipulations performed. Sequences of the regions of interest (celA and *crtCDF*) were included in Appendix 2-2 of the original GRAS Notice. KnipBio performed a BLAST search of the *M. extorquens* genome sequence against the Comprehensive Antibiotic Resistance Database (https://card.mcmaster.ca/) and did not find any hits (data can be provided on request).

On page 9 of Document 2017.4935, EFSA says:

> Although we reference only the 2017.4935 document, there are similar or identical statements in the 2017.4936 document as well.
Bioinformatic analysis did not show any biologically relevant similarity to known allergens or toxins for any of the putative peptides that might be produced from the open reading frames ...

KnipBio performed a BLAST analysis of the entire *M. extorquens* genome against the database of toxins, and the results of that analysis were included in Appendix 2-2 of the original GRAS Notice. The *M. extorquens* genome has no homology to any known toxins. The question of similarity to allergens is of lower importance when fish are the target species. In addition, KnipBio has not introduced any heterologous open reading frames into the production organism, so there would not be expected to be any impact of the genetic engineering that might have introduced sequences coding allergens or toxins.

Finally, we note that also on page 9 of Document 2017.4935, EFSA makes the following comment which, contrary to the implication of the passages cited by CVM in the Meeting Minutes, is a confirmation that in spite of the hypothetical concerns, EFSA concluded that the *E. coli* strain in question could be used to produce an animal feed ingredient:

Therefore, the product PL73 (TM), obtained from *E. coli* BP-10942, does not give rise to any safety concern with regard to the genetically modified strain from which it is made.

In conclusion, KnipBio maintains that there is nothing in the FEEDAP documents that implicates *M. extorquens* or any other specific gram-negative organism as being inherently hazardous or unsuited for use in production of animal feed ingredients, other than mere speculation. The FEEDAP documents make no assertions of lack of safety, nor do they remotely point to any specific features of any microorganism that might raise concerns. The documents merely call for such feed materials to be “assessed for safety”, and that is exactly the process which FDA is currently undertaking, using the data and literature evidence presented by KnipBio.

*Molecular biology:*

*CVM indicated the notice states on page 8 that the spirilloxanthin pathway was deleted as described in published U.S. patent application US 14/454,816 (Feinberg and Marx, 2015), whereas on page 40 the patent is described as U.S. patent application 20150044327A1. The notifier should provide a copy of the patent.*

A copy of this patent application is attached as Appendix 8. By way of clarification, 20150044327A1 is the Publication Number of this pending patent application, and USSN 14/454,816 is the Serial Number of this application. Thus, both numbers describe the same patent application. KnipBio regrets any confusion this differing nomenclature may have caused.
Thank you very much for the opportunity to address these questions. Please contact the under-signed if there are any additional questions we can address.

Sincerely,

Larry Feinberg
CEO

List of Appendices

Appendix 1. Spirilloxanthin methods and analysis (Confidential).

Appendix 2. Information about anti-foaming agent.

Appendix 3. ETA Letter re anti-foaming agent.

Appendix 4. Verification of PHB Assay (Confidential).

Appendix 5. Verification of Methanol and Formaldehyde Assay (Confidential).

Appendix 6. Copy of Hardy et al. paper.

Appendix 7. Corroborative shrimp data-FDA.

References:


ATTN: Dr Carlacci
Center for Veterinary Medicine
Division of Animal Feeds
7519 Standish Place HFV220
Rockville MD 20855

8/9/18

Dear Dr Carlacci and team,

Please find enclosed KnipBio’s Amendment to the GRAS notification AGRN26 including a copy of the appendices & references on this enclosed CD.

Thank you,

Larry Feinberg
CEO
KnipBio INC
110 Canal Street
Lowell MA 01852
Chelsea please file this amendment for submission M000059
Thank you.
Lou

Louis Carlacci, Ph.D.
Chemist
Ingredient Safety Team (HFV-224)
Division of Animal Feeds
Center for Veterinary Medicine
Ph 240-402-2921

Dear Dr Wong and Carlacci,

please find enclosed KnipBio's response to the question raised about the amendment to GRAS notice AGRN 26.
We are also attaching a revised Appendix 5 as well as a copy of 2 new references that were used in our response.
We would like to thank the committee for their thorough review of our submission.

Please let us know should you have any question.

Sincerely,

KnipBio

--

Catherine J. Pujol-Baxley, PhD
VP of R&D
Louis Carlassi, Ph.D.
Chemist
Ingredient Safety Team (HFV-224)
Division of Animal Feeds
Center for Veterinary Medicine
Ph 240-402-2921

From: Kristi Smedley <smedley@cfr-services.com>
Sent: Tuesday, October 02, 2018 1:29 PM
To: Carlassi, Louis <Louis.Carlassi@fda.hhs.gov>; 'Catherine Pujol-Baxley' <cpb@knipbio.com>
Cc: Wong, Geoffrey K <Geoffrey.Wong@fda.hhs.gov>; 'Larry Feinberg' <lfeinberg@knipbio.com>
Subject: RE: KnipBio Amendment AGRN 26

Lou:

Thank you for your call. You requested clarification on page 4, second paragraph (last sentence). That sentence you cited included two typos, and was intended to state “We have corrected the specification in Table 3 above to say that there is less than 0.3 mg methanol per gram of biomass.”

The changes are in red (above)

We apologize for the oversight on our part. We have supported the safety specification specific to 0.3 mg methanol/gram of biomass (as provided in Table 3 on page 3).

Kristi O. Smedley, Ph.D.
Center for Regulatory Services, Inc.
5200 Wolf Run Shoals Rd.
Woodbridge, VA 22192

Ph. 703-590-7337
Cell (b) (6)...
Fax 703-580-8637
Hi Kristi.
Based on our phone conversation this morning, would you respond to this email with the notifier’s clarification. In the amendment dated September 27, 2018, the pdf file named 180927 FDA Amendment Final on page 4 of 9 states that the notifier has “corrected the specification in Table 9 above to say that there is less than 0.2 mg methanol per gram of biomass.” However, this pdf file does not contain a Table 9 and the acceptance criterion established for methanol content in the provided specification (Table 3 page 3) is 0.300mg/gm.

Please do not send an updated file. Just provide the clarification in an email. I will delete the emails you sent this morning to clarify the issue.

Thank you.

Lou

Louis Carlacci, Ph.D.
Chemist
Ingredient Safety Team (HFV-224)
Division of Animal Feeds
Center for Veterinary Medicine
Ph 240-402-2921
September 27, 2018

Louis Carlacci, Ph.D.
Chemist, Ingredient Safety Team
Division of Animal Feeds
Center for Veterinary Medicine
U.S. Food and Drug Administration
7519 Standish Place
Rockville, MD 20855

RE: GRAS Notice No. AGRN 26

Dear Dr. Carlacci:

KnipBio, Inc., would like to thank you and your colleagues at CVM for the efficient conference call on September 18, 2018 regarding the amendment to GRAS Notice AGRN 26 and your request for response. We have received the meeting minutes for the call and have written our response to the issues raised below. In the remainder of this letter, CVM’s comments and questions are shown in bold italics, followed by KnipBio’s response. In some cases, revisions or differences from previously-submitted information are highlighted in yellow.

Background

The substance is Methylobacterium extorquens protein (or KBM) derived from genetically engineered Methylobacterium extorquens strain KB203 through fermentation and spray drying the biomass. This notice was filed February 7, 2018. FDA received an amendment dated August 9, 2018. The notice informs the FDA of KnipBio’s view that Methylobacterium extorquens protein is GRAS through scientific procedures when used as a protein source in food for aquaculture species and when used at an intended use rate of up to 10% of the diet. The substance is intended to replace soybean or fish meal in the aquaculture diet. Minutes CVM indicated that we are interested in clarification on the data and information contained in the amendment dated August 9, 2018. We indicated that we believe that these can be addressed by the notifier in an additional amendment to the notice. The chemistry, manufacturing, and controls and target animal safety sections of the notice will need to be addressed in the amendment.

Chemistry, Manufacturing and Controls:

1. We note that the notice currently states that the lead content is ‘<0.05[ppm]’ but that a release specification does not include a test for lead. We recommend that a test for lead be included in the specification. If your firm concludes that a specification test for lead is appropriate, please provide a complete specification for the notified substance that includes the test for lead, acceptance criteria, and the AOAC method used for testing. Given the current finding of <0.05ppm lead, we recommend less than 0.05ppm lead. Given that a) methanol is the carbon source used for growth of
Methylobacterium extorquens strain KB203, b) the specification for methanol (contained in Table 1 in the amendment dated August 9, 2018) has the lead content at no more than 1 ppm. c) in the description of the source methanol contained in Table 2, the actual content of heavy metals as lead is 0.200 ppm, and d) the measured lead content in the notified substance is less than 0.05 ppm (which is the method detection limit), it is not clear from the description of the manufacture where the accumulated lead is separated from the manufactured substance and how this is controlled. Thus, we recommend a specification for the notified substance that includes a specification test for lead.

KnipBio provides the following response, to replace or supplement the response to FDA's question #3 in the August 9, 2018 Amendment.

The following Table shows the analysis of heavy metals in 3 batches of the notified substance, as performed by (b) (4) The column in the Table entitled "Methods" indicates the methods used by NJFL, identified by their AOAC reference numbers (http://www.aoac.org/).

Table 4 from the August 9, 2018 amendment. Heavy metal analysis in three batches of the notified substance.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Arsenic ppm</td>
<td>AOAC 990.08</td>
<td>(b) (4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lead ppm</td>
<td>AOAC 990.08</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mercury ppm</td>
<td>NJFL MERC.001</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cadmium</td>
<td>AOAC 967.61</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

As a quality control (QC) measure, KnipBio will determine at regular intervals (as determined necessary for assuring safety) that the amount of heavy metals (as lead) in each manufactured batch is below 0.05 ppm, using the AOAC method above.

