Stop TB Partnership

New Diagnostics Working Group

Annual Meeting 2014

Barcelona, 29 October 2014

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Co-Chair, NDWG

New Diagnostics Working Group

Fostering development of new diagnostic tools for TB

Vision

High quality diagnosis of tuberculosis and drug resistance is available for all people in all settings.

Mission

Foster development and evaluation of new diagnostics for tuberculosis by serving as a coordination, communication and advocacy platform for all stakeholders in TB diagnostic research and development.

Connecting partners

The NDWG serves as **a forum for stakeholders**, provides a coordination and communication platform for effective collaboration and develops technical resources towards delivery of new TB diagnostics, by

1. Assuring coordination between partners
2. Establishing mechanisms for strategic information and knowledge sharing
3. Identifying and promoting promising innovation
4. Advocating for new TB diagnostics, for increased funding for TB diagnostic R&D and for evidence-based decision making to drive WHO policy

Five priority actions to address the MDR-TB crisis

By 2020 DST UNIVERSAL COVERAGE

LARGE SCALE IMPLEMENTATION OF CULTURE DST LABORATORIES

LARGE SCALE IMPLEMENTATION OF MOLECULAR DIAGNOSTICS

Main differences

CULTURE BASED DST

- Culture based
- Evaluate the growth of bacteria (or a proportion of the overall inoculum)in the presence of an established concentration of drug

MOLECULAR BASED DST

- Detects mutations in genes relevant for the mechanism of action:
  - Synonymous mutations
  - Mutations not interfering with the mechanism of action of the drug
  - Mutations highly interfering with the DRUG pathway

Class of drug

Single drug

The current challenge

To develop a process by which mutations in MTB can in a systematic and transparent manner be shown to have adequate objective evidence to support a claim indicative of the mutation either causing or being associated with resistance to a known and identified drug and / or drug class

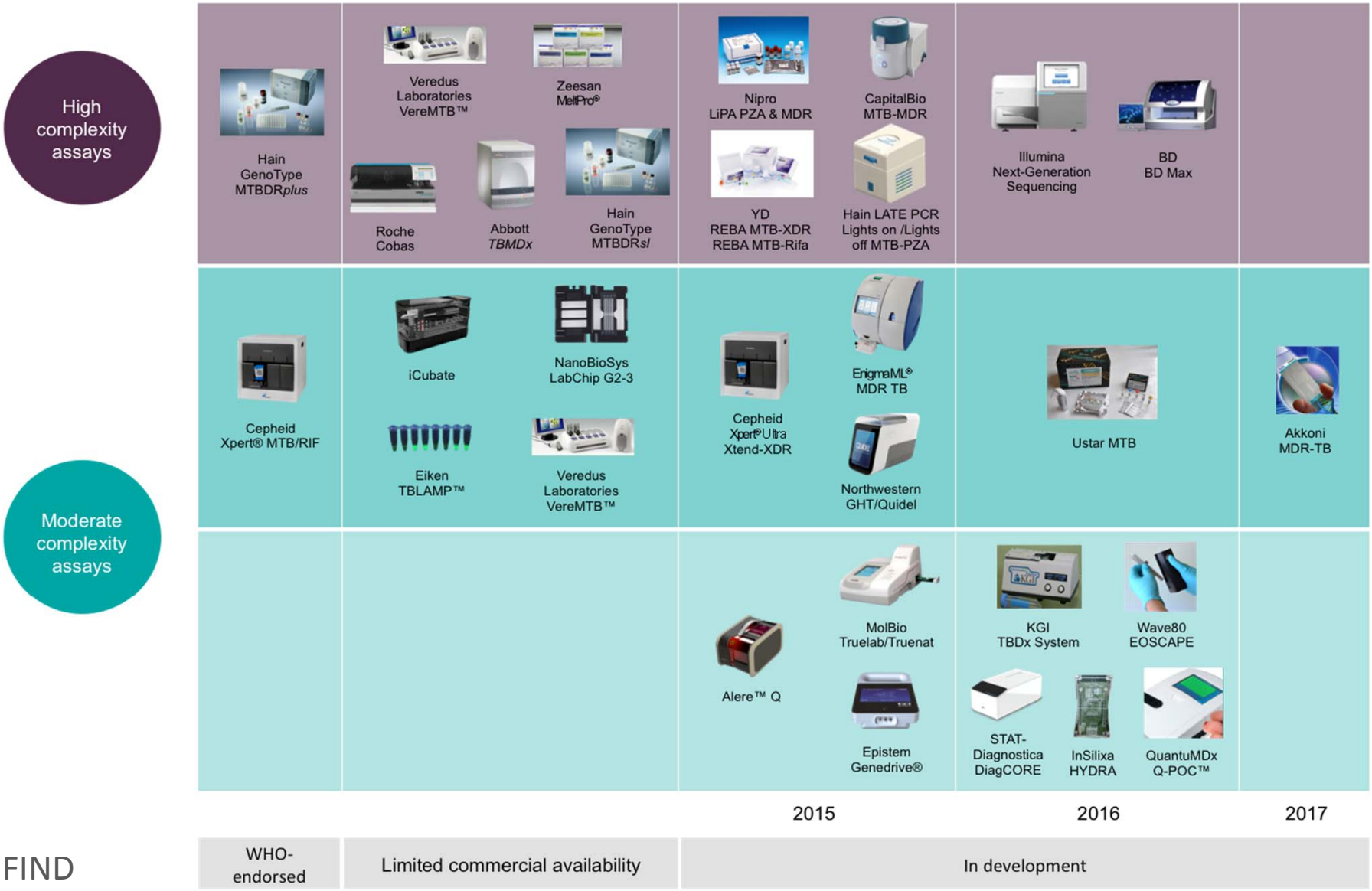
Link between sequencing data (Sanger? NGS) high quality phenotypic (gold standard??) data and clinical outcome on large sets of DRUG RESISTANT and DRUG SENSITIVE strains

