Many Hosts of Mycobacteria – a ‘One Health’ Approach to Mycobacterial Diseases

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Tuberculosis

- Spread by aerosol route
- One third of world’s population is infected
- 4,000+ deaths every day from TB
- 8-10 million new infections every year
- Increasing incidence of TB in HIV-endemic areas
- Leading attributable cause of death in HIV infected individuals
- Worldwide emergence of drug-resistant TB (MDR-TB & XDR-TB)
- WHO-Declared Global Health Emergency

White Plague
Consumption

King Tutankhamen
John Keats
Elizabeth Barrett Browning
Edgar Allen Poe
Frederic Chopin
Ralph Waldo Emerson
Emily Bronte
Robert Louis Stevenson
Eleanor Roosevelt
George Orwell
Sanatorium for Tuberculosis in New York

Saranac Lake – 1875

Bronx – 1952
Mycobacteria

- *Mycobacterium tuberculosis* = TB
- *Mycobacterium leprae* = Leprosy
- *Mycobacterium avium* = common infection in AIDS patients
- *Mycobacterium bovis* = TB in livestock, wildlife and humans
- *Mycobacterium ulcerans* = Burili ulcer
Tuberculosis Infection and Disease Therapeutics

- Infection
- Initial containment – 95%
- Early Disease Progression - 5%
- Late Disease Progression - 5%
- Self-Cure – 90%
Tuberculosis Infection and Disease Therapeutics

Diagnostics

Vaccines

Drugs

Initial containment – 95%

Self-Cure – 90%

Late Disease Progression - 5%

Early Disease Progression - 5%

Infection

Initial containment – 95%

Self-Cure – 90%
Virulent *M. bovis* from tuberculous cow (1908) \( \times \) 231 passages on ox bile media over 13 years = BCG (1921)
BCG Vaccine Endorsed by the League of Nations in 1929
BCG: live attenuated *Mycobacterium bovis*

Limited and variable efficacy
Not recommended in HIV+ or immuno-suppressed infants

Protects infants against TB meningitis

Estimated 80-90% of infants worldwide receive BCG vaccine at birth
Better than BCG?

Is BCG the best vaccine platform?

Would a human adapted *Mycobacterium tuberculosis* derived vaccine can protect better against TB infection than an *M. bovis* (BCG) strain?
M. tuberculosis and Attenuation of M. bovis

RD1 = region of difference 1
Rational Attenuation of Mycobacteria

Virulent *Mycobacterium tuberculosis* from bovine mastitis infection

→ Passage 231 times on ox bile media

→ Attenuated *Mycobacterium bovis* vaccine (BCG)

→ Rationally attenuated *Mycobacterium tuberculosis* vaccine (*Mtb* ∆*leuCD* ∆*panCD* or *Mtb* ∆*RD1* ∆*panCD*)

Virulent *Mycobacterium bovis* from bovine mastitis infection

→ Precise null gene deletions (∆*RD1* and/or essential biosynthetic genes)
Pre-clinical animal models for TB vaccine development
Pre-clinical animal models for TB vaccine development
Neonates are not miniaturized adults

Giotto, ~1320

Raphael, ~1509
Overcoming Meeting Silos for Mycobacteria
Experimental and Natural Mycobacterial Infections

- Humans
- M. tuberculosis
- Mice
- M. bovis
- Guinea pigs
- M. leprae
- Cotton rats
- M. marinum
- Rabbits
- M. avium spp paratuberculosis
- Non-human primates
- M. ulcerans
- Cattle
- M. mungi
- Deer
- M. mungi
- Possum
- M. mungi
- Elephants
- M. mungi
- Armadillos
- M. mungi
- Fish
- M. mungi
- Mongoose
Many Hosts of Mycobacteria Meeting Series

- Small (70-90 people)

- Discussion based meeting
  - Very limited powerpoint
  - Discuss/debate big questions
  - NOT everyone giving their standard 20 or 40 minute talk

- Diverse perspectives
  - Basic Researchers
  - Human Clinicians
  - Veterinary Medicine Clinicians
  - Veterinary Medicine Researchers

- Range of research/clinical/funding settings
  - Academic researchers
  - Clinical microbiology
  - Government (NIH, USDA, VHLS)
  - Zoos
  - National Parks
  - Biotech
  - NGOs

- Priority
  - Early/mid-career
  - Attendees from mycobacterial disease endemic areas
  - Women and/or minorities
## Many Hosts of Mycobacteria (MHM) Meetings