Expressing the amount of methanol in mg/g of biomass, a revised Specification of the notified substance is shown in Edited Table 3 of the August 9, 2018 AGRN amendment.
Edited Table 3: Specification of the notified substance

<table>
<thead>
<tr>
<th></th>
<th>Method</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moisture %</td>
<td>AOAC 930.15</td>
<td>&lt;7</td>
</tr>
<tr>
<td>Protein (crude) %</td>
<td>AOAC 990.03</td>
<td>&gt;50</td>
</tr>
<tr>
<td>PHB %</td>
<td>Adapted from Karr et al. (1983)</td>
<td>&lt; 25</td>
</tr>
<tr>
<td>Methanol (mg/g)</td>
<td>Adapted from Anthon et al. (2004)</td>
<td>&lt;0.3</td>
</tr>
<tr>
<td>Lead ppm</td>
<td>AOAC 990.08</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Total coliform (cfu/g)</td>
<td>MFHPB-34</td>
<td>&lt;5</td>
</tr>
<tr>
<td>Appearance (color)</td>
<td></td>
<td>Light pink to reddish color</td>
</tr>
<tr>
<td>Appearance (form)</td>
<td></td>
<td>Fine powder</td>
</tr>
</tbody>
</table>

2. Please clarify the interpretation of the methanol testing data in the amendment dated August 9, 2018. In Tables 3 and 7 on pages 4 and 8 (and other locations) in pdf file Appendix 5, the units for methanol content is reported as "% (w/v)." However, the content units are actually mg/ml, which is verified by multiplying the methanol content as % w/v by 792mg/ml (density of methanol) and dividing by 100%. As a result, the maximum methanol content in the notified substance as reported in Table 7 (and in the specification) is 0.00396mg/ml and not 0.00396% (w/v). In addition, the linearity higher limit in Table 3 is incorrectly stated. It should be 0.025%v/v. Please verify the following calculation to determine the methanol content in units of milligrams methanol per milligrams of the notified substance (which is the form requested in the specification). The sample solutions used in testing were derived from sonication of a solution containing 20mg dry cell biomass per milliliter of solution and separation of the supernatant. The sample solution is diluted to give the test solution. According to Table 7 on page 8, the maximum possible methanol content in the sample solution is 0.0005%v/v or 0.00396mg methanol per milliliter sample solution. The amount of methanol in the dried biomass is 0.020% (w/v) (or (100% × 0.00396mg/ml) / (20mg biomass/ml)). Note, the notice states that there is less than 0.00125% MeOH (0.01mg/mL) in the notified substance. We recommend the specification acceptance criterion for methanol content in terms of mg methanol per mg dried biomass (or corresponding percentage or ppm).

The following is KnipBio’s response:

KnipBio would like to thank Dr Caracci and the committee for detecting the unit inconsistencies and the edits to capture these changes are highlighted below as well as in the Revised Appendix 5 attached with this letter.


Methanol is not expected to be in high concentrations at the end of methanol fermentation of *Methylobacterium extorquens* due to the residual enzyme activities from multiple methanol oxidases and formate activating enzyme. Moreover, methanol which is much more volatile than water (vapor pressure 13.02 kPa vs 2.34 kPa at 20 °C), would be expected to evaporate during spray drying, drum drying, or lyophilization.
The extracted methanol was detected in volume percent (% v/v). Using the density of methanol (0.792 g/mL), volume percent was converted to mg per mL methanol. To determine the mg methanol per gram biomass, the mg/mL methanol value was divided by the mg/mL of the suspended biomass that was extracted and the number was multiplied by 1000.

Based on these calculations, we edited the tables from Appendix 5 of Amendment AGRN 26 (A revised version of Appendix 5 is attached at the end of this letter). Edits are highlighted below. More specifically, we have corrected the issues of units in Tables 3, 5, and 7, and also added the calculated mg methanol per gram of biomass. We have also clarified the units in the text and the table columns throughout Appendix 5. We have corrected the specification in Table 9 above to say that there is less than 0.2 mg methanol per gram of biomass.

The “linearity higher limit” in Table 3 is 0.25% v/v as was described in the text. Table 1 in Appendix 5 had an error and has been corrected to reflect that the standard range used in experiments was 0.005% to 0.25% (v/v) methanol.

The edited Table 3 from Appendix 5 of the August 9, 2018 amendment below summarizes the Linearity and LOD of the methanol measurement in the standard assay.

**Edited Table 3. Linearity and LOD summary.**

<table>
<thead>
<tr>
<th>MW Methanol: 32.04 g/mol</th>
<th>% (v/v)</th>
<th>mM</th>
<th>% (w/v)</th>
<th>mg/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Linearity lower limit</td>
<td>0.005</td>
<td>1.23</td>
<td>0.00396</td>
<td>0.0396</td>
</tr>
<tr>
<td>Linearity higher limit</td>
<td>0.25</td>
<td>61.74</td>
<td>0.198</td>
<td>1.98</td>
</tr>
<tr>
<td>Limit of detection</td>
<td>0.0003125</td>
<td>0.077</td>
<td>0.0002475</td>
<td>0.002475</td>
</tr>
</tbody>
</table>

**Edited Table 5. Maximum possible methanol possible in cell biomass from Experiment 2.**

<table>
<thead>
<tr>
<th>Sample</th>
<th>Feed</th>
<th>OD</th>
<th>DCW (mg)</th>
<th>(mg/mL) cell susp.</th>
<th>MeOH measured (v/v)</th>
<th>MeOH measured (mg/mL)</th>
<th>mg MeOH / g biomass</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Before</td>
<td>2.16</td>
<td>2.59</td>
<td>13.0</td>
<td>&lt; 0.00125</td>
<td>&lt; 0.0099</td>
<td>&lt; 0.76</td>
</tr>
<tr>
<td>1</td>
<td>After</td>
<td>3.96</td>
<td>4.75</td>
<td>23.8</td>
<td>&lt; 0.00125</td>
<td>&lt; 0.0099</td>
<td>&lt; 0.42</td>
</tr>
<tr>
<td>2</td>
<td>Before</td>
<td>3.18</td>
<td>3.82</td>
<td>19.1</td>
<td>&lt; 0.00125</td>
<td>&lt; 0.0099</td>
<td>&lt; 0.52</td>
</tr>
<tr>
<td>2</td>
<td>After</td>
<td>4.33</td>
<td>5.20</td>
<td>26.0</td>
<td>&lt; 0.00125</td>
<td>&lt; 0.0099</td>
<td>&lt; 0.38</td>
</tr>
</tbody>
</table>

The amount of methanol in 3 batches of spray dried biomass were measured:

1. Sample 1 – June 2015 run
2. Sample 2 – May 2016 run
3. Sample 3 – October 2016 run

All the samples had very low, but linear increases ($r^2$ > 0.8 to 0.98) in absorbance with increasing sample volume consistent with them having low amounts of methanol.
The amount of Methanol in spray dried powder samples is presented in Table 7. Conversion in mg methanol/g of biomass was done by using the standard methanol density of 0.792 g/mL.

**Edited Table 7: Maximum possible methanol possible in cell biomass.**

<table>
<thead>
<tr>
<th>Sample</th>
<th>mg/mL cell resuspension</th>
<th>MeOH measured (% v/v)</th>
<th>MeOH measured (mg/mL)</th>
<th>mg MeOH/g biomass</th>
</tr>
</thead>
<tbody>
<tr>
<td>P1 (June 2015 run)</td>
<td>20.0</td>
<td>0.00038</td>
<td>0.00301</td>
<td>0.15</td>
</tr>
<tr>
<td>P2 (May 2016 run)</td>
<td>20.0</td>
<td>&lt;0.0003125</td>
<td>&lt;0.002475</td>
<td>&lt;0.12</td>
</tr>
<tr>
<td>P3 (Oct. 2016 run)</td>
<td>20.0</td>
<td>0.00050</td>
<td>0.00396</td>
<td>0.20</td>
</tr>
</tbody>
</table>

**Target Animal Safety:**

1. **Within the amendment to your GRAS Notice, please clarify the target animal safety section (TAS) item 7 on pages 24 to 26 to better connect the different aspects of your safety argument. CVM notes, in specific, that the firm should delete any statements indicating that the agency is conducting a safety assessment of their notified substance. The TAS narrative should be revised to make the firm’s argument clear and comprehensive.**

KnipBio provides the following revised version of the section of the TAS found on pages 24-26 of the August 9, 2018 amendment:


We note that these two publications ("the FEEDAP documents") are largely positive statements about the safe use in the European Union of certain strains of modified E. coli to produce a substance for use in animal feed. Although these documents expressed some uncertainties, there were few or no assertions that the E. coli biomass would have adverse effects on animals, or on humans ingesting products derived from such animals. Indeed, the panel’s conclusions in both the FEEDAP documents included the statement "The recipient strain E. coli K-12S B-7 is considered to be safe." (emphasis added). The documents suggested that other Gram-negative bacterial biomass could not rely on the safety assessment for the E. coli K-12S B-7 and should undergo a safety assessment.

KnipBio has completed a safety assessment for the use of M. extorquens, a Gram-negative organism. We note that it does not share any of the potentially problematic traits of certain other gram-negative microorganisms.
In particular, there are biological, physiological and taxonomic differences between *E. coli* and *M. extorquens*. There is no evidence that *M. extorquens* produces harmful endotoxins, lipopolysaccharides (LPS), or any other substance identical or similar to such substances that are produced by some strains of *E. coli* or other Gram-negative microorganisms that are known to be pathogens. This assertion is based on the literature search as described in Part 6 of the original GRAS notification and details provided in the appendices to support section 6. This review covered several hundred of peer-reviewed literature characterizing the fundamental biology of this organism. It is KnipBio's position that we thoroughly established in the Narrative section of the original GRAS Notice that there is no evidence in the scientific literature implicating *M. extorquens* as having any pathogenic, toxic or other negative characteristics.