Use of phenotypic tests as “absolute” standard and the poor quality of some results has biased our comparative evaluation of molecular tools

Analysis on extremely large data sets (>50.000 genomes) can compensate for phenotypic DST errors

Stucki, Gagneux; Tuberculosis (Edinb). 2013 Jan;93(1):30-9.

Molecular Diagnostic Pipeline

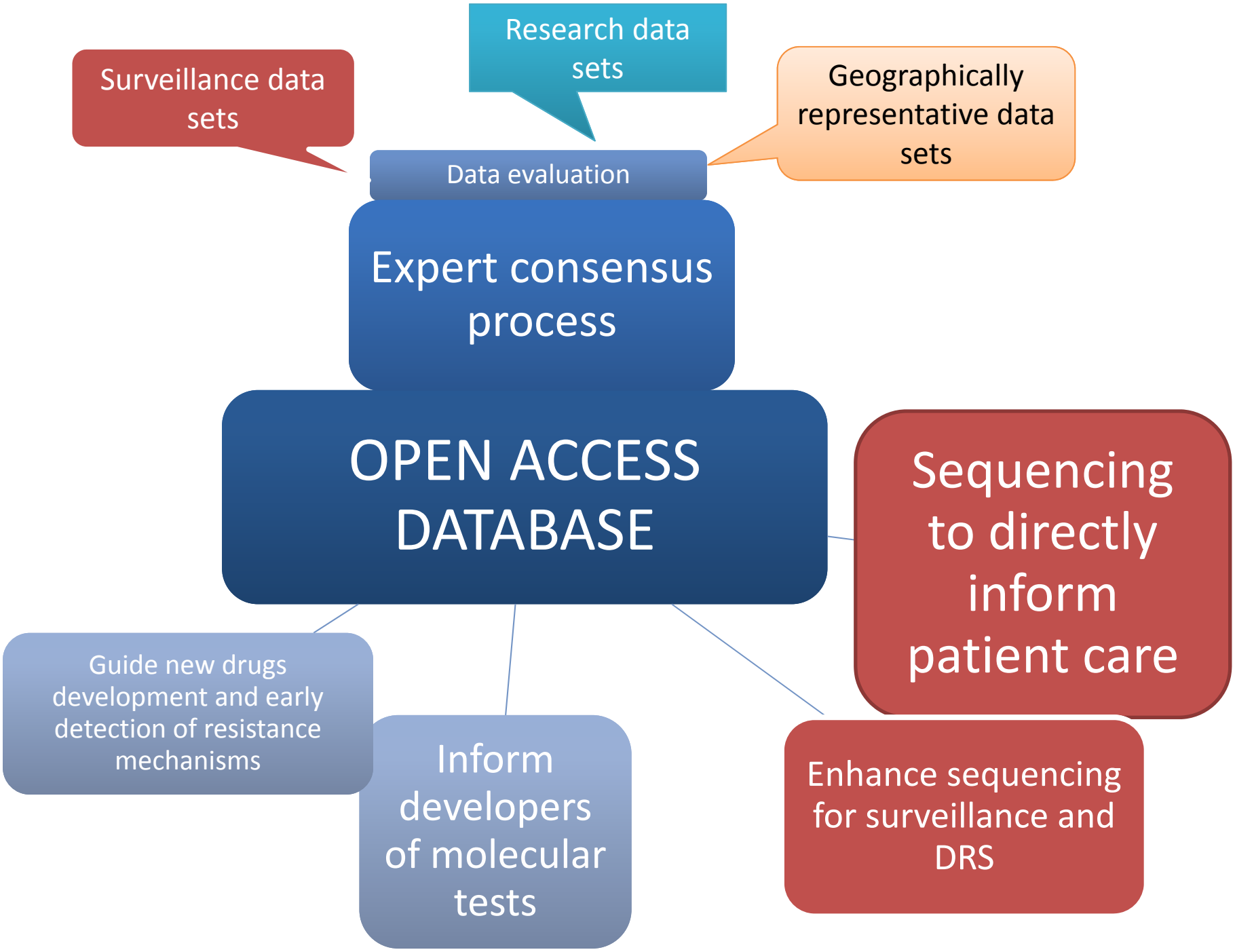


Aligning diagnostics with treatment to provide the best available therapeutic options

Joining forces

Sharing data

Avoid duplication


Surveillance data sets
Research data sets
Geographically representative data sets
Data evaluation
Expert consensus process
OPEN ACCESS DATABASE
Sequencing to directly inform patient care
Guide new drugs development and early detection of resistance mechanisms
Inform developers of molecular tests
Enhance sequencing for surveillance and DRS

The Process

- **Consensus based (HIV-1 resistance database for TruGene)**
  - Expert Panel
