TB/HIV Research Scale-Up for the Next 10 Years: An NIH Perspective

Anthony S. Fauci, M.D.
Director
National Institute of Allergy and Infectious Diseases
National Institutes of Health
July 21, 2012
Tuberculosis and HIV/AIDS

- Of 34 million people living with HIV, ~1/3 are co-infected with TB

- TB is the leading cause of death among HIV-infected people worldwide

- TB accelerates the replication of HIV

- HIV accelerates progression of TB
Key TB Research Areas in the Era of HIV/AIDS

- Pathogenesis
- Diagnostics
- Therapeutics
- Prevention
Key TB Research Areas in the Era of HIV/AIDS

- Pathogenesis
- Diagnostics
- Therapeutics
- Prevention
TB Pathogenesis

- Bridge basic and clinical research to understand fundamental questions, e.g., mechanisms of latency, correlates of immunity

- A better understanding of TB pathogenesis will inform the development of new interventions

- Need for TB biomarkers

- Need to understand the host, the pathogen and their complex interactions -- systems biology
Key TB Research Areas in the Era of HIV/AIDS

- Pathogenesis
- Diagnostics
- Therapeutics
- Prevention
Sensitive Detection of TB and Rifampin Resistance in < 2 hours with Minimal Hands-on Time

Rapid Molecular Detection of Tuberculosis and Rifampin Resistance

CC Boehme, DA Alland, MD Perkins, et al.
Severe Limitations in TB Diagnostics

- In most settings, diagnostics are antiquated

- Critical needs:
  - Point-of-care
  - Simple, accurate, inexpensive
  - Relevant for clinical specimens from multiple body sites
Key TB Research Areas in the Era of HIV/AIDS

- Pathogenesis
- Diagnostics
- Therapeutics
- Prevention
TB Therapeutics: Current Challenges

- 6-9 month regimens with multiple drugs
- Patient noncompliance and insufficient medical monitoring
- Drug resistance
- Drug-drug interactions, e.g., antiretrovirals
TB Drug Discovery

1940-1943 Streptomycin
1948 PAS
1952 Isoniazid
1954 Pyrazinamide
1955 Cycloserine
1957 Kanamycin
1960 Ethionamide
1961 Ethambutol
1963 Capreomycin
1963 Rifampicin

49 Years

Adapted from Ma and Lienhardt, Clin Chest Med, 2009
Key Goals in TB Drug R&D

- Shorten duration and simplify treatment regimens for drug-sensitive and MDR/XDR TB
- Expand drug pipeline against old and new targets
- Test drugs as combinations
- Expand clinical trials capacity
- Improve TB drug regimens used in treating HIV/TB co-infected individuals
Integration of Antiretroviral Therapy with Tuberculosis Treatment
Salim S. Abdool Karim, et. al.

Timing of Antiretroviral Therapy for HIV-1 Infection and Tuberculosis
Diane V. Havlir, et. al.

Earlier versus Later Start of Antiretroviral Therapy in HIV-Infected Adults with Tuberculosis
Francois-Xavier Blanc, et. al.
Key TB Research Areas in the Era of HIV/AIDS

- Pathogenesis
- Diagnostics
- Therapeutics
- Prevention
Antiretrovirals and Isoniazid Preventive Therapy in the Prevention of HIV-Associated Tuberculosis in Settings with Limited Health-Care Resources

SG Lawn, GJ Churchyard et al.

**ART** reduced TB incidence by 67% in 9 observational cohorts; n = ~38,000
Tuberculosis Vaccine

- BCG not effective in preventing adult pulmonary TB, the most transmissible form of the disease

- BCG no longer recommended in HIV co-infected children

- New safe and effective vaccines against all forms of TB are urgently needed
Tuberculosis Vaccines: A Strategic Blueprint for the Next Decade

MJ Brennan and J Thole

Transforming Biomedical Research to Develop Effective TB Vaccines: The Next Ten Years

C Sizemore and AS Fauci
“I am in the process of exploring the possibility... of utilizing our HIV/AIDS clinical trials networks for the implementation of similar clinical trials capacities for TB as well as other infectious diseases.”
### Six Major NIAID-Funded HIV/AIDS Clinical Trials Networks

<table>
<thead>
<tr>
<th>Network</th>
</tr>
</thead>
<tbody>
<tr>
<td>AIDS Clinical Trials Group (ACTG)</td>
</tr>
<tr>
<td>HIV Prevention Trials Network (HPTN)</td>
</tr>
<tr>
<td>HIV Vaccine Trials Network (HVTN)</td>
</tr>
<tr>
<td>International Maternal Pediatric Adolescent AIDS Clinical Trials Group (IMPAACT)</td>
</tr>
<tr>
<td>International Network for Strategic Initiatives in Global HIV Trials (INSIGHT)</td>
</tr>
<tr>
<td>Microbicide Trials Network (MTN)</td>
</tr>
</tbody>
</table>

**Expanded to include TB**
TB/HIV Research Scale-Up for the Next 10 Years: Reasons for Optimism

- Commitment to funding
- Robust research pipelines
- Powerful new research tools
- Progress in HIV-TB management
- Increased TB clinical trial capacity through HIV/AIDS networks
- Partnerships, e.g., PEPFAR