We would also like to highlight several features of *M. extorquens* that address certain comments in the FEEDAP documents. KnipBio has confirmed through whole-genome sequencing of the production organism that there is no antibiotic resistance gene present in the production organism. Similarly, this whole-genome sequencing showed that there was no unexpected genetic rearrangement after the genetic manipulations performed. Sequences of the regions of interest (celA and crtCDF) were included in Appendix 2-2 of the original GRAS Notice. KnipBio performed a BLAST search of the *M. extorquens* genome sequence against the Comprehensive Antibiotic Resistance Database (https://card.mcmaster.ca/) and did not find any hits (data can be provided on request).

Also, on page 9 of Document 2017.4935, the FEEDAP document expressed the importance of ascertaining that there were no putative peptides encoded by the microorganism that have similarity to allergens or toxins. KnipBio performed a BLAST analysis of the entire *M. extorquens* genome against the database of toxins, and the results of that analysis were included in Appendix 2-2 of the original GRAS Notice. The *M. extorquens* genome has no homology to any known toxins. The question of similarity to allergens is of lower importance when fish are the target species. In addition, KnipBio has not introduced any heterologous open reading frames into the production organism, so there would not be expected to be any impact of the genetic engineering that might have introduced sequences coding allergens or toxins.

Finally, we note that also on page 9 of Document 2017.4935, the FEEDAP document makes the following comment which we believe is a confirmation that in spite of the hypothetical concerns, EFSA concluded that the *E. coli* strain in question could be used to produce an animal feed ingredient:

> Therefore, the product PL73 (TM), obtained from *E. coli* BP-10942, does not give rise to any safety concern with regard to the genetically modified strain from which it is made.

Some Gram-negative microorganisms are used as fish feed or to produce fish feed substances. For example, a species of *Methyllococcus capsulatus* has been approved as a fish feed for use in the EU (product name: FeedKind). Although this species does not use methanol as a carbon source, it uses methane (which is converted to methanol by a methane monooxygenase enzyme with high requirement in copper). A recently-published review article (Gamboa-Delgado, J. and Márquez-Reyes, J. M. (2018) 'Potential of microbial-derived nutrients for aquaculture development', *Reviews in Aquaculture*, 10(1), pp. 224–246) summarizes the safe use of a variety of microbial species for aquaculture feed.
In conclusion, KnipBio maintains that they have assessed the safety of *M. extorquens*, a Gram-negative microorganism, as suggested by the FEEDAP document. Our review confirms the safety of *M. extorquens* for use in production of aquaculture feed ingredients. The documents merely call for such feed materials to be "assessed for safety", an assessment that has been conducted by KnipBio, and is a part of the notice being provided to FDA.

*We recommend that you consider the safety of methanol as a contaminant based on the manufacturing chemistry question raised on the expected higher maximum methanol content. You should present a clear discussion with data to support that higher maximum methanol content does not present a safety concern for your notified substance.*

The following are KnipBio’s responses:

The maximum level of methanol in the notified substance is 0.3 mg/g.

(It is important to note that although the specifications for methanol have been changed to be expressed as mg/gram of biomass, the overall level of methanol has not changed)

The following are revisions to those portions of the Target Animal Safety sections of the original GRAS Notice specific for methanol, as indicated.

Revision to PART 3 “Target Animal Exposure” of the original GRAS Notice, beginning on page 28.

*Concentration of methanol in the notified substance.* Although methanol is used as a feedstock in the fermentation of the microorganism comprising the notified substance, concentrations of methanol in the notified substances are expected to be extremely low, if detectable at all. As fermentation progresses, methanol in the growth media is converted to microbial biomass or otherwise metabolized and is therefore expected to be depleted in the natural course of the fermentation. Further, when collecting cells by centrifugation at the end of the run, it would be expected that any remaining methanol would primarily be retained in the supernatant rather than the cell pellet.

Methanol levels have been tested in preparations of the notified substance. Dried KBM from the three 1500L batches run was resuspended in a 20mg/mL 0.05X PBS and assayed for methanol according to the Nash Reagent Absorbance and Alcohol oxidase method (See Appendix 3-4). Based on the extrapolation of a standard curve established with known amounts of methanol, this assay potentially allows the detection of methanol in the samples at concentrations as low as 0.005% (v/v) or 0.04mg/ml. Since the samples were run at a 16X concentration compared to the standards, where the highest signal seen was equivalent to 0.0005% (v/v) or 0.004mg/ml, the highest amount of methanol detected in the samples was 0.2mg per gram biomass. KnipBio is confident there is less than 0.3 mg methanol/gram biomass or 300 ppm in the notified substance. Since KBM will constitute no more than 10% of the total feed, the total potential methanol concentration will be less than 0.03 mg methanol/gram feed (30 ppm) of the diet.

Methanol is a normal part of the diet as it is a component of fruits, vegetables and grains (EPA, 2013), and it is also a normal metabolite from food digestion. Based on various oral administration studies, EPA (EPA, 2013) determined that the NOAEL level was 500 mg/Kg bodyweight, based on subchronic studies
reviewed. Chronic studies exposing rats to methanol in drinking water (0-20,000 ppm) throughout their lifetime had no impact of viability. ("Overall, there was no pattern of compound-related clinical signs of toxicity, and the available data did not provide any indication that the control group was not concurrent with the treated group."). The review of these safety studies demonstrates that methanol is not toxic at levels found in potential methanol contaminated feed ingredients.

FDA’s past regulatory actions appear to agree with EPA’s overall safety assessment, that low levels of methanol in diet are not hazardous. Methanol contamination has been assessed in a number of products intended for animals. The most significant level of “contamination” is the use of methanol as a stabilizer in formalin (formaldehyde solution of 37%), in which methanol (USP, 2006) is generally added as a stabilizer at levels of 10-12%.

FDA has determined the safety of formalin as an animal drug for aquatic species and as a feed preservative in all feeds. 21 CFR 529.1030 permits the bathing of animals in concentrations of formalin at levels up to 2000 ul/l (which is equivalent to 200 ul methanol/liter) for brief periods of time. This level of methanol exposure is difficult to compare to feed specific methanol but suffice it to say the aquatic exposure for aquaculture species is magnitudes higher than a maximum level of 50 ppm in the complete feed.

21 CFR 573.460 covers the assessed level of formaldehyde in animal feed for various uses. The use as described in 21 CFR 573.460 (b)(1) is for maintaining feed Salmonella-negative. The permitted uses are for 2.5 Kg/ton of feed. Assuming that the formaldehyde product is stabilized by 10% methanol, this would be exposure of 0.25 Kg methanol/ton of feed or 0.025% methanol (250 ppm). This level of methanol contamination was permitted for all complete feeds for all animals.

Furthermore, according to a 2011 Position Paper from the UK Advisory Committee on Animal Feedingstuffs (UK Advisory Committee on Animal Feedingstuffs, 2011), citing (EFSA Panel on Contaminants in the Food Chain (CONTAM), 2010):

In December 2010, EFSA published an Opinion on the use of glycerine as a co-product from biodiesel production from Category 1 animal by-products (ABP) and vegetable oils. EFSA stated that inclusion rates of glycerol are usually up to 15% of the diet of ruminants and up to 10% in non-ruminant diets, with no adverse effects on animal health. It also found that residual amounts of methanol (up to 0.5%) and sodium (up to 1%) had no adverse effects on animal health. However, a maximum level of 0.2% methanol is proposed for the EU Catalogue of Feed Materials required under Regulation 767/2009, but we envisage that any MPLS should only apply to category 3 tallow.

KnipBio therefore expects that methanol levels in the notified substance, which each batch below the limit of detection in the assay described above, will be below the maximum allowed concentration of 0.3 mg methanol/gram of biomass. This level of contamination will not provide a hazard.
Revision to PART 6. Narrative, Section 5(c)(ii), second paragraph, of the original GRAS Notice, beginning on page 50.

ii) Other Potential Contaminants

* * * * *

As discussed above, the concentrations of methanol and formaldehyde, which might arise in the notified substance due to its method of manufacture, are expected to be no more than 0.03% (300 ppm) and 0.0025% (25 ppm) respectively. Both substances are therefore expected to be present at levels below the maximum allowed under applicable regulations: for example 21 CFR 573.460(b)(1) for formaldehyde and methanol, as discussed in Section 3(a)(3) above.

2. Intended Use: The firm should clarify the intended target animal species. CVM notes that in Part 1, the firm indicates the notified substance will be used in fish diets, but use in other animal species is discussed elsewhere in the notice including the target animal safety section. The firm should address these inconsistencies and revise the notice.

KnipBio appreciates the committee’s keen eye: in the review of Part 1 section 4, the intended use is in aquaculture feed.

Revision to Part 1(4) “Intended conditions of use of the notified substance” of the Original GRAS Notice

The substance will be used as a replacement or soybean or fish meal, to constitute up to 10% of the diet in aquaculture feed.

Thank you very much for the opportunity to address these questions. Please contact the under-signed if there are any additional questions we can address.

Sincerely,

Larry Feinberg
CEO

References:

USP, 2006. Formaldehyde Solution. Page 967
U.S. PHARMACOPEIA

Search USP29

Formaldehyde Solution
CH₃O  30.03

Formaldehyde.
Formaldehyde  [50-00-0].

» Formaldehyde Solution in bulk containers contains not less than 37.0 percent, by weight, of formaldehyde (CH₂O), with methanol added to prevent polymerization. Formaldehyde Solution in small containers (4 liters or less) contains not less than 36.5 percent, by weight, of formaldehyde (CH₂O), with methanol present to prevent polymerization.

