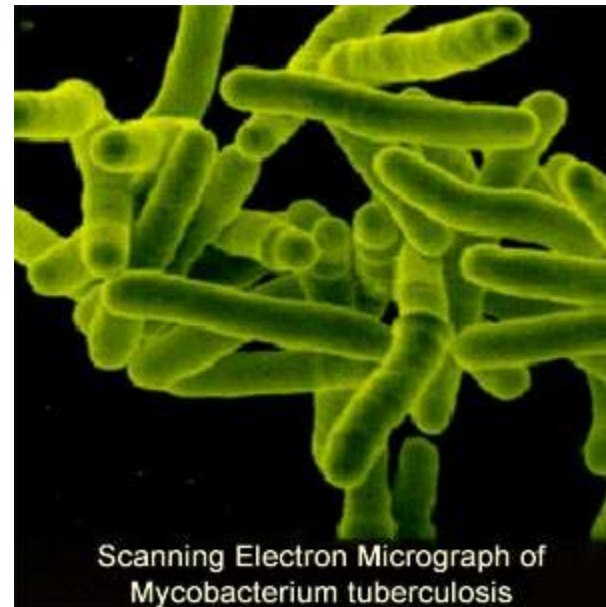


Strategies for mitigating the global health threat of TB

www.stonybrook.edu

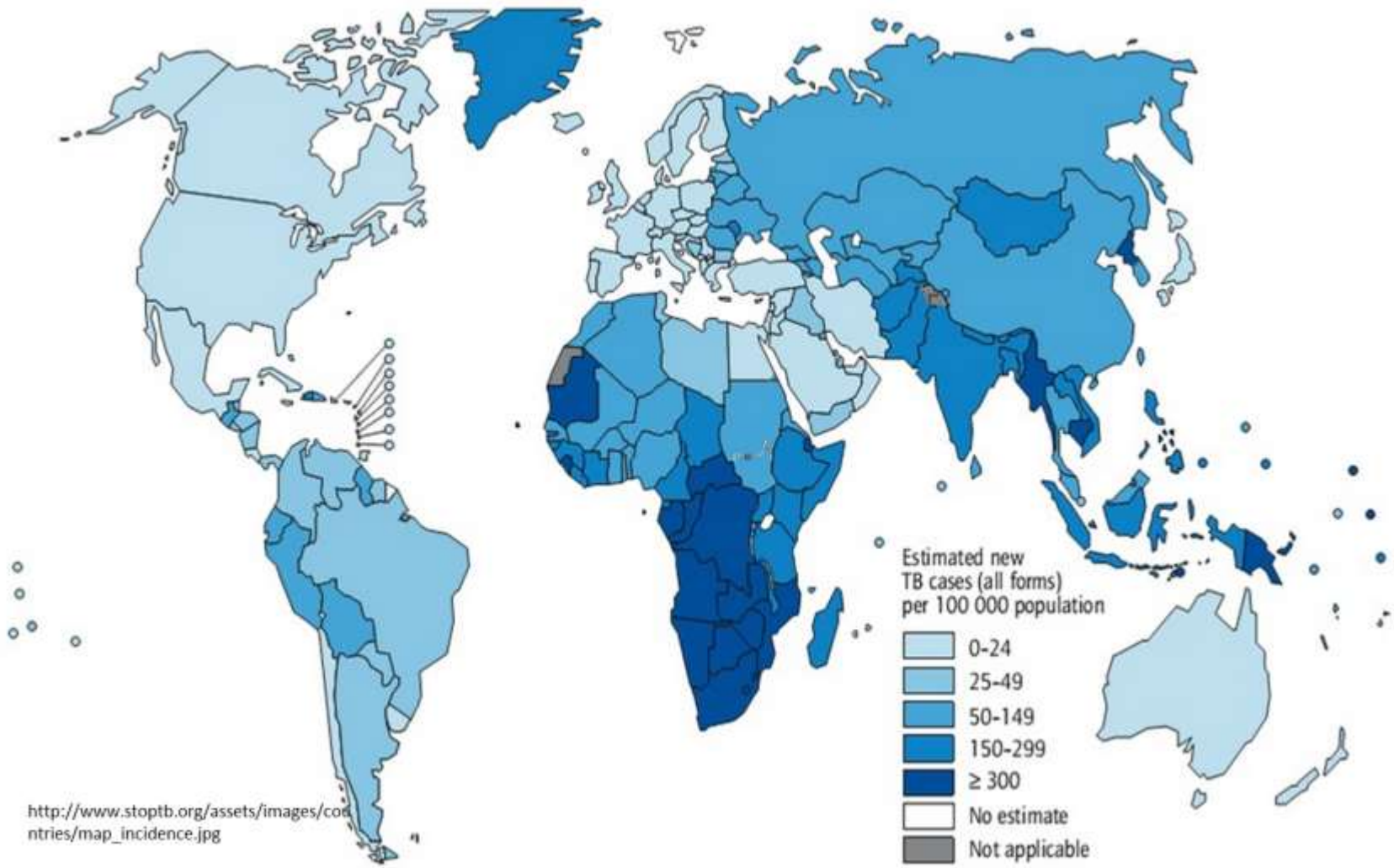
Vassie C. Ware, Ph.D.
Bioscience in the 21st Century
November 8, 2013



