



Partnership Between TB Diagnostics and Vaccines: The Promise and Reality

Richard O'Brien, FIND

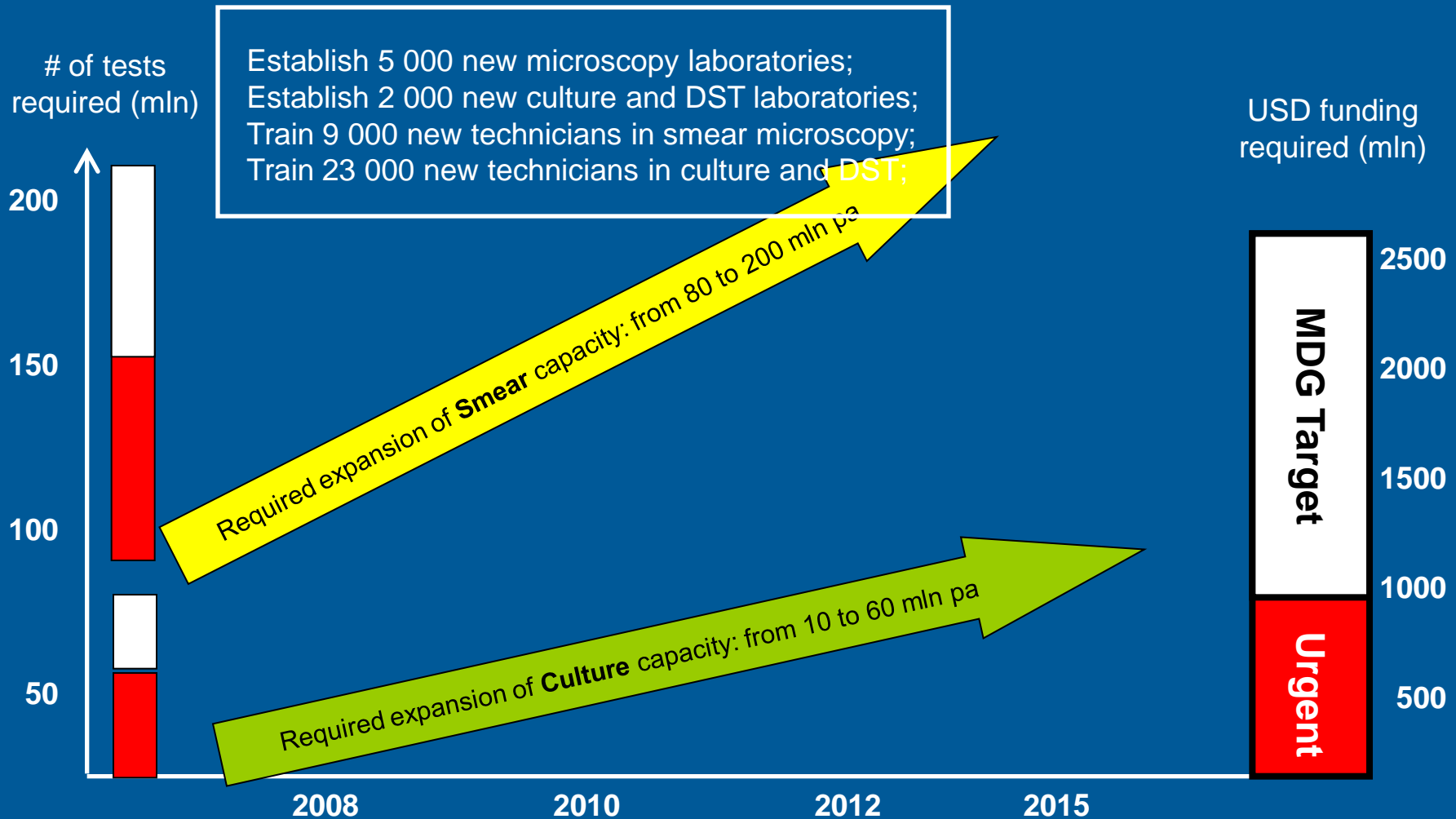
TB Vaccines – A Second Global Forum

23 September 2010, Tallinn, Estonia

Partnering for better diagnosis for all