Packaging and storage— Preserve in tight containers, and preferably store at a temperature not below 15º.

Labeling— The label of bulk containers of the Solution directs the drug repackager to demonstrate compliance with the USP Assay limit for formaldehyde of not less than 37.0%, by weight, immediately prior to repacking.

Identification—

A: Dilute 2 mL with 10 mL of water in a test tube, and add 1 mL of silver-ammonia-nitrate TS: metallic silver is produced either in the form of a finely divided, gray precipitate, or as a bright, metallic mirror on the sides of the test tube.

B: Add 2 drops to 5 mL of sulfuric acid in which about 20 mg of salicylic acid has been dissolved, and warm the liquid very gently; a permanent, deep-red color appears.

Acidity— Measure 20.0 mL into a flask containing 20 mL of water, add 2 drops of bromothymol blue TS, and titrate with 0.1 N sodium hydroxide VS: not more than 10.0 mL of 0.1 N sodium hydroxide is consumed.

Assay— Transfer about 3 mL of Solution to a tared flask containing 10 mL of water, insert the stopper in the flask tightly, and accurately determine the weight of the Solution taken. Slowly and quantitatively add a mixture of 50.0 mL of 1 N sodium hydroxide VS and 50 mL of hydrogen peroxide TS that has been previously neutralized to bromothymol blue TS with 1 N sodium hydroxide. Heat the contents of the flask cautiously on a steam bath for 15 minutes, shaking it occasionally with a rotary motion. Allow the mixture to cool, rinse the funnel and the inner wall of the flask with water, and after allowing it to stand for 30 minutes, add 2 to 5 drops of bromothymol blue TS, and titrate the excess alkali with 1 N sulfuric acid VS.

Perform a blank determination (see Residual Titrations under Titrimetry (541)). Also make a correction based upon the acidity found in the test for Acidity. Each mL of 1 N sodium hydroxide is equivalent to 30.03 mg of CH₂O.

Auxiliary Information— Staff Liaison: Tina S. Morris, Ph.D., Senior Scientist
Expert Committee: (BBV05) Biologics and Biotechnology - Vaccines and Virology
USP29—NF24 Page 967
Phone Number: 1-301-816-8397

http://www.pharmacopeia.cn/v29240/usp29nf24s0_m34300.html
Appendix 5
Amendment to AGRN 26 Revision

1. Background and Overall Summary

The purpose of the method is to test the amounts of methanol and formaldehyde in spray dried batches of biomass by adapting a colorimetric method commonly used for quantifying methanol in aqueous solutions that was published by Anthon and Barret (1). To test for methanol, an alcohol oxidase from Pichia pastoris is first used to convert methanol to formaldehyde prior to adding the Nash reagent (2). The Nash reagent is a mixture of acetylatedone and ammonia which reacts specifically with formaldehyde to produce a chromophore that can be detected with absorbance or fluorescence. To test for formaldehyde, samples are simply mixed with the Nash reagent.

Formaldehyde and methanol are not expected to be in high concentrations at the end of methanol fermentation of Methylobacterium extorquens due to the residual enzyme activities from multiple methanol oxidases and formate activating enzyme (3-5). Furthermore, any residual formaldehyde is expected to react with proteins, lipids, and other compounds in the biomass. Methanol which is much more volatile than water (vapor pressure 13.02 kPA vs 2.34 kPa at 20 °C), would be expected to evaporate during spray drying, drum drying, or lyophilization.

Summary:
Below are several experiments in which we adapt and verify a published method (1) to measure methanol and formaldehyde in dried cellular biomass. Our modifications are:

(1) To extract any cellular methanol or formaldehyde, we resuspend the dried biomass in dilute phosphate buffered saline (PBS) and subject the cellular material to freeze thaw cycles that is frequently used to lyse bacterial cells. The mixture is pelleted, and the resulting supernatant is tested for methanol or formaldehyde as described above.

(2) To test for lower amounts of methanol or formaldehyde, we include higher amounts of the sample in the reaction relative to the standards. If we add 2ul of a standard and 16ul of a sample and correct for volume changes, we should be able to measure formaldehyde or methanol 8 folds lower.

However, based on the data herein, we can state that the levels of methanol and formaldehyde detected from extractions of resuspended biomass samples (20 mg/mL) are less than 0.0004% (w/v) and below the limit of detection (0.00004 % w/v), respectively. These equate to less than 0.2 mg methanol or 0.02 mg formaldehyde per gram biomass.

2. Methanol Summary

In Experiments 1-3 below, we show our modification and verification of the method of Anthon and Barret (1) to attempt to measure methanol in spray dried biomass.
CONTAINS CONFIDENTIAL INFORMATION OF KNIPBIO, INC.

Method verification: Methanol and Formaldehyde

We established the linearity of the detection between (b)(4) and (b)(4) (w/v) and demonstrate that by increasing sample volumes relative to standards, it is possible to detect methanol as low as 0.002475% (w/v). We show that the methanol detected is specific in spray dried samples when spiked in at 0.05 and 0.005% (v/v).

Three powder biomass samples were resuspended to 20mg/mL and subjected to freeze thaw lysis to ensure the methanol present is in solution and tested exhaustively to try and determine the amount of methanol present. Based on the data in this experiment, the safest estimate of methanol present is less than 0.004% (mg/mL) or 0.0004% (w/v) per 20 mg biomass. These equate to less than 0.2 mg methanol per gram biomass (200ppm).

3. **Experiment 1: Determining linearity and LOD**

Rationale:

(1) Determine the linearity of methanol method using standards of (b)(4) to (b) MeOH (v/v) (b)(4) mM).

(2) Determine the effects on linearity of increasing sample volume relative to standard volume to detect lower amounts of methanol.

Acceptance criteria:

Linearity is achieved if the standards from 0.005 to 0.25% (v/v) methanol have a $r^2 > 0.99$. For testing if increased samples give responses that are linear with their expected concentration a $r^2 > 0.95$ is considered acceptable.

Results:

Table 1 below shows at least three assays for three different users where linearity was achieved. When linearity is below our acceptance criteria of $r^2 < 0.99$ (bolded values), it is usually due to the highest standard of 0.25% MeOH. When this standard is removed $r^2$ increases to over 0.99. Typically, samples measuring outside the acceptable linear range, such as those giving values above 0.25% or below 0.005%, are discarded. They are retested following dilution, or a larger amount of the sample is compared to the standard (see below). As in (1), 0.25% ethanol, acetone, or 2-propanol did not have any signal above the alcohol free blank (data not shown).

<table>
<thead>
<tr>
<th>User</th>
<th>$r^2$</th>
<th>% y intercept of 0.1% MeOH response</th>
<th>Standard range used in experiments (% v/v)</th>
<th>$r^2$ without 0.25% standard</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>User 1</td>
<td>(b)(4)</td>
<td></td>
<td></td>
<td></td>
<td>170627</td>
</tr>
<tr>
<td>User 1</td>
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CONTAINS CONFIDENTIAL INFORMATION OF KNIPBIO, INC.
Method verification: Methanol and Formaldehyde

<table>
<thead>
<tr>
<th>User 3</th>
<th>(b) (4)</th>
<th></th>
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<td>180726</td>
</tr>
<tr>
<td>User 3</td>
<td></td>
<td>180727</td>
</tr>
</tbody>
</table>

The standard reaction uses 2uL of the standard solution in a total volume of 202 ul, making the effective concentration of the standards between 0.0122 to 0.611mM. To measure lower concentrations, 4, 8, 16, or 32uL of sample can be used. After taking into account the increased volume, the percent methanol can be measured below 0.005% (v/v).

Table 2 below lists three experiments where the volume of the lower concentration standards was increased to 4, 8, 16, or 32uL. A linear fit between the expected value and the corrected response was generally good with $r^2 > 0.975$. Thus, increasing the sample amount relative to the standard allows measuring methanol in the ug/mL range.

<table>
<thead>
<tr>
<th>Experiment</th>
<th>% (v/v) Standard diluted</th>
<th>vol standards within range</th>
<th>$r^2$</th>
<th>Lowest Detectable % (v/v)</th>
<th>Lowest Detectable (mM)</th>
<th>Lowest detectable (mg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1A</td>
<td>(b) (4)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1A</td>
<td></td>
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</tr>
</tbody>
</table>

Table 3. Linearity and LOD summary

<table>
<thead>
<tr>
<th></th>
<th>% (v/v)</th>
<th>mM</th>
<th>% (w/v)</th>
<th>mg/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Linearity lower limit</td>
<td>0.005</td>
<td>1.23</td>
<td>0.00396</td>
<td>0.0396</td>
</tr>
<tr>
<td>Linearity higher limit</td>
<td>0.25</td>
<td>61.74</td>
<td>0.198</td>
<td>1.98</td>
</tr>
<tr>
<td>Limit of detection</td>
<td>0.0003125</td>
<td>0.077</td>
<td>0.0002475</td>
<td>0.002475</td>
</tr>
</tbody>
</table>

MW Methanol: 32.04 g/mol  
Density: 0.792 g/mL

4. **Experiment 2: Determination of the specificity and accuracy measurement.**

**Rationale:**
Test for specificity, accuracy, linearity, and limit of detection of methanol from cells grown in flask in absence of presence of methanol. Determine specificity using methanol spiked samples

**Experimental Design:**
We utilized the following samples:
1. KB203 grown with methanol as the sole carbon source.
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Method verification: Methanol and Formaldehyde

- Culture used for inoculation was grown in minimal medium with 0.5% methanol.
- Culture used for assay was inoculated with preculture of OD$_{600}$ 0.05 into minimal media amended with 0.5% methanol.
- Cultures were fed an additional 0.5% methanol after 23 hours growth.
- Cell pellets from 4ml culture and culture supernatants were collected before feeding, where most of the initial methanol was depleted, and 3.5 hours after feeding.