    - Geographic diversity
    - Representative areas of expertise
  - Develop quality metrics and requirements for
    - Data inclusion for the database for mining
      - Genotypic
      - Phenotypic
      - Metadata
    - Data weighting system
    - Validation algorithm/process for association to resistance
      - Validity criteria
      - Acceptance criteria
  - WHO endorsement of the ‘validated’ resistance mutation

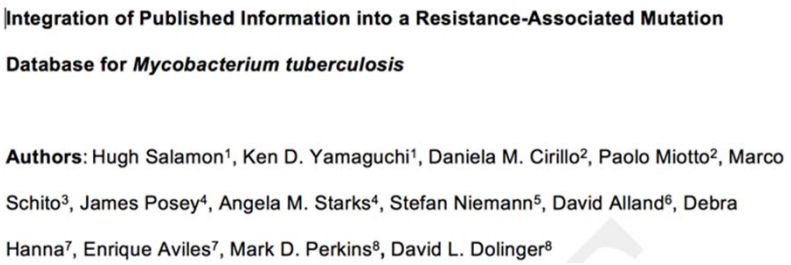
The Panel

- **Expert Panel**
  - Geographic diversity
    - Five (5) core members
    - Up-to ten (10) co-opted members
  - Representative areas of expertise
  - Initially meetings will be up to 4 times per year
  - Supervised by FIND and NDWG (the persons acting as coordinating chairs will have no voting rights)
    - Coordinate dates of meetings
    - Setup and run the meeting
    - Prep data packages

Two Step Approach

FIRST Step

- What do we know now?