Global Laboratory Capacity Gap

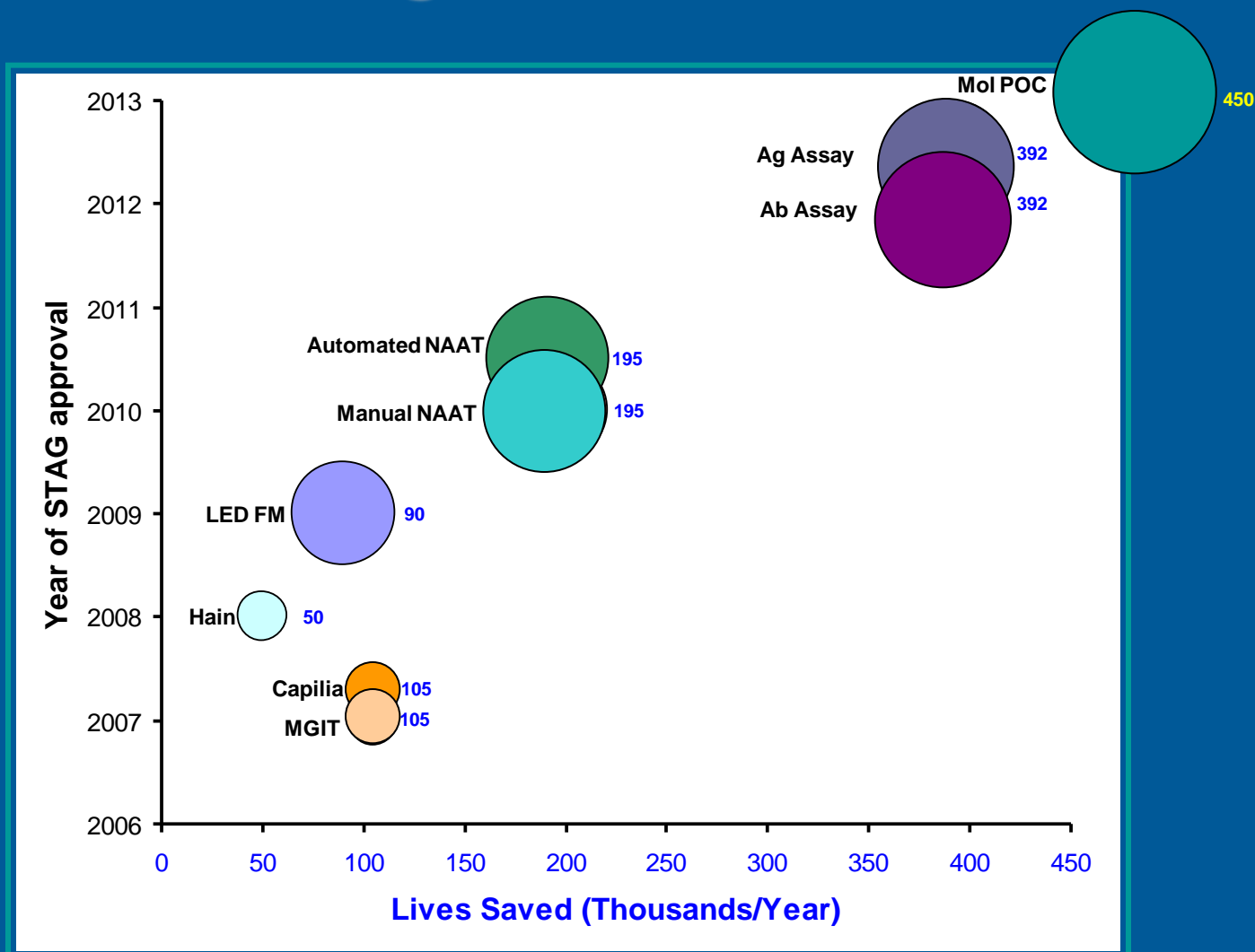
To reach MDG targets, a global capacity need of **120 million smears**, **60 million cultures** and **6 million DST investigations** must be met by 2015, requiring at least **6.1 billion USD** by 2015