Scanning Electron Micrograph of
Mycobacterium tuberculosis

- **TB FACTS**
- **WHO STOP TB STRATEGY 2006-2015**
- **RECALL LESSONS LEARNED: Key concepts from previous infectious disease lectures**
- **Challenges in diagnosis, prevention, and cure of TB**
- **Selected Highlights in TB Research**
 - **Mycobacterial physiology**
 - **Diagnostic devices**
 - **Mycobacteriophage genomics**
 - Hatfull video clip (iBioseminar series, part 3)**
 - Phages and TB diagnostics**
 - Phages and therapy: challenges**
 - Lehigh's SEA-PHAGES Program**
- **Acknowledgments**

Tuberculosis FACTS



http://www.stoptb.org/assets/images/countries/map_incidence.jpg

World Health Organization 2006 TB Facts

- **Nearly 2 million deaths are caused by TB every year**
- **TB is curable but kills 5000 people every day**
- **TB is a disease of poverty; virtually all TB deaths are in the developing world affecting mostly young adults who are poor and malnourished**
- **TB is leading killer among those infected with HIV. 250,000 deaths are HIV-associated (most in Africa)**
- **Global TB incidence is still growing due to rapid increase in Africa**
- **2 BILLION people (1/3 of world's population) are infected with TB microbes**
- **Multi-drug-resistant TB does not respond to standard drug treatment. MDR-TB is found globally with 450,000 new cases arises every year. Highest rates of MDR-TB in countries of the former Soviet Union and China.**

- Tuberculosis (TB) is second only to HIV/AIDS as the greatest killer due to a single infectious agent.
- In 2011, 8.7 million people fell ill with TB and 1.4 million died from TB.
- In 2010, there were about 10 million orphan children as a result of TB deaths among parents.
- Over 95% of TB deaths occur in low- and middle-income countries.

WHO GOALS

The TB targets:

2005: detect at least 70% of sputum smear (+) and treat successfully 85% of detected cases

2015: Millennium Development Goals to have halted and begun to reverse TB incidence; and halve prevalence and deaths in comparison to 1990

The NEW STOP TB STRATEGY

- Pursue expansion of DOTS (directly observing therapy-short course)
- Address TB/HIV, MDR-TB
- Contribute to health system strengthening
- Engage all care providers
- Empower people with TB and communities
- Enable and promote research