2. KB203 grown with succinate as the sole carbon source.
- Culture used for inoculation was grown in minimal medium with 30mM succinate.
- Culture used for assay was inoculated with preculture of OD$_{600}$ 0.05 into minimal media amended with 30mM succinate.
- Cultures were fed an additional 30mM succinate after 23 hours growth.
- Cell pellets from 4 ml culture and culture supernatants were collected before feeding, where most of the initial succinate was depleted, and 3.5 hours after feeding.

Sample processing:
All cell pellets were washed with 1mL 0.05X PBS. Following re-pelleting and removing the wash, the pellets were saved at -20°C until analysis. For analysis, cell pellets were resuspended by adding 200ul 0.05X PBS and mixing by pipetting.

To one tube of each cell pellet and culture supernatant, 1uL of 10% Methanol was added to spike in ~0.05% methanol. To one tube of each cell pellet after feeding, 10ul of 1mg/mL formaldehyde was added to spike in approximately 1.6mM formaldehyde (~0.048%) (see experiment 5). All cell pellet resuspensions were subjected to three freeze thaw cycles of at least ten minutes in a dry ice ethanol slurry and three minutes of bath sonication at room temperature. Following centrifugation at 15,000xG for 2 minutes, approximately 150ul of supernatant was transferred to a second tube and tested or methanol or formaldehyde levels. Samples were tested at 2, 4, 8, volumes relative to the 2ul standard volume.

Acceptance criteria:
Specificity is met if samples grown without methanol (succinate) have no detectable methanol in their supernatant and no detectable methanol in their cells. Spiked samples of methanol in succinate supernatants should be within 10% of the theoretical value. Accuracy is met if spiking of methanol results in methanol response that is within 10% of the theoretical value. Linearity is met if $r^2 > 0.95$ when comparing the measured methanol concentration of samples with increased volume relative to standards to their expected concentration.

Results:
None of the cells grown in methanol or succinate showed any detectable methanol (See Table 4). As expected the supernatant of the succinate grown cultures did not have detectable levels of methanol.

In the MeOH spiked samples, less MeOH than expected was seen for all cells, including succinate, suggesting possible residual methanol oxidase activity. Evidence that this activity is ablated in the spray drying process is given in Experiment 3 below. The succinate sample 2, did
have the expected amount of methanol in the spiked supernatant samples from before and after feeding, suggesting it did not have extracellular methanol oxidase activity.

In most cases, the linearity was acceptable when comparing the theoretical and measured amounts when samples were measure at 2, 4, and 8 ml. Exceptions (bold in Table 4) were found in samples where the higher volume gave responses that were outside the linear range. Sample can thus be measured to at least 0.00125% (v/v) methanol.

### Table 4. Specificity and accuracy of addition of samples spiked with Methanol

<table>
<thead>
<tr>
<th>Sample</th>
<th>Feed</th>
<th>% (v/v) MeOH</th>
<th>Linearity check</th>
<th>Expected (% v/v)</th>
<th>Result (% v/v)</th>
<th>%Diff.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>(b)</td>
<td>(4)</td>
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</table>

Using the data above and the limit of detections tested, none of the cells from samples grown in flask had methanol greater than 0.76 mg per gram biomass (see Table 5 below). In subsequent experiments 3 and 4 below, we were able to determine methanol is even lower in dried powder because we use higher volumes of sample relative to the standards.

### Table 5. Maximum possible methanol possible in cell biomass from Experiment 2

<table>
<thead>
<tr>
<th>Sample</th>
<th>Feed</th>
<th>OD (mg)</th>
<th>DCW (mg)</th>
<th>(mg/mL) cell susp.</th>
<th>MeOH measured (% v/v)</th>
<th>MeOH measured (mg/mL)</th>
<th>mg MeOH / g biomass</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>(b)</td>
<td>(4)</td>
<td></td>
<td></td>
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<td>1</td>
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<td>2</td>
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</tbody>
</table>
5. **Experiment 3: Testing for methanol and formaldehyde in spray dried biomass**

**Rationale:**
(1) Measure methanol and formaldehyde in spray dried biomass using the following samples:
   1. Powder 1 – June 2015 run
   2. Powder 2 – May 2016 run
   3. Powder 3 – October 2016 run
(2) Determine the minimum amount of methanol detectable by testing linearity of increasing sample volumes relative to standard volumes.

**Sample Processing:**
Powder was weighed and resuspended with 0.05X PBS to reach a concentration of 20mg/mL. The resuspension was aliquoted into two tubes of 200uL. To one tube of each powder, 1uL of 10% Methanol was added to spike in 0.05% methanol. All six tubes were subjected to three freeze thaw cycles of at least ten minutes in a dry ice ethanol slurry and three minutes of bath sonication at room temperature. Following centrifugation at 15,000xG for 2 minutes, approximately 150uL of supernatant was transferred to a second tube and tested or methanol. Samples were tested at 2, 4, 8, 16, 32uL volumes relative to the 2uL standard volume.

**Acceptance criteria:**
Linearity is met if \( r^2 > 0.95 \) when comparing the measured methanol concentration of samples with increased volume relative to standards to their expected concentration. Accuracy is met if spiking of methanol results in methanol response that is within 10% of the theoretical value.

**Results:**
All of the powders had very low, but linear increases (\( r^2 > 0.8 \) to 0.98) in absorbance with increasing sample volume consistent with them having low amounts of methanol (Table 6). However, this increase in absorbance may also be due to proteins and other components.

The spiked samples had measured values that were on average 5.6% of the expected values (Table 6). Unlike the cells in Experiment 2 above, the spray dried powder has very little or no residual methanol oxidase activity. This is likely due to denaturation caused by heating during the spray dried process. The spiked samples also had acceptable linearity with increasing sample volumes (\( r^2 > 0.995 \)).
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Method verification: Methanol and Formaldehyde

Table 6: Specificity and accuracy of samples of resuspended dried powder (20mg/mL) spiked with methanol at 0.05% (v/v)

<table>
<thead>
<tr>
<th>% (v/v) MeOH</th>
<th>Sample vol. used</th>
<th>Total vol.</th>
<th>Adjusted % (v/v) MeOH</th>
<th>Spike</th>
<th>( r^2 )</th>
<th>sample volumes in range</th>
<th>Expected from spike (%v/v)</th>
<th>Measured from spike (%v/v)</th>
<th>%Diff</th>
</tr>
</thead>
<tbody>
<tr>
<td>P1</td>
<td>(b) (4)</td>
<td></td>
<td></td>
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</tbody>
</table>

The amount of Methanol in spray dried powders is presented in Table 7.

Table 7: Maximum possible methanol possible in cell biomass from Experiment 3

<table>
<thead>
<tr>
<th>Sample</th>
<th>mg/mL cell resuspension</th>
<th>MeOH measured (% v/v)</th>
<th>MeOH measured (mg/mL)</th>
<th>mg MeOH / g biomass</th>
</tr>
</thead>
<tbody>
<tr>
<td>P1 (June 2015 run)</td>
<td>(b) (4)</td>
<td></td>
<td></td>
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<tr>
<td>P2 (May 2016 run)</td>
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<tr>
<td>P3 (Oct. 2016 run)</td>
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</table>

6. Experiment 4: Formaldehyde

Rationale:
(1) Determine the linearity of formaldehyde method using standards.
(2) Determine the effects on linearity of increasing sample volume.
(3) Determine the lowest amount of formaldehyde possible.

Acceptance criteria:
Linearity is achieved if the standards from 0.01 mg/mL (0.33mM) to 0.5 mg/mL (16.7mM) have a \( r^2 > 0.99 \). For testing if increased samples give responses that are linear with their expected concentration a \( r^2 > 0.95 \) is considered acceptable.

Results:
We generally have acceptable linearity when using formaldehyde standards of 0.01 mg/mL (0.001% w/v) to 0.5 mg/mL (0.05% w/v). Table 8 below shows several assays from different users. When linearity is below our acceptance criteria of \( r^2 < 0.99 \), it is usually due to a pipetting error. Samples outside the acceptable linear range, such as those giving values above 0.5 mg/mL or below 0.01 mg/mL are discarded. They are retested following dilution, or a larger amount of the sample is compared to the standard (see below). As expected (1), acetaldehyde did not increase response above background (not shown).

As in the Methanol assay, the amount of formaldehyde measured can be lowered by using more sample than standard. When tested between 0.00004% and 0.001% (w/v) linearity was an acceptable \( r^2 > 0.9918 \). Linearity of the samples describe in experiment 2 using 2, 10, 20uL sample
that were not outside the linear range were consistent with being able to measure lower concentrations by increasing sample volume ($r^2 > 0.9551, 0.9532$).

None of the extractions from the powders had any response above the LOD (0.00004% w/v) even when sample were 25 times greater than the formaldehyde standard (50uL sample volume).