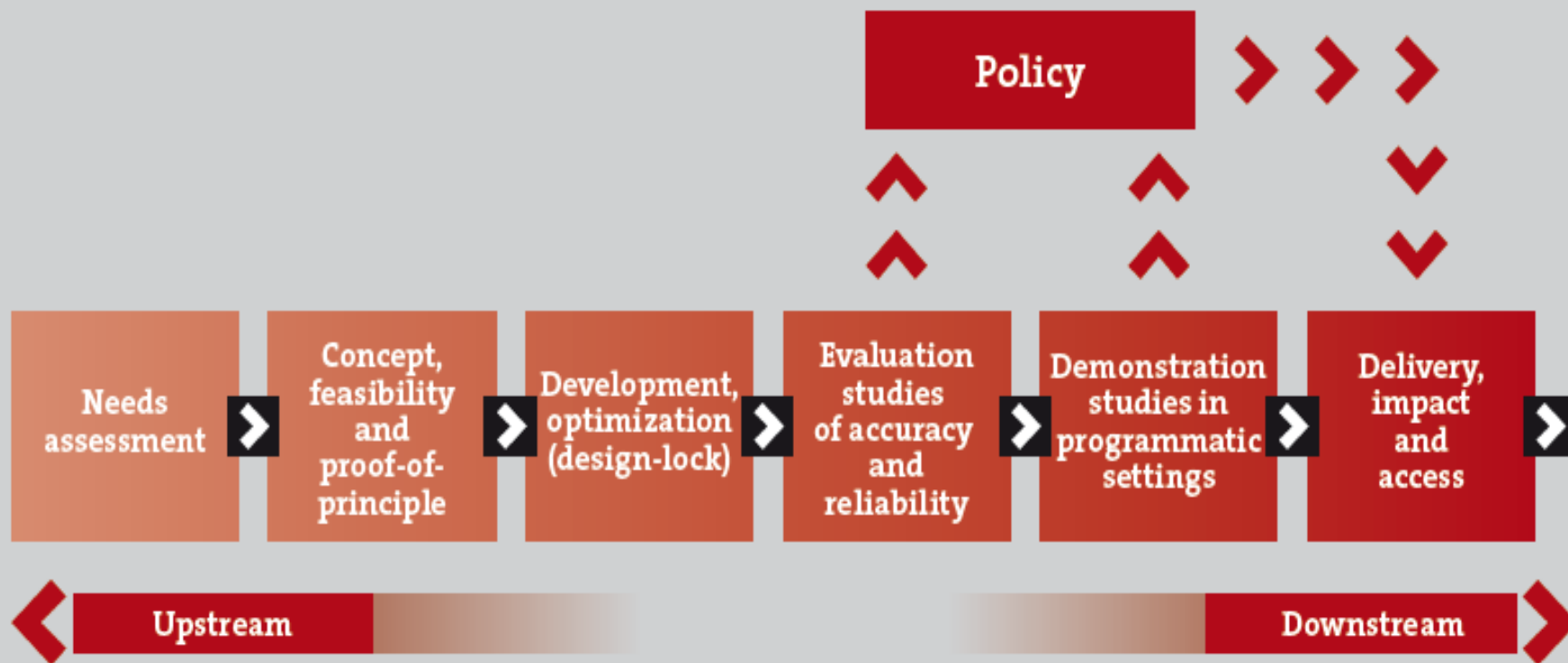
TB Diagnostic Research Priorities

- Point of care test for case finding
- Rapid detection of drug resistance
- Rapid test for AFB smear-negative TB: HIV-infected persons, children, EPTB
- Assessment of new diagnostic algorithms
- Impact assessment
 - Case detection
 - M/XDR TB detection
 - LTBI detection
- Predictive test for LTBI