Integration of Published Information into a Resistance-Associated Mutation Database for *Mycobacterium tuberculosis*

Authors: Hugh Salamon[1], Ken D. Yamaguchi[1], Daniela M. Cirillo[2], Paolo Miotto[2], Marco Schito[3], James Posey[4], Angela M. Starks[4], Stefan Niemann[5], David Alland[6], Debra Hanna[7], Enrique Aviles[7], Mark D. Perkins[8], David L. Dolinger[8]

- TPP development
- Identification of high confidence markers of resistance
- Inform developers of molecular tests

SECOND Step

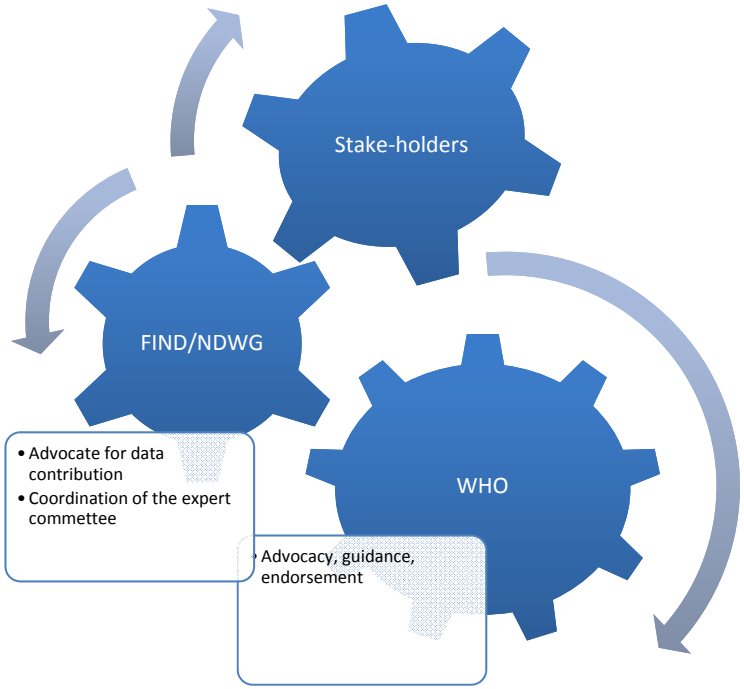
- Enhance sequencing for surveillance
  - Country capacity strengthening
  - Integration of data in database
- Sequencing to directly inform patient care
  - Optimization of sample preparation for sequencing
  - Development of more automated solutions

The role of the NDWG

To provide the coordination and communication with stakeholders

In partnership with lead experts in the field

- Ensure the quality of the data
- Drive the development of criteria for the validation of mutations
- Create a 'living' list of mutations
- Define algorithms for the interpretation of genotypic data and their correlation with clinically relevant resistance in *M. tuberculosis*.



TB Drug Resistance Data Sharing Platform

- CPTR - a strong partner
  - With established capabilities in management of large amounts of data
  - With linkage to drug development

NDWG Core Group

Co-Chairs

Dr. Catharina Boehme, FIND

Dr. Daniela Cirillo, San Raffaele Research Institute

Core Group Members (and constituency)

- Dr. Martina Casenghi, MSF (NGOs)
- Dr. Anne Detjen, IUATLD/TB TREAT, USA (IUATLD)
- Dr. Christopher Gilpin, WHO Global TB Programme (WHO)
- Dr. Rumina Hasan, Aga Kahn University, (GLI)
- Philippe Jacon, Cepheid (Industry)
- Dr. Stefan Niemann, Borstel Research Institute (Academia)
- Dr. Mark Perkins, FIND (Diagnostic Developers)
- Dr. John Ridderhof, CDC Atlanta, (CDC)
- Dr. Charles Sandy, National TB Program, Zimbabwe (NTP)

Subgroups and Coordinators

Point-of-Care Diagnostics	Dr. Ruth McNerney (LSHTM)
Diagnosis of Latent TB Infection	Dr. Keertan Dheda (University of Cape Town) and Dr. Philip Hill (University of Otago) (jointly)
Evidence Synthesis and Policy	Dr. Karen Steingart (Cochrane Infectious Diseases Group)
Childhood TB and Diagnostics	Dr. Anneke Hesseling (Stellenbosch University)
Community, Poverty and Advocacy	Mayowa Joel (Communication for Development)

Secretariat Alessandra Varga, FIND

Thank you

WHO
CPTR
C-PATH
BMGF

FIND
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Claudia Denkinger
David Dolinger

NDWG
Alessandra Varga
Stefan Niemann
John Ridderhof

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http://www.stoptb.org/wg/new_diagnostics/