**Table 8: Linearity results from two users of formaldehyde method standards**

<table>
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<tr>
<th>$r^2$</th>
<th>Background Corrected Response of 10mM</th>
<th>b</th>
<th>Percent y intercept of response</th>
<th>Standard range used (w/v)</th>
<th>Date</th>
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<tbody>
<tr>
<td>User 1</td>
<td>(b) (4)</td>
<td></td>
<td></td>
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<tr>
<td>User 1</td>
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<td>User 2</td>
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<td>User 3</td>
<td></td>
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**References**
TOXICOLOGICAL REVIEW

OF

METHANOL (NONCANCER)

(CAS No. 67-56-1)

In Support of Summary Information on the
Integrated Risk Information System (IRIS)

September 2013

U.S. Environmental Protection Agency
Washington, DC
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<td>AUC</td>
<td>area under the curve, representing the cumulative product of time and</td>
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<td>concentration for a substance in the blood</td>
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<td>BMD for response one standard deviation from control mean</td>
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<td>Center for the Evaluation of Risks to Human Reproduction at the NTP</td>
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<td>d, δ, Δ</td>
<td>delta, difference, change</td>
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<td>F344</td>
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<tr>
<td>FAD</td>
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<td>FAS</td>
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<td>FD</td>
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FP  folate paired
FR  folate reduced
FRACIN  fraction inhaled
FS  folate sufficient
FSH  follicular stimulating hormone
γ-GT  gamma glutamyl transferase
g  gravity
g, kg, mg, µg  gram, kilogram, milligram, microgram
G6PD  glucose-6-phosphate dehydrogenase
GAP43  growth-associated protein (neuronal growth cone)
GD  gestation day
GFR  glomerular filtration rate
GI  gastrointestinal track
GLM  generalized linear model
GLP  good laboratory practice
GSH  glutathione
HAP  hazardous air pollutant
HCHO  formaldehyde
HCOO  formate
Hct  hematocrit
HEC  human equivalent concentration
HED  human equivalent dose
HEI  Health Effects Institute
HERO  Health and Environmental Research Online (database system)
HH  hereditary hemochromatosis
5-HIAA  5-hydroxyindolacetic acid
HMGS-H  S-hydroxymethylglutathione
Hp  haptoglobin
HPA  hypothalamus-pituitary-adrenal (axis)
HPLC  high-performance liquid chromatography
HSDB  Hazardous Substances Databank
HSP70  biomarker of cellular stress
5-HT  serotonin
IL  interleukins
i.p.  intraperitoneal (injection)
IPCS  International Programme on Chemical Safety
IQ  intelligence quotient
IRIS  Integrated Risk Information System
IUR  inhalation unit risk
i.v.  intravenous (injection)
k₁  first-order urinary clearance
k₁C  first-order urinary clearance scaling constant; first order clearance of methanol from the blood to the bladder for urinary elimination
k₅  first order uptake from the intestine
k₆  first order methanol oral absorption rate from stomach
kₑ  rate constant for urinary excretion from bladder
kₑv  respiratory/cardiac depression constant
K₁LH  keyhole limpet hemocyanin
K₁L  alternate first order rate constant
Kₘ  apparent Michaelis-Menten constant; substrate concentration at half the maximum velocity (Vₘₐₓ)
kₙ  first order transfer between stomach and intestine
L, dL, mL  liter, deciliter, milliliter
LD₅₀  median lethal dose
LDH  lactate dehydrogenase
LH  luteinizing hormone
LLF  (maximum) log likelihood function
LMI  leukocyte migration inhibition (assay)
LOAEL  lowest-observed-adverse-effect level
M, mM, µM  molar, millimolar, micromolar
MeOH  methanol
MLE  maximum likelihood estimate
M-M  Michaelis-Menten
MN  micronuclei
MOA  mode of action
4-MP  4-methylpyrazole (fomepizole)
MRI  magnetic resonance imaging
mRNA  messenger RNA
MTBE  methyl tertiary butyl ether
MTX  methotrexate
N₂O/O₂  nitrous oxide
NAD⁺  nicotinamide adenine dinucleotide
NADH  reduced form of nicotinamide adenine dinucleotide
NBT  nitroblue tetrazolium (test)
NCEA  National Center for Environmental Assessment
ND  not determined
NEDO  New Energy Development Organization (of Japan)
NIEHS  National Institute for Environmental Health Sciences
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<td>NIOSH</td>
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<tr>
<td>nmol</td>
<td>nanomole</td>
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<tr>
<td>NOAEL</td>
<td>no-observed-adverse-effect level</td>
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<td>NOEL</td>
<td>no-observed-effect level</td>
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<td>NTP</td>
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<td>NZW</td>
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<td>OR</td>
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<td>OU</td>
<td>oculus uterque (each eye)</td>
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<td>P, p</td>
<td>probability</td>
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<td>ppb, ppm</td>
<td>parts per billion, parts per million</td>
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<td>body:blood partition coefficient</td>
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<td>PWG</td>
<td>Pathology Working Group of the NTP of NIEHS</td>
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<td>Q wave</td>
<td>the initial deflection of the QRS complex</td>
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<td>cardiac output scaling constant</td>
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<td>pulmonary (alveolar) ventilation</td>
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<td>QRS</td>
<td>portion of electrocardiogram corresponding to the depolarization of ventricular cardiac cells.</td>
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<td>square of the correlation coefficient, a measure of the reliability of a linear relationship.</td>
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<td>SOP</td>
<td>standard operating procedure(s)</td>
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<td>T; T₁₉₅</td>
<td>time; half-life</td>
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<td>T wave</td>
<td>the next deflection in the electrocardiogram after the QRS complex; represents ventricular repolarization</td>
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<td>WOE</td>
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<td>w/v</td>
<td>weight (mass of solute)/volume of solution</td>
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<td>χ²</td>
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## AUTHORS, CONTRIBUTORS, AND REVIEWERS

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Jeffrey Gift, Ph.D. (Chemical Manager)  
J. Allen Davis, MSPH  

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Paul Schlosser, Ph.D.  

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<td>Research Triangle Park, NC</td>
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# Production Team

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# Executive Direction

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# Reviewers

The methanol (noncancer) assessment was provided for review to scientists in EPA’s Program and Region Offices. Comments were submitted by:

- Office of Air Quality and Planning Standards, Research Triangle Park, NC
- Office of Children’s Health Protection, Washington, DC
- Office of Policy, Economics, and Innovation, Washington, DC
- Office of Solid Waste and Emergency Response, Washington, DC
- Office of Water, Washington, DC

The methanol (noncancer) assessment was provided for review to other federal agencies and the Executive Office of the President. Comments were submitted by:

- Agency for Toxic Substances Disease Registry, Centers for Disease Control and Prevention, Department of Health & Human Services
- Council on Environmental Quality, Executive Office of the President
- National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention, Department of Health & Human Services
- Office of Management and Budget, Executive Office of the President
- United States Department of Defense
The methanol (noncancer) assessment was released for public comment in April 2011 and a revised assessment was released for public comment in May 2013. A summary and EPA's disposition of the comments from the public is included in Appendix A. Comments were received from the following entities:

<table>
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<th>Name</th>
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<td>Paul Noe</td>
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<td>Greg Dolan</td>
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<td>Andrew G. Salmon M.A., D.Phil.*</td>
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*Members of the 2011 peer review panel, who also provided public comments on the 2013 revised draft of the methanol (noncancer) toxicological review.

The methanol (noncancer) assessment was peer reviewed by independent expert scientists external to EPA and a peer-review meeting was held on July 22, 2011. A follow-up peer review was completed in July 2013 to obtain feedback from members of the original 2011 peer review panel (identified with an asterisk below) on the 2013 revised draft methanol (noncancer) toxicological review and EPA's response to the 2011 peer review comments. The original and follow-up external peer-review comments are available on the IRIS Web site. A summary and EPA's disposition of the comments received from the independent external peer reviewers is included in Appendix A.

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**Members of the original 2011 peer review panel, who also reviewed the 2013 revised draft of the methanol (noncancer) toxicological review.
EXECUTIVE SUMMARY

Introduction

Methanol is a high production volume chemical with many commercial uses. It is a basic building block for numerous chemicals. Many of its derivatives are used in the construction, housing or automotive industries. Consumer products that contain methanol include varnishes, shellacs, paints, windshield washer fluid, antifreeze, adhesives, and deicers.

Methanol can be formed in the mammalian organism as a metabolic byproduct. Endogenous background levels [naturally generated from within the body] are not the same as exogenous exposure (exposure from a source outside the body), but the combination of endogenous background levels of methanol plus exogenous methanol exposure can lead to toxicity. Diet can contribute to background levels of methanol, principally from the ordinary ingestion of fruits and vegetables. This Toxicological Review provides scientific support and rationale for a hazard identification and dose-response assessment of the noncancer effects associated with chronic exposures to exogenous sources of methanol that add to background levels of methanol. For the purpose of this methanol (noncancer) assessment, EPA estimates that a diet that includes fruits and vegetables would not increase methanol blood levels above 2.5 mg/L (see discussion in Section 5.3.6). Thus, for a population with background blood levels of methanol at or below 2.5 mg/L, the inhalation reference concentration (RfC) and oral reference dose (RfD) that are derived in this assessment represent estimates (with uncertainty spanning perhaps an order of magnitude) of daily exposures to the human population (including sensitive subgroups) that are likely to be without an appreciable risk of deleterious effects during a lifetime. In Section 5 (Dose Response Assessments), the basis for a RfC of $2 \times 10^1$ mg/m$^3$ and a RfD of 2 mg/kg-day are described.

This health assessment does not assess the potential carcinogenicity of methanol, or the health effects associated with background levels of methanol that arise from metabolic and dietary sources such as vegetables, fruits and juices that naturally contain methanol or have components (e.g., plant pectin) that convert to methanol. Hence, as discussed in Section 3.4.3.2 (Model Structure), responses observed in oral and inhalation studies of laboratory animals exposed to methanol are evaluated against blood concentrations of methanol after subtracting an estimate of the background blood levels in control animals.
Chemical and Physical Information

Methanol is the smallest member of the family of aliphatic alcohols. Also known as methyl alcohol or wood alcohol, among other synonyms, it is a clear, colorless, very volatile, and flammable liquid. Methanol is widely used as a solvent in many commercial and consumer products. It is freely miscible with water and other short-chain aliphatic alcohols but has little tendency to distribute into lipophilic media.