Potential Impact of New TB Diagnostics



TB Diagnostics Pathway*

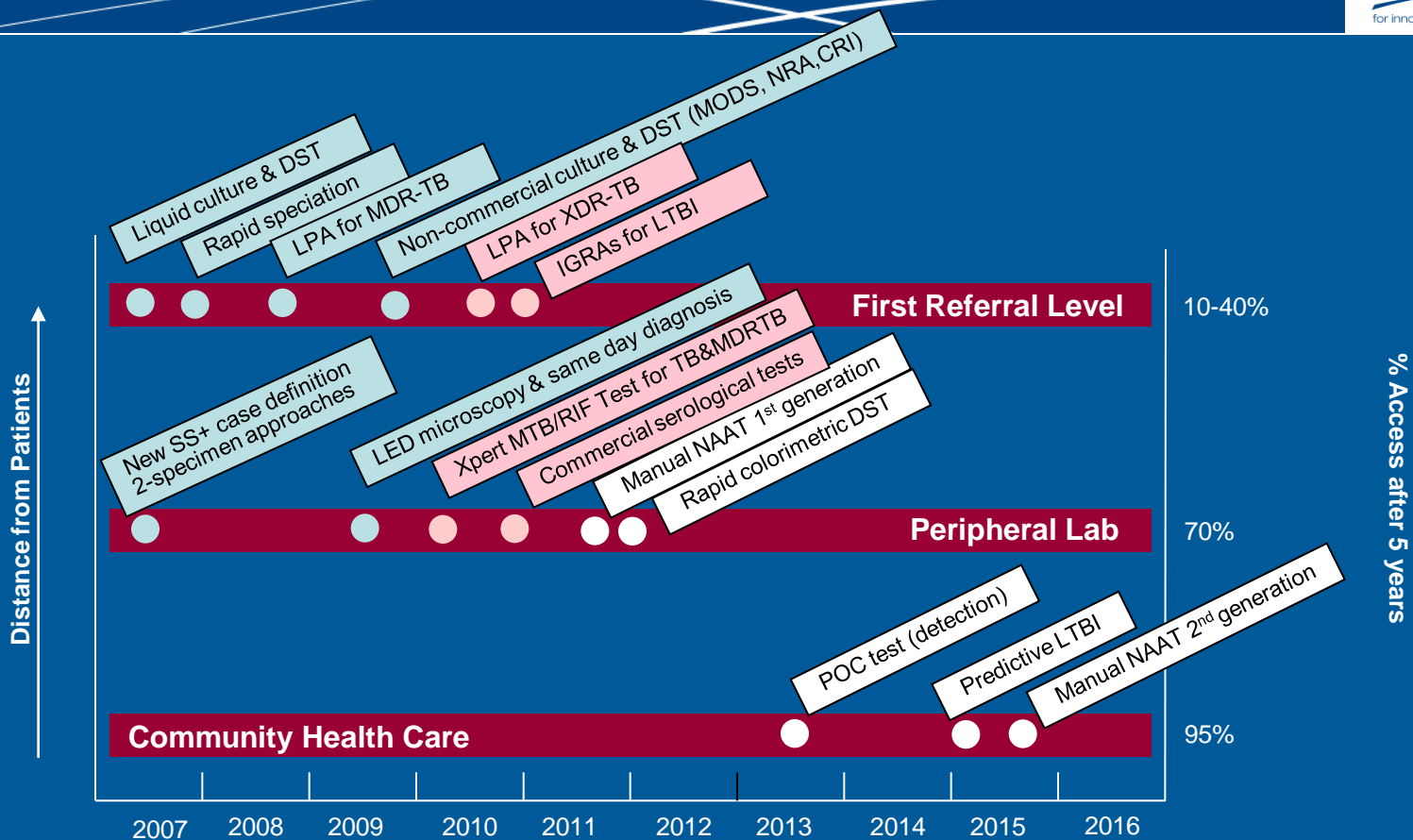


*Stop TB New Diagnostics Working Group: A blueprint for the development of TB Diagnostics, 2009

WHO Policy on Implementing New Tools*

- Identifying the need for a policy change
 - WHO monitoring of technical developments
 - Requests from interested outside parties
- Reviewing the evidence
 - Use of standardized criteria for assessing available data
 - Systematic review and meta-analyses
 - GRADE approach for rating the strength of a recommendation
- Convening an expert panel to review evidence and draft recommendations
- Assessing draft policy and evidence by STAG-TB
- Formulating and disseminating policy

*http://www.who.int/tb/advisory_bodies/research_to_policy/en/index.html



Abbreviations

- DST: Drug Susceptibility Test
- NAAT: Nucleic Acid Amplification Test
- LTBI: Latent TB Infection
- POC: Point of Care
- MODS: Microscopic observation drug-susceptibility
- NRA: Nitrate reductase assay
- CRI: Colorimetric redox indicator assay
- LED: Light-emitting diode
- LPA: Line probe assay

- Technologies or processes endorsed by STAG/WHO
- Technologies for which WHO review is in process

Collaboration in TB Vaccine and Diagnostics Research

- Discovery
- Sharing biobanks
- Maximizing clinical trials resources
- Assessment of new TB diagnostic tests in vaccine clinical trials
- Advocacy and resource mobilization

