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Over-the-Counter Drug Products
Part 15 Hearing; June 28-29, 2000

EpicYTE Pharmaceutical, Inc.
5810 Nancy Ridge Drive
Suite 150
San Diego, California, 92121

EpicYTE Pharmaceutical Summary: June 29, 11:30 am

Presenter: Kevin J Whaley, PhD
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EpicYTE Pharmaceutical, Inc. (San Diego, CA) intends to develop and market products that prevent transmission of infectious diseases. Infectious diseases are the leading cause of mortality worldwide and account for nearly half of all deaths for people under age 45.

Since 90% of all infectious diseases begin at a mucosal site, there is a real need for products to protect mucosal surfaces (oral, gastrointestinal, respiratory, genitourinary) and prevent transmission of infectious diseases.

The active agent in EpicYTE prevention products are plantibodies. Plantibodies are human antibodies produced in plants at low cost and at large capacity. The plantibodies are purified from plants and formulated as pharmaceuticals. Plantibodies will supplement and mimic the prevention role of mucosal antibodies. Healthy humans produce antibodies in large quantities (approximately 4 g/day, more than all other antibody types combined) at mucosal surfaces.

One example of the need for personal protection technology for preventing transmission of infectious pathogens is the expanding AIDS epidemic. The world community has had limited options for preventing sexual transmission of HIV and other pathogens. Vaginal microbicides are an emerging technology for preventing the sexual transmission of these pathogens. EpicYTE's contribution to this product category will be a vaginal immunoprotectant for blocking STD/HIV transmission. EpicYTE is also developing plantibodies that will prevent mucosal transmission of respiratory and gastrointestinal pathogens.

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Although some of the plantibody-based products that prevent transmission will be used in hospitals and other medical settings, the broader healthy population is constantly at risk for acquiring infectious disease. We believe that the best interests of individuals and public health will be served by making one venue of availability for transmission preventives to be over-the-counter. EpicYTE intends to include the Division of OTC at the FDA during the development and clinical evaluation of plantibodies for the prevention of transmission of infectious diseases.

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Over-the-Counter Drug Products

- Kevin J. Whaley, PhD
- Epicyte Pharmaceutical, Inc.
5810 Nancy Ridge Drive, Suite 150
San Diego, CA 92121
- FDA/CDER
- Over-the Counter Drug Products, Part 15 Hearing
June 28-29, 2000
8:30-4:30 pm

Mucosal Antibodies and Prevention

- 90% of all infections begin on a mucosal surface
- Mucosal antibodies help prevent mucosal infections

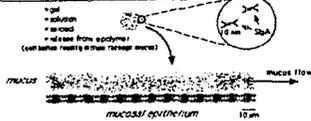
Examples of Mucosal Protection

Pathogen	Species	Route	Prevention
Virus			
Herpes Simplex	mouse	vaginal rectal	100%
100%			
Influenza	ferret	oral	100%
Rotavirus	human	oral	100%
Respiratory syncytial	monkey	nasal	3 to 4 log reduction in virus titre
Bacteria			
Chlamydia trachomatis	mouse	vaginal	90%
Clostridium difficile	hamster	oral	100%
Escherichia coli	human	oral	100%
Porphyromonas gingivalis	human	oral	100%
Shigella flexneri	human	oral	100%
Staphylococcus aureus	mouse	nasal	3 to 4 log reduction in CFU
Streptococcus mutans	human	oral	100%
Vibrio cholerae	mouse	oral	100%
Fungal			
Candida albicans	mouse	vaginal	50% reduction in CFU
Parasite			
Cryptosporidium parvum	mouse	oral	77% reduction in parasites

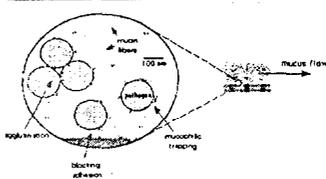
Prospective Double-Blind, Placebo Controlled Passive Immunization Studies for Prevention of Disease in Humans

Pathogen	Antibody	Route of antibody delivery	Prevention efficacy (%)
Escherichia coli	polyclonal	oral	100
P. gingivalis	monoclonal	oral	100
Rotavirus	polyclonal	oral	100
Shigella flexneri	polyclonal	oral	100
S. mutans	monoclonal	oral	100

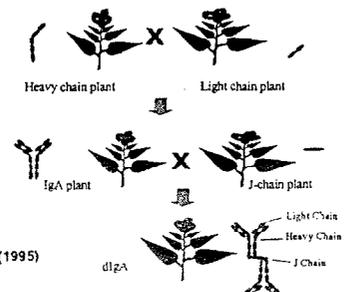
Antibodies can be delivered to mucosa via