Lessons learned for today's TB discussion

Infectious agents: bacteria, viruses

Emerging disease

Multi-drug resistance

Antibiotic resistance

Role of multiple drug cocktails

Dearth of new antibiotics

Low cost diagnostic tools

Spread of TB

TB disease progression

TB latent infection

Challenges in diagnosis, prevention, and cure of TB

DISCUSSION

SELECTED HIGHLIGHTS in TB RESEARCH

- **Mycobacterial Physiology**

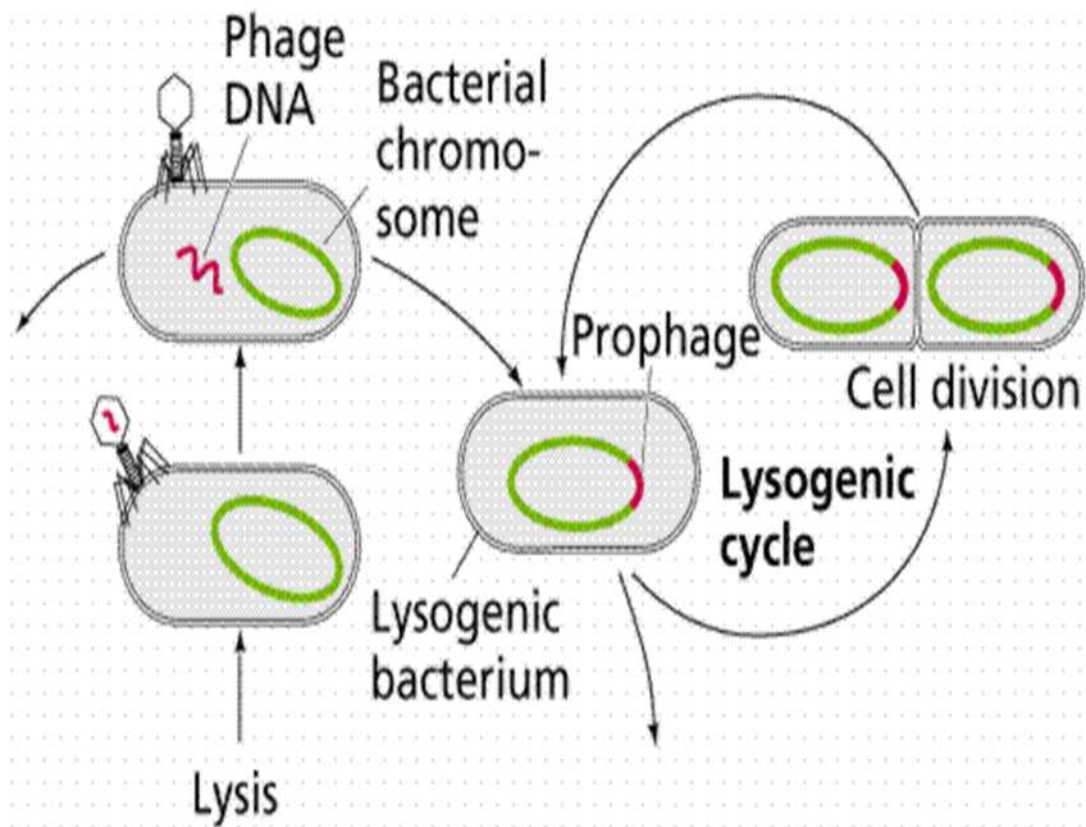
Identification of key enzymes in the metabolism of carbon within the bacterial cell. Biochemical and genetics studies to mutate enzymes to determine effect on bacterial viability within lung tissue (see McKinney iBioseminar, part 4)

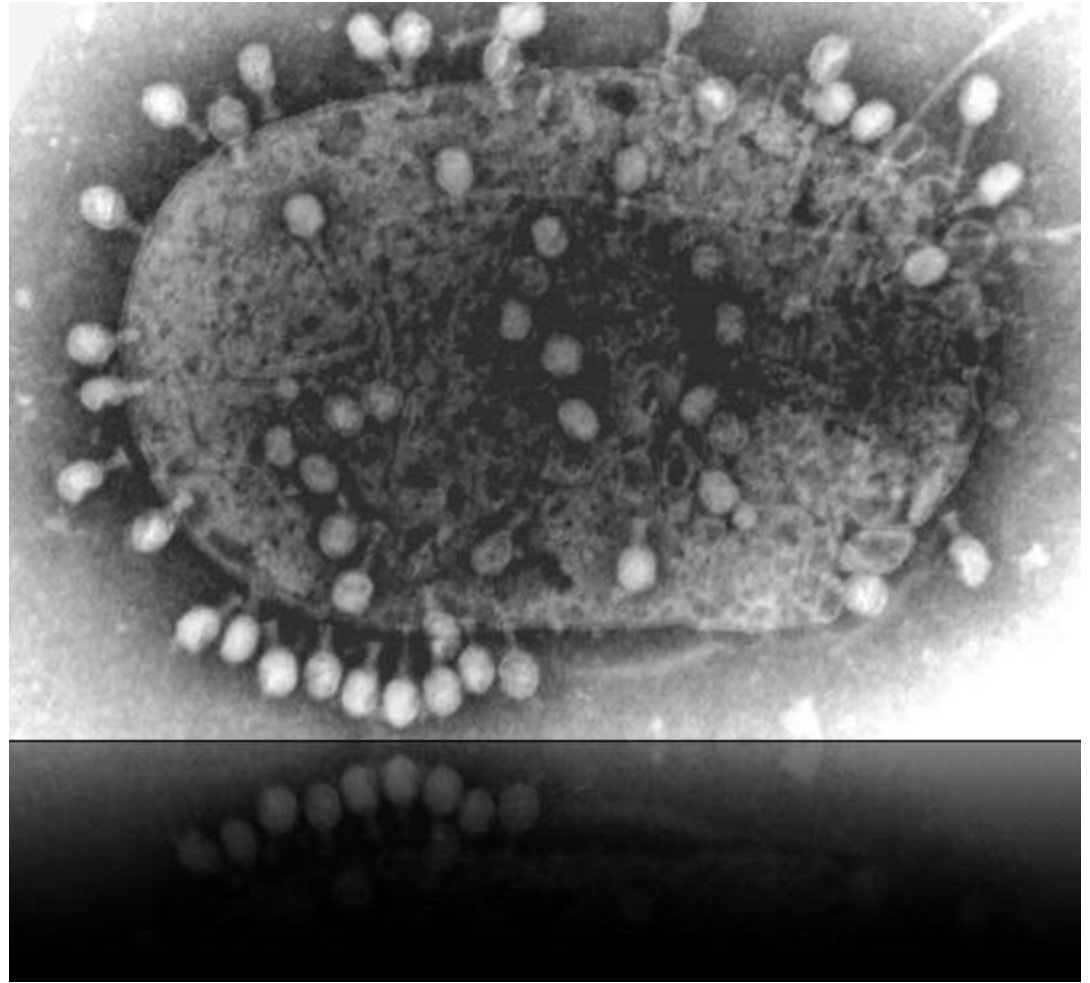
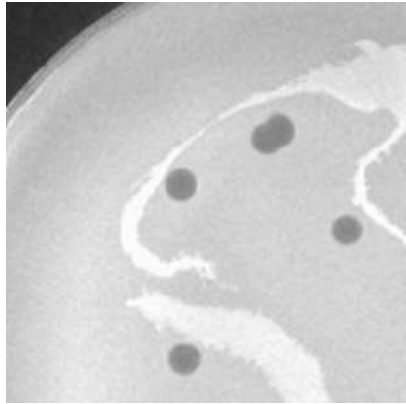
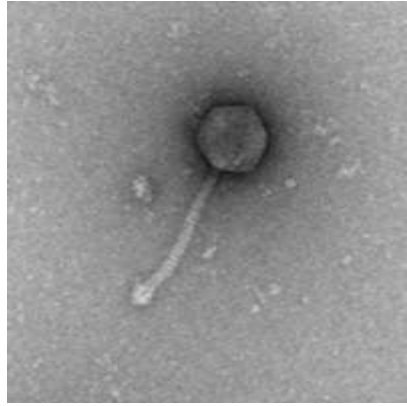
- **Diagnostic Devices**