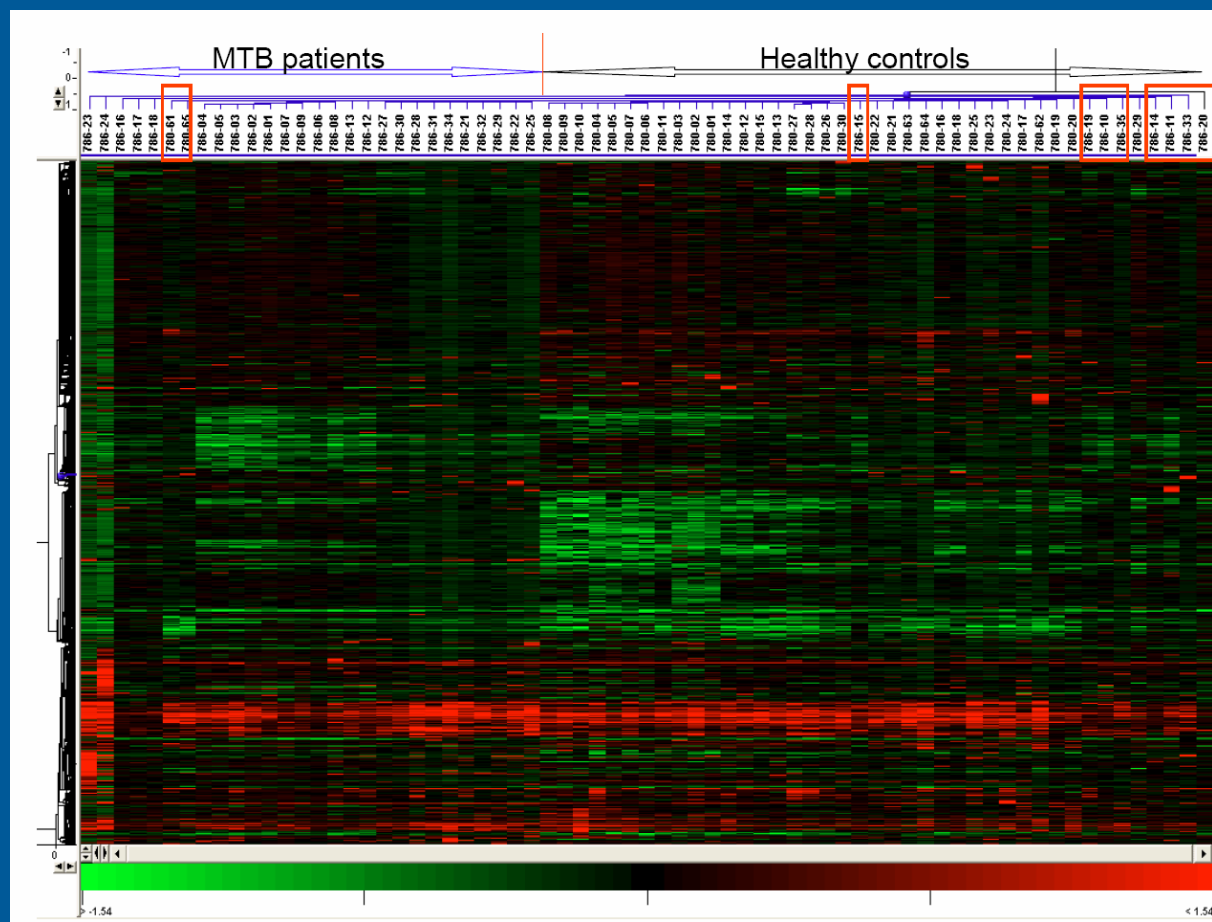
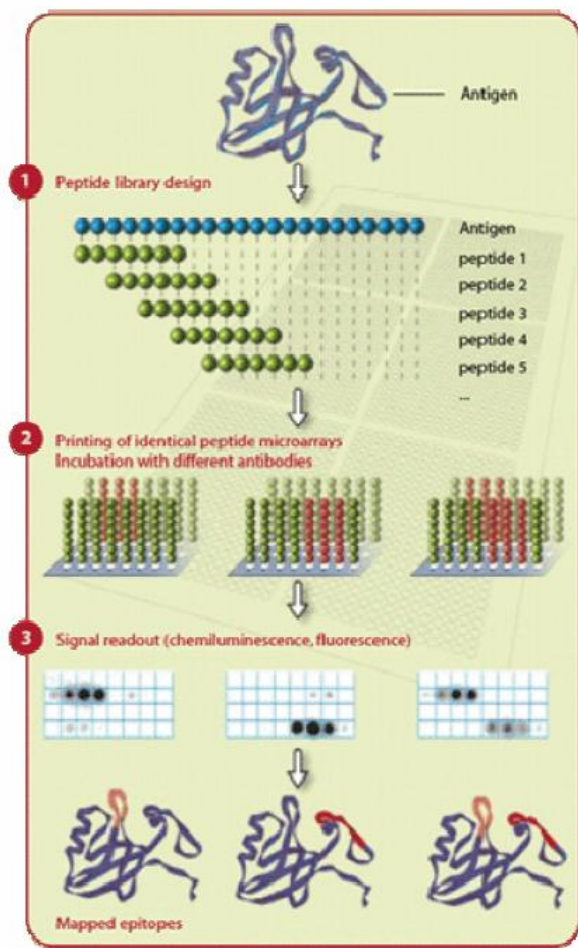
Collaboration in TB Vaccine and Diagnostics Research

