Pathogenesis of

Pseudomonas

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Nothing to disclose
Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases, Updated Edition, 221, 2518-2531.e3
P. aeruginosa physiology

• Ubiquitous
• Minimal growth requirements
• Temperature
• Can grow anaerobically with arginine or nitrate
• Resistant to antimicrobials
  • Permeability barrier
  • Numerous efflux pumps
  • Acquired resistance
What is available to the field?

• Strains
  • First sequenced *P. aeruginosa* strain, PAO1 (Stover et al. Nature 2000)
    • Large genome, single circular chromosome, ~6.6 Mb
    • >5580 ORF
    • 66% G+C

• Bioinformatic analysis

• Ordered transposon (Tn) libraries
  • PAO1, Jacobs et al. PNAS 2003
  • PA14, Liberati et al. PNAS 2006

• State of the art genetic tools
  • Reagents for the construction of specific mutations
  • Tnseq
  • RNAseq
The International Pseudomonas Consortium Database

Linking metadata, genomics and human health

IPCD is a repository of thousands of *Pseudomonas aeruginosa* isolates from the environment (soil and water), plants, animals and human infections, with a strong emphasis on Cystic Fibrosis. It was created for metadata analyses linking bacterial phenotype, genotype and clinical data, with a clear focus on the development of prognostic approaches to treating Cystic Fibrosis infections.

IPCD currently contains 1588 isolates. Draft genomes have been produced for 979 of them.

The content of IPCD can be accessed [here](http://www.pseudomonas.com/)

Other useful resources:

- PATRIC, The bacterial bioinformatics database and analysis pipeline: [www.patricbrc.org](http://www.patricbrc.org)
- The Comprehensive antibiotic resistance database: [http://arpcard.mcmaster.ca/](http://arpcard.mcmaster.ca/)
- The Public databases for molecular typing and microbial genome diversity: [http://pubmlst.org/](http://pubmlst.org/)
- In silico serotyping: PAst 1.0 (upcoming)
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The Pseudomonas Genome Database collaborates with an international panel of expert Pseudomonas researchers to provide high quality updates to the PA01 genome annotation and make cutting edge genome analysis data available.
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P. aeruginosa is an opportunistic pathogen

- Infections generally occur in the context of breach of the innate immune system
- Healthy animals like healthy humans are typically resistant to infection
Eye infections
Chronic respiratory infections (particularly, cystic fibrosis)
Hospital-acquired pneumonia
Bloodstream and catheter-related infections
Urinary tract infections
Intra-abdominal infections
Skin and soft tissue infections

*Pseudomonas aeruginosa*

Clinical Presentation
Pathogenesis

Pathogenesis in *P. aeruginosa* is mediated by various adhesins and secreted toxins, proteases, effector proteins and pigments that facilitate adhesion, modulate or disrupt host cell pathways and target the extracellular matrix.

*Pseudomonas aeruginosa*
Early (Acute) Infection

- Flagella
- Type IV pili
- Secreted toxins and enzymes
- Complete LPS ("Smooth")
- Low level of alginate

Chronic Infection

- Decreased secretion
- Defective LPS ("Rough")
- Deacylated lipid A
- Auxotrophy
- Overexpression of alginate
- LasR (quorum-sensing) mutants

Adaptation During Chronic Lung Infection In Cystic Fibrosis
Considerations for development of animal models of \textit{P. aeruginosa}

- Normal healthy animals are generally resistant to infection
  - Some acute infections can disseminate
  - Other infections stay localized
- \textit{P. aeruginosa} adapts during chronic respiratory infections in cystic fibrosis (CF)
  - There are >1700 recognized disease-associated mutations in \textit{CFTR} in the human population (with F508del being most common), but not all are equivalent
- Strains from particular sources may express distinct constellations of pathogenic factors that may be essential at different infection sites
Thanks