<table>
<thead>
<tr>
<th>Meeting</th>
<th>Year</th>
<th>Location</th>
<th>Theme</th>
</tr>
</thead>
<tbody>
<tr>
<td>MHM I</td>
<td>2007</td>
<td>National Animal Diseases Center (USDA), Ames, IA</td>
<td>Many Hosts of Mycobacteria</td>
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<tr>
<td>MHM II</td>
<td>2008</td>
<td>Gettysburg, PA</td>
<td>Immunopathology</td>
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<tr>
<td>MHM III</td>
<td>2009</td>
<td>Former Leprosy Sanatorium, Carville, LA</td>
<td>Comparative Mycobacteriology</td>
</tr>
<tr>
<td>MHM IV</td>
<td>2011</td>
<td>Lowry Park Zoo, Tampa, FL</td>
<td>Biomarkers</td>
</tr>
<tr>
<td>MHM V</td>
<td>2012</td>
<td>NIH, Bethesda, MD</td>
<td>Translational Science</td>
</tr>
<tr>
<td>MHM VI</td>
<td>2015</td>
<td>Tulane National Primate Center, Covington, LA</td>
<td>Host Specificity and Disease Dynamics</td>
</tr>
<tr>
<td>MHM VII</td>
<td>2017</td>
<td>Colorado State University, Ft. Collins, CO</td>
<td>Bringing Science into the Community</td>
</tr>
<tr>
<td>MHM VIII</td>
<td>2019</td>
<td>Albert Einstein College of Medicine, Bronx, NY</td>
<td>Back to the Future</td>
</tr>
</tbody>
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**MHM VIII: ‘Back to the Future’** Albert Einstein College of Medicine, Bronx, NY  
March 4-6<sup>th</sup>, 2019  
Please contact michelle.larsen@einstein.yu.edu if you or a colleague are interested.
Many Hosts of Mycobacteria
Tuberculosis, Leprosy and other Mycobacterial Diseases of Man and Animals

Edited by Harshini Mukundan, Mark A. Chambers, W. Ray Waters and Michelle H. Larsen
Banded mongoose (Mungos mungo)
Wildlife-Associated MtbComplex Organisms

- gr. 1, TbD1 intact- "ancestral" *M. tuberculosis*
- gr. 1, e.g. Beijing
- gr. 2, e.g. CDC1551
- gr. 3, e.g. H37Rv

TbD1 deleted- "modern" *M. tuberculosis*

- *M. africanum* subtype 1 (b) (West-African 1 Lineage)
  - *M. africanum* subtype 1(a) sublineage 1
  - *M. africanum* subtype 1(a) sublineage 2
  - *M. africanum* subtype 1(a) sublineage 3

- Chimpanzee bacillus
- *M. mungi* (banded mongoose bacillus)
- Dassie bacillus
- *M. suricatae* (meerkat bacillus)
  - *M. oryxis* (oryx bacillus)
  - *M. microti* (vole bacillus)
  - *M. pinnipedii* (seal bacillus)
  - *M. caprae* (goat bacillus)
  - *M. bovis* (bovine bacillus)
  - *M. bovis* BCG

Wildlife-associated lineage six MtbC

☆ = known outbreak of wildlife-associated lineage six MtbC
Emerging Tuberculosis Pathogen Hijacks Social Communication Behavior in the Group-Living Banded Mongoose (Mungos mungo)

Kathleen A. Alexander, Claire E. Sanderson, Michelle H. Larsen, Suelee Robbe-Austerman, Mark C. Williams, Mitchell V. Palmer

Department of Fish and Wildlife Conservation, Virginia Tech, Blacksburg, Virginia, USA; C and Land Use, Kasane, Botswana; Department of Medicine, Albert Einstein College of Medicine, New York, USA; Veterinary Services Laboratories, Ames, Iowa, USA; University of Pretoria, Onderstepoort Disease Center, Pretoria, South Africa
**Mycobacterium mungi**

The only known MTBC species that has not been successfully cultured in vitro.

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**Draft Genome Sequence of the Mycobacterium tuberculosis Complex**

Pathogen *M. mungi*, identified in a Banded Mongoose (*Mungos mungo*) in Northern Botswana

Kathleen A. Alexander,* Michelle H. Larsen,* Svelee Rööbe-Austerman,* Tod P. Stubber,* Patrick M. Camp*
RD1 Deletions in Wildlife-Associated MtbC
One Health and Mycobacterial Diseases

We shall not cease from exploration. And the end of all our exploring Will be to arrive where we started And know the place for the first time.

T.S. Eliot
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Many Hosts of Mycobacteria Book
Many Hosts of Mycobacteria Meetings
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