- Discovery research – similar tools but different biologic approaches
- Sharing biobanks
- Maximizing clinical trials resources
- Assessment of new TB diagnostic tests in vaccine clinical trials
- Advocacy and resource mobilization

Anti-Mtb Antibody Profiling

Overlapping Peptide Arrays

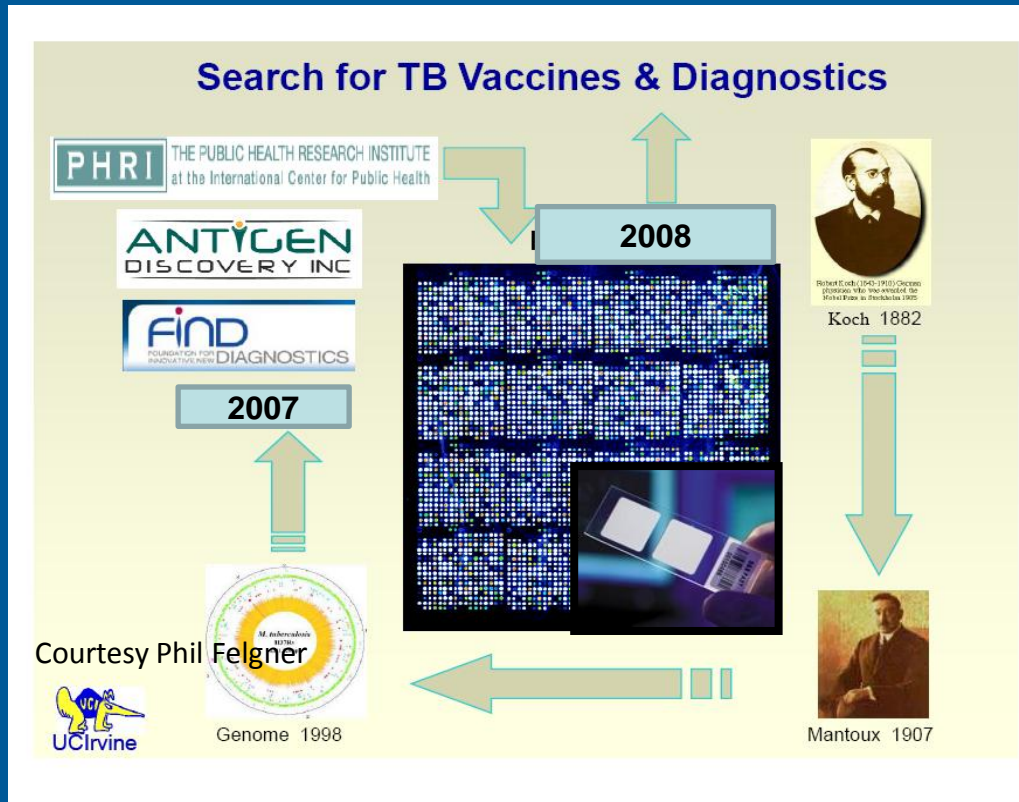
Courtesy of Markus Maeurer



Collaboration in TB Vaccine and Diagnostics Research

- Discovery research
- Sharing biobanks – desired biologic specimens come from different populations
- Maximizing clinical trials resources
- Assessment of new TB diagnostic tests in vaccine clinical trials
- Advocacy and resource mobilization