Toxicokinetics

Due to its very low oil:water partition coefficient, methanol is taken up efficiently by the lung or the intestinal tract and distributes freely in body water (blood volume, extracellular and intracellular fluid, etc.) without any tendency to accumulate in fatty tissues. Methanol can be metabolized completely to CO₂ but may also, as a regular byproduct of metabolism, enter the formic acid C₁-pool (1-carbon unit pool), and become incorporated into biomolecules. Animal studies indicate that blood methanol levels increase with the breathing rate and that metabolism becomes saturated at high exposure levels. Because of its volatility methanol can be exhaled with air, and also excreted unchanged via urine. As discussed in Section 3.1 (Toxicokinetics Overview), the enzymes responsible for metabolizing methanol are different in rodents and primates (Figure 3-1). Several published rat, mouse, and human PBPK models which attempt to account for these species differences are described in Section 3.4.2 (Methanol PBPK Models).

The development of methanol PBPK models was organized around a set of criteria, described in Section 3.4.1.2 (Criteria for the Development of Methanol PBPK Models), that take into account the dose routes used in key toxicity studies, the availability of pharmacokinetic information necessary for PBPK model development and the most likely toxicological mode of action (MOA). Specifically, EPA developed new PBPK models or modified the existing ones, which allowed for the estimation of monkey and rat internal dose metrics. A human model was also developed to extrapolate those internal metrics to inhalation and oral exposure concentrations that would result in the same internal dose in humans (human equivalent concentrations [HECs] and human equivalent doses [HEDs]). The procedures used for the development, calibration and use of these EPA models are summarized in Section 3.4 (Physiologically Based Pharmacokinetic Models), with further details provided in Appendix B, "Development, Calibration and Application of a Methanol PBPK Model."

Developmental malformations and anomalies in gestationally exposed fetal mice (and developmental neurotoxicity, as indicated by reduced absolute brain weight, in gestationally and lactationally exposed fetal and neonate rats) observed in inhalation studies are sensitive endpoints considered in the derivation of an RfC. However, questions remain regarding the
relative involvement of parent methanol, formaldehyde, and reactive oxygen species (ROS) in the MOA for these developmental effects. Given the reactivity of formaldehyde and the lack of relevant pharmacokinetic information, PBPK models that predict levels of formaldehyde (or subsequent metabolites of formaldehyde) in the blood would be difficult to validate. However, the high reactivity of formaldehyde (see Section 3.1 [Toxicokinetics Overview]) would limit its unbound and unaltered transport as free formaldehyde from maternal to fetal blood (see discussion in Section 3.4.1.1 [MOA and Selection of a Dose Metric] and 4.7.1 [Role of Methanol and Metabolites in the Developmental Toxicity of Methanol]), and the ROS MOA requires the presence of methanol to alter embryonic catalase activity. Hence, it is likely that all of these MOAs require methanol to be present at the target site. For this reason, and because adequate pharmacokinetic information was available, PBPK models that estimate levels of parent methanol in blood were developed and validated for rats and humans. Because actual measured internal blood methanol levels suitable for use as estimates of peak concentrations (C$_{\text{max}}$) in mice were provided in the Rogers et al. (1993b) study, and these data were considered better than a predictive model, the mouse PBPK model was not used or discussed in detail in this toxicological review. A simple PK model for monkey methanol kinetics was also developed and used to evaluate the results of monkey developmental studies (Burbacher et al., 2004a; 2004b; 1999a; 1999b).

A pregnancy-specific PBPK model does not exist for methanol and limited data exist for the development and validation of a fetal/gestational/conceptus compartment. For this reason, and because levels of methanol in non-pregnant and pregnant adult females, and fetal blood (all measures of maternal exposure) are expected to be similar following the same oral or inhalation methanol exposure (see discussion in Section 3.4.1.2 [Criteria for the development of Methanol PBPK Models]), EPA developed and used non-pregnancy models for the appropriate species and routes of exposure for the derivation of candidate RfC's and RfDs. It is recognized that these models may not accurately represent neonate blood levels following the gestation, lactation and inhalation exposure regimen used in one of the key rat studies (NEDO, 1987), but they are considered appropriate for use in deriving HEC values from this study assuming the ratio of maternal to offspring blood methanol would be similar in rats and humans (see discussion in Sections 5.1.3.2.2 [Animal-to-Human Extrapolation UF$_{\lambda}$]).

The rat and human methanol PBPK models fit multiple data sets for inhalation, oral, and i.v. exposures, from multiple research groups using consistent parameters that are representative of each species but are not varied within species or by dose or source of data. Also, a simple PK

---

1 The PBPK models developed by EPA estimate total amount of methanol cleared by metabolic processes, but this has limited value as a metric of formaldehyde or formate dose since it ignores metabolic processes that may differ between species and between the mother and the fetus/neonate.
model calibrated to non-pregnant (NP) monkey data, which were shown to be essentially indistinguishable from pregnant monkey PK data, was used to estimate blood methanol area under the curve (AUC) values (internal doses) in that species. In the case of the mouse, a PK model developed from in vivo blood methanol levels in (Rogers et al., 1993b) resulted in more reliable estimates compared to the PBPK model and was used for derivation of effect levels in this species. Section 5 (Dose Response Assessments and Characterization) describes how the human PBPK model was used in the derivation of candidate RfCs and RfDs.

Hazard Identification

In humans, acute central nervous system (CNS) toxicity can result from relatively low ingested doses (as low as 3-20 mL of methanol), which can metabolize to formic acid and lead to metabolic acidosis. The resulting acidosis can potentially cause lasting nervous system effects such as blindness, Parkinson-like symptoms, and cognitive impairment. These effects have been observed in humans with blood methanol levels as low as 200 mg/L (Adair et al., 2005).

CNS effects have not been observed in rodents following acute exposures to methanol, and NEDO (1987) reported that methanol blood levels around 5,000 mg/L were necessary to cause clinical signs and CNS changes in cynomolgus monkeys. The species differences in toxicity from acute exposures appear to be the result of a limited ability of humans to metabolize formic acid.

Occupational studies and case reports offer valuable information on the effects of methanol following acute human exposures, but the relatively small amount of data for subchronic, chronic, or in utero human exposures are inconclusive. However, a number of reproductive, developmental, subchronic, and chronic toxicity studies have been conducted in mice, rats, and monkeys.

Data regarding effects from oral exposure in experimental animals exist, but they are more limited than data from the inhalation route of exposure (see Sections 4.2 [Acute, Subchronic, and Chronic Studies in Animals – Oral and Inhalation], 4.3 [Reproductive and Developmental Studies – Oral and Inhalation], and 4.4 [Neurotoxicity]). Two oral studies in rats (Soffritti et al., 2002; TRL, 1986), one oral study in mice (Apaja, 1980) and several inhalation studies in monkeys, rats and mice (NEDO, 1987, 1985a, b) of 90-days duration or longer have been reported. Some noncancer effects of methanol exposure were noted in these studies, principally in the liver and brain tissues, but they occurred at relatively high doses.

A number of studies have used the inhalation route of exposure to assess the potential of reproductive or developmental toxicity of methanol in mice, rats, and monkeys (see Section 4.3.2 [Inhalation Reproductive and Developmental Studies]). These studies indicate that fetal and
neonate toxicity occurs at lower doses than maternal toxicity. At exposure concentrations of 5,000 ppm or above, methanol has been shown to cause an increase in litters with resorptions (Bolon et al., 1993), and severe malformations (encephaly and cleft palate) in mice, the most sensitive gestational days being GD6 and GD7 (i.e., early organogenesis) (Rogers and Mole, 1997; Rogers et al., 1993a; Rogers et al., 1993b). Increased occurrences of ossification disturbances and skeletal anomalies were observed at exposure concentrations of 2,000 ppm in mice (Rogers et al., 1993b) and at 10,000 ppm in rats (Nelson et al., 1985). NEDO (1987) conducted a series of developmental and reproductive studies, including a two generation and a follow-up one generation reproductive toxicity study in rats, which used exposure times of 20 hours/day or more at concentrations between 100 and 5,000 ppm. Details were not reported (e.g., means, variances, sample sizes, pup-to-litter correlations) that would allow for an analysis of the findings from this study. However, a follow-up one-generation study conducted by NEDO (1987) contained enough information to confirm and quantify the primary endpoint identified, pup brain weight changes. This developmental neurotoxicity study is discussed in Section 4.4.2 (Inhalation Neurotoxicity Studies). Section 4.4.2 also describes another key developmental neurotoxicity study conducted in pregnant cynomolgus monkeys exposed to 200-1,800 ppm methanol for 2.5 hours/day throughout pre-mating, mating, and gestation (Burbacher et al., 2004a; 2004b; 1999a; 1999b). Potential compound-related effects noted were a shortening of the gestation period by less than 5%, and developmental neurotoxicity (particularly delayed sensorimotor development) in the monkeys.

As discussed in Section 4.6.1.2 (Key Studies, Inhalation), due largely to the lack of clear dose-response information, the data from the monkey developmental study are not conclusive, and there was insufficient evidence to determine if the primate fetus is more sensitive, or less sensitive, than rodents to the developmental or reproductive effects of methanol. Taken together, however, the NEDO (1987) rat study and the Burbacher et al. (2004a; 2004b; 1999a; 1999b) monkey study suggest that prenatal exposure to methanol can result in adverse effects on developmental neurology pathology and function, which can be exacerbated by continued postnatal exposure. Among an array of findings indicating developmental neurotoxicity and developmental malformations and anomalies that have been observed in rodents, a decrease in the brain weights of gestationally and lactationally exposed neonatal rats (NEDO, 1987) and an increase in the incidence of cervical ribs of gestationally exposed fetal mice (Rogers et al., 1993b) are considered the most robust endpoints for the purposes of RfD and RfC derivation. See Section 4.6 (Synthesis of Major Noncancer Effects) for a more extensive summary of the dose-related effects that have been observed following subchronic or chronic exposure.