If pathogens arrive, antibodies bind and trap them in mucus



ASSEMBLY OF ANTIBODIES BY CROSSING

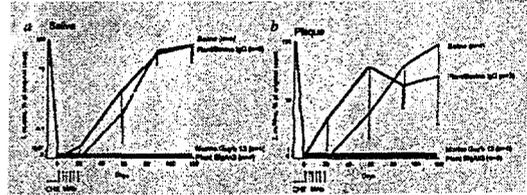


Science 268: 718-9 (1995)

A clinical trial with plantibody: anti-*Streptococcus mutans*

Ma et al., 1998. Characterization of a recombinant plant monoclonal secretory antibody and preventive immunotherapy in humans. *Nat Med* 4:601-606.

- Oral delivery of secretory plantibody
- 6 applications over 20 days
- Total plantibody delivered = 25 mg
- Clinical endpoint: preventing recolonization



- Recolonization prevented in 4 of 4 patients
- No adverse side effects
- No serum anti-plantibody response

Plantibodies as Mucosal Immunoprotectants

- Plantibodies are human antibodies produced in plants at low cost and at large capacity
- Plantibodies are purified from plants and formulated as pharmaceuticals
- Plantibodies will supplement and mimic the prevention role of mucosal antibodies

First Generation Plantibody Prevention Products

- A lubricant that prevents sexual transmission of HSV2
- A microbicide that prevents horizontal and vertical transmission of HIV
- An inhalant that prevents RSV infections in infants and the elderly
- An oral solution that prevents *C. difficile*

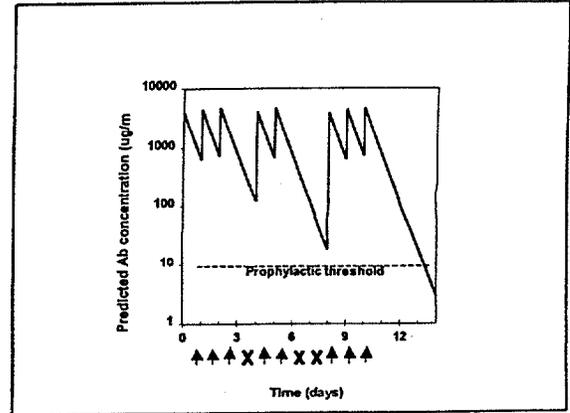
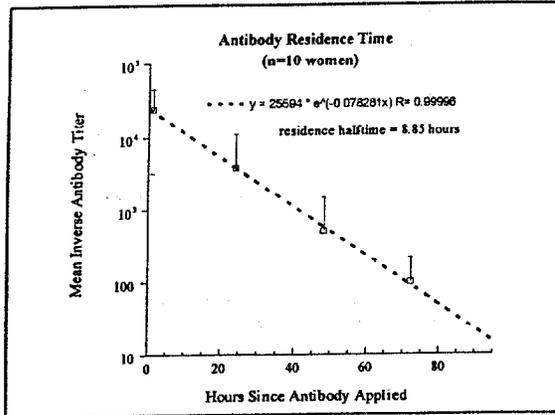
A Public Health and Market Opportunity for Microbicides

In 1999, 15.4 million people in the US acquired a new STD; STDs cause infertility, pregnancy complications, cervical cancer, infant mortality

- A safe, effective microbicide is viewed as a priority technology by women's health advocates, WHO, UNAIDS and NIH
- If vaginal microbicides can be made more user friendly and less prone to user failure, then acceptability and efficacy may be enhanced

Vaccines or Cures for STD Pathogens

Pathogen	Vaccine	Cure	Drug Resistance
<i>Chlamydia trachomatis</i>	no	yes	
<i>Haemophilus ducreyi</i>	no	yes	yes
Herpes simplex virus	no	no	yes
HIV	no	no	yes
Human papilloma virus	no	yes/no	
<i>Neisseria gonorrhoeae</i>	no	yes	yes
<i>Treponema pallidum</i>	no	yes	
<i>Trichomonas vaginalis</i>	no	yes	yes



Mucosal Protectants

- 1st Generation Plantibody Products: single target, one to several plantibodies
- 2nd Generation Plantibody Products: multiple targets, multiple plantibodies

Mucosal Protectants

- Individuals are exposed to a range of mucosal pathogens on a daily basis
- Strategies and technologies for preventing transmission of infectious diseases at mucosal surfaces are limited.
- Because accessibility is important for personal protection, one venue for transmission prevention products should be over-the-counter