On the way to a POC – The search for AB sets



- Whole proteome screen completed
- 1000 samples from 10 countries
- Target protein set identified for HIV+/HIV-
- IP filed

What's next:

- Validation of identified Ab patterns w Luminex / overlapping peptide approach
- Final Ab sets will require confirmatory testing in large sample set
- Prototype assays for first field studies expected for July 2010

Collaboration in TB Vaccine and Diagnostics Research

- Discovery research
- Sharing biobanks
- Maximizing clinical trials resources, e.g., trial sites, use of CROs
- Assessment of new TB diagnostic tests in vaccine clinical trials
- Advocacy and resource mobilization

Collaboration in TB Vaccine and Diagnostics Research

- Discovery research
- Sharing biobanks
- Maximizing clinical trials resources
- **Assessment of new TB diagnostic tests in vaccine clinical trials – limited opportunities**
- Advocacy and resource mobilization

Title: Tuberculin skin test and Interferon- γ release assay in infants and young children suspected of having tuberculosis in a high incidence setting

Study team:

¹Sizulu Moyo, ¹Fatima Isaacs, ³Sebastian Gelderbloem, ²Suzanne Verver, ³Anthony Hawkrige, ¹Mark Hatherill, ¹Michele Tameris, ¹Hennie Geldenhuys, ¹Lesley Workman, ⁴Madhukar Pai, ¹Gregory Hussey, ¹Willem A. Hanekom, ¹Hassan Mahomed

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²KNCV Tuberculosis Foundation, the Netherlands and CINIMA, Academic Medical Centre Amsterdam, The Netherlands.

³Aeras Global Tuberculosis Vaccine Foundation, USA,

⁴Department of Epidemiology & Biostatistics, McGill University, Canada

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The SATVI study compared TST and QFT in children <3 years old evaluated for TB disease in SA. Among 397 children with both TST and QFT results, 68 (17%) were QFT positive and 72 (18%) were TST positive (≥ 10 mm). Agreement between the tests was excellent (94%; kappa = 0.79(95% CI 0.69-0.89). TB disease was diagnosed in 52/397 (13%) of participants: 3 classified as definite, 35 probable, and 14 possible TB. QFT sensitivity and specificity for any TB disease were 38% and 81% respectively, while TST sensitivity and specificity were 35% and 84% respectively.

Title: A comparison of the QuantiFERON Gold In-Tube assay with the tuberculin skin test in TB infection and disease in South Indian infants

Study team:

Nelson J¹, Sumithra RS¹, Kenneth J¹, Bennet S², Doherty M³, Pai M⁵, Vaz M^{1*}, Grewal HMS^{4*}: TB Trials Study Group†

1. St. John's Research Institute, Bangalore, India.
2. Aeras Global TB Vaccine Foundation, Rockville, MD, USA.
3. Statens Serum Institute Copenhagen, Denmark.
4. The Gade Institute, University of Bergen and Haukeland Hospital, Bergen, Norway.
5. McGill University, Montreal, Canada

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Of the 641 infants admitted in the case verification ward, 43 infants (6.7%) were TST positive at a cut off of 10mm, 269 infants (42%) were TST positive at cut off of 5 mm and 32 infants (5%) were QFT positive. The indeterminate rate for QFT was 1.25% (8/641). The single bacteriologically confirmed infant with TB disease was TST positive and QFT positive. Of the 9 probable TB cases, none were QFT positive or TST positive at a cut off of 10 mm. This study did not have the power to determine the role of QFT in active TB diagnosis, but the fact that none of the probable cases were QFT or TST (10mm) positive suggests that all immune-based LTBI tests may perform poorly in this subgroup.

Collaboration in TB Vaccine and Diagnostics Research

- Discovery research
- Sharing biobanks
- Maximizing clinical trials resources
- Assessment of new TB diagnostic tests in vaccine clinical trials
- **Advocacy and resource mobilization – Stop TB Partnership**