Sections 4.7 (Noncancer MOA Information) and 5.3.5 (Choice of Species/Sex), provide a discussion of the uncertainty regarding human relevance of the mouse and rat developmental
studies due to differences in the way humans and rodents metabolize methanol. Adult humans metabolize methanol principally via alcohol dehydrogenase (ADH1) and rodents via catalase and ADH1. Recent studies in mice have demonstrated that high catalase activity can reduce, and low catalase activity can enhance, methanol’s embryotoxic effects. However, the MOA for these effects, and the role of catalase, have not been determined. Further, while catalase does not appear to be involved in adult human methanol metabolism, less is known about the metabolism of methanol in human infants (see Section 3.3 [Human Variability in Methanol Metabolism]). Thus, the effects observed in rodents are considered relevant for the assessment of human health.

**Dose-Response Assessment and Characterization**

As discussed above and in Section 5.1.1 (Choice of Principal Study and Critical Effect[s]), reproductive and developmental effects are considered the most sensitive and quantifiable effects reported in studies of methanol. Because the oral reproductive and developmental studies employed single and comparatively high doses (i.e., oral versus inhalation), the developmental effects observed in the inhalation studies were used to derive the RfC and, using a route-to-route extrapolation, the RfD.

Clearly defined toxic endpoints at moderate exposure levels have been observed in inhalation studies of reproductive and developmental toxicity (see Section 5.1.1.2 [Selection of Critical Effect[s]]). Three endpoints from inhalation developmental toxicity studies were critically evaluated for derivation of the RfC: (1) increased occurrences of ossification disturbances and skeletal abnormalities (i.e., formation of cervical ribs) in CD-1 mice exposed to methanol during organogenesis (Rogers et al., 1993b); (2) reduced brain weights in rats exposed to methanol from early gestation through 8 weeks of postnatal life (NEDO, 1987); and (3) deficits in sensorimotor development in the offspring of monkeys exposed to methanol throughout gestation (Burbacher et al., 2004a; 2004b; 1999a; 1999b).

Rogers et al. (1993b) exposed CD-1 mice to air concentrations of 0, 1,000, 2,000, and 5,000 ppm methanol for 7 hours/day on GD7 to GD17. A lower limit of a one-sided 95% confidence interval on the BMD (BMDL) of 43 mg/L was estimated for the internal peak blood methanol (Cmax) associated with 5% extra risk for the formation of cervical ribs (see Section 5.1.2.3 [BMD Approach Applied to Cervical Rib Data in Mice] and Appendix D [RfC Derivation Options]). This BMDL05 was then divided by 100 to account for uncertainties associated with human variability (UFH), the animal-to-human extrapolation (UFa) and the database (UFd), and to reduce it to a level that is within the range of blood levels for which the human PBPK model was calibrated (see discussion in Section 5.1.3.2 [Application of UF]). The PBPK model was then used to convert this adjusted internal BMDL05 of 0.43 mg/L to a human equivalent.
candidate RfC of 20.0 mg/m³ (see Section 5.1.3 [Rfc Derivation – Including Application of Uncertainty Factors]) and a candidate RfD of 1.9 mg/kg-day (see Section 5.2.2 [Rfd Derivation – Including Application of Uncertainty Factors]).

NEDO (1987) exposed fetal Sprague-Dawley rats and their dams to air concentrations of 0, 500, 1,000 and 2,000 ppm methanol from the first day of gestation (GD1) until 8 weeks of age, and brain weights were determined at 3, 6, and 8 weeks of age. A BMDL of 858 mg-hr/L was estimated for the area under the curve (AUC) internal blood methanol dose, associated with a brain weight reduction at 6 weeks equal to one standard deviation (SD) from the control mean (see Section 5.1.2.2 [BMD Approach Applied to Brain Weight Data in Rats], and Appendix D [Rfc Derivation Options]). This BMDL was then divided by 100 to account for uncertainties associated with human variability (UFH), the animal-to-human extrapolation (UFa) and the database (UD), and to reduce it to a level that is within the range of blood levels for which the human PBPK model was calibrated (see discussion in Section 5.1.3.2 [Application of UF (s)]. The PBPK model was then used to convert this adjusted internal BMDLSD of 8.58 mg-hr/L to a human equivalent candidate RfC of 17.8 mg/m³ (see Section 5.1.3 [Rfc Derivation – Including Application of Uncertainty Factors]) and a candidate RfD of 5.2 mg/kg-day (see Section 5.2.2 [Rfd Derivation – Including Application of Uncertainty Factors]).

Burbacher et al. (2004a; 2004b; 1999a; 1999b) exposed M. fascicularis monkeys to 0, 200, 600, or 1,800 ppm methanol 2.5 hours/day, 7 days/week during pre-mating/mating and throughout gestation (approximately 168 days). A BMDLSD of 19.6 mg/L was estimated for the blood methanol Cmax associated with a one SD delay in sensorimotor development in the offspring as measured by a visually directed reaching (VDR) test (see Appendix D [Rfc Derivation Options]). However, only the unadjusted VDR response for females exhibited a response that could be modeled and the dose-response was marginally significant, with only the high dose exhibiting a response significantly different from controls. Although, the metabolism of methanol in monkeys is comparable to humans (Section 3.1 [Toxicokinetics Overview]) and a delay in VDR is a potentially relevant CNS effect (Section 4.4.2 [Inhalation Neurotoxicity Studies]), EPA concluded that the use of this data for RfC/D derivation was not preferable, given the availability of more reliable dose-response data from the Rogers et al. (1993b) and NEDO (1987) rodent studies.

In summary, after the evaluation of different species, different endpoints, different protocols and different data sources, the Rogers et al. (1993b) mouse, NEDO (1987) rat, and Burbacher et al. (2004a; 2004b; 1999a; 1999b) monkey studies exhibited developmental effects at similar doses, providing consistent results. As described in Sections 5.1.1.2 (Selection of Critical Effects) and 5.2.1.1 (Expansion of the Oral Database by Route-to-Route Extrapolation), because the Rogers et al. (1993b) and NEDO (1987) studies identified relevant effects in relevant
species that could be adequately quantified in a dose-response analysis, they are considered the most appropriate studies for use in the RfC and RfD derivation. The candidate RfC of $2 \times 10^1$ mg/m$^3$ based on decreased brain weight observed in the NEDO (1987) rat developmental study (see Table 5-4 [Summary of POD values for critical endpoints, application of UF$s$ and conversion to candidate RfCs using PBPK modeling]) was selected as the RfC for methanol. The candidate RfD of 2 mg/kg-day based on the formation of extra cervical ribs observed in the Rogers et al. (1993b) mouse developmental study (see Table 5-6 [Summary of POD values for critical endpoints, application of UF$s$ and conversion to candidate RfDs using PBPK modeling]) was selected as the RfD for methanol. As described in Sections 5.1.3 (RfC Derivation – Including Application of Uncertainty Factors) and 5.2.2 (RfD Derivation – Including Application of Uncertainty Factors), the UF$s$ employed for both the RfC and RfD derivations include a UF$_H$ of 10 for intraspecies variability, a UF$_A$ of 3 to address pharmacodynamic uncertainty and a UF$_D$ of 3 for database uncertainty.

**Relationship of the RfC and RfD to Background Methanol Blood Levels and Monkey Blood Levels Associated with Effects of Uncertain Adversity**

In Section 5.3.6, PBPK model predictions for the increase in methanol levels in blood resulting from exposure to methanol at the level of the RfC or RfD are compared to background blood levels of methanol estimated from (1) daily endogenous production and dietary exposure estimates from the U.K. report (COT, 2011) and (2) a sample background distribution derived from relevant study groups in Table 3-1 of this toxicological review. Both the EPA and the U.K. data are consistent with approximately 2.5 mg/L representing a high end of the range of background (as defined in Section 5.3.6) methanol blood levels. EPA estimates that the shift in EPA's sample background methanol blood level distribution that would be associated with daily exposures of the entire population to methanol at the RfC or the RfD would increase the number of individuals with peak methanol blood levels at or above 2.5 mg/L from ~7% to ~14%. EPA's PBPK model predicts that a continuous daily methanol exposure at the RfD or RfC would raise the peak methanol blood level of an individual with a high end background methanol blood level of 2.5 mg/L to just under 3 mg/L. As discussed in Section 5.3.7, this 3 mg/L methanol blood level is at the low end of the range of methanol blood levels that have been reported in monkey chronic and gestational exposure studies to be associated with CNS and reproductive/developmental effects of uncertain, but potential adversity.
1. INTRODUCTION

This document presents background information and justification for the Integrated Risk Information System (IRIS) Summary of the hazard and dose-response assessment of methanol. IRIS Summaries may include oral reference dose (RdD) and inhalation reference concentration (RfC) values for chronic and other exposure durations, and a carcinogenicity assessment.

The RdD and RfC, if derived, provide quantitative information for use in risk assessments for noncancer health effects known or assumed to be produced through a nonlinear (presumed threshold) mode of action (MOA). The RdD (expressed in units of milligrams per kilogram per day [mg/kg-day]) is defined as an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. The inhalation RfC (expressed in units of milligrams per cubic meter [mg/m³]) is analogous to the oral RdD but provides a continuous inhalation exposure estimate. The inhalation RfC considers toxic effects for both the respiratory system (portal-of-entry) and for effects peripheral to the respiratory system (extrarespiratory or systemic effects). Reference values are generally derived for chronic exposures (up to a lifetime), but may also be derived for acute (≤ 24 hours), short-term (>24 hours up to 30 days), and subchronic (>30 days up to 10% of lifetime) exposure durations, all of which are derived based on an assumption of continuous exposure throughout the duration specified. Unless specified otherwise, the RdD and RfC are derived for chronic exposure duration.