Development of new microfluidic devices using Bio-Micro-Electro-Mechanical Systems (MEMS) technology for faster and better diagnoses of TB infection. Using molecular biology techniques for detection, these devices will provide a TB diagnosis in < 1 day (compared to minimum of 1 week for some traditional methods). Systems are disposable-type testing cartridge for rapid preparation of a sputum sample that mixes with premixed reagents and media. TB tester project is a collaboration between industry (InterScience, Inc.) and academia (UAlbany, Albert Einstein College of Medicine, SUNY Downstate Medical Center).

- **Mycobacteriophage genomics**

Hatfull iBioseminar clip, part 3 (view first 7 minutes of iBioseminars.org)





Mycobacteriophage genomics continued:

Phages and TB diagnostics:

- Molecular biology engineering of phage genome to include gene for luciferase (firefly) or green fluorescent protein (jelly fish). Infection of Mycobacterium with phage (carrying “light” gene) allows amount of light to be measured when there is a productive infection (indicates Mycobacteria are present in patient sample). The amount of light is correlated with the numbers of live bacteria.

- Use of “light-carrying” phage to determine sensitivity of Mycobacteria in patient sample to drugs. Add drug and determine if light goes “out” (indicative of dead bacteria killed by the drug) or if light stays “on” (indicates bacteria are still alive and resistant to drug).

Phages and TB therapy: advantages and challenges

Advantages:

- Phages typically infect one bacterial type (or very closely related types)
- Phages are plentiful in the biosphere (10^{31} !!!)
- Phages require bacteria for replication; therefore they replicate where the pathogen resides (if accessible)
- Generally thought to be safe (commonly used prior to antibiotic revolution after WWII)
- Indiscriminate against antibiotic-sensitive and antibiotic-resistant bacteria

Challenges:

- More research needed to determine efficacy and safety
- Accessibility challenges for pathogens that are intracellular (like TB at certain stages)
- Delivery challenges to get to target and to avoid neutralization by immune system
- Can be carriers of other genetic material and deliver to bacterial pathogen (transduction)

Lehigh's contributions to the TB Story:



AND

Mountaintop TB Pilot Summer 2013

Lehigh.edu/~insea

See Lehigh.edu for news stories about Mountaintop Pilot Projects

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Professor Kelly Austin (Department of Sociology & Anthropology)

Global Health Students

HHMI