The urgent need for TB point-of-care testing – Where do we stand?

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On behalf of
Point of Care Subgroup
NDWG Meeting
16 October 2008, Paris
Point-of-care testing for TB - Rationale

**WHAT**
- Simple &
- Accurate &
- Robust &
- Rapid Test
- For qualitative TB case detection

**WHERE**
- At or near the site of patient care
- Lowest level of health system: the health posts

**WHY**
- 4 M undiagnosed cases
  - WHO Global TB Report 2008
- Diagnostic delays fuel transmission & severity
  - Liam, 1997, Int J Tub & Lung Dis
- Widely deployed rapid test could save 0.5 M lives/year
  - Keeler, 2006, Nature
Technology needs for patient-centered approach

Reference Lab
- Surveillance
  - 5%

Regional Lab
- Auto. LC 15d
- Manual C 15d
- LPA 1d
  - LJ - 40d
  - 10%

Peripheral Lab
- LED +10%
- Manual NAAT +25%
- Auto NAAT +40%
  - Smear - 60%
  - 25%

Clinic / Health Post
- AG/AB
- Molecular
- VOC
  - Symptoms
  - 60%

Faster than solid culture
More sensitive than microscopy
Simpler than microscopy

Technology needs for patient-centered approach
Point-of-care approaches for TB (1)

**Antigen detection**

**Strategic approach**

**Improved LAM AB**

- Sandwich catcher 171 detector 178

![Graph showing % positive control vs. LAM (ng/ml)]

<table>
<thead>
<tr>
<th>X= 0.5ng/0 ng value</th>
<th>1.1</th>
<th>2.0</th>
<th>5.4</th>
</tr>
</thead>
<tbody>
<tr>
<td>X= 2.5ng/0 ng value</td>
<td>1.4</td>
<td>5.4</td>
<td>25.1</td>
</tr>
</tbody>
</table>

**Novel targets**

- Catcher 24 detector 29
- Catcher 29 detector 24
- Catcher 171 detector 178

**Better detection technology**

- Feasibility study to start Nov 08
- Apply new tools for AG discovery
- Fluorescence labeled LFI with reader
Point-of-care approaches for TB (2)

**Antibody detection**

**Strategic approach**

<table>
<thead>
<tr>
<th>Identify diagnostic AB pattern</th>
<th>Suitable detection technology</th>
</tr>
</thead>
</table>

- Microarray-based screening using high-throughput expression systems
- Multiplexing in point-of-care format
Point-of-care approaches for TB (3)

Volatile Organic Compound detection

<table>
<thead>
<tr>
<th>Strategic approach</th>
<th>MTB-specific VOC</th>
<th>Field-applicable detection technology</th>
</tr>
</thead>
</table>

- Use of high end MS devices
- Miniaturization of sensitive MS

<table>
<thead>
<tr>
<th>VOC in</th>
<th>Author/Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breath</td>
<td>Phillips, 2007</td>
</tr>
<tr>
<td>HS of culture</td>
<td>Trevejo, 2007</td>
</tr>
<tr>
<td>HS of culture</td>
<td>Syhre, 2008</td>
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Point-of-care approaches for TB (4)

Molecular detection

**Strategic approach**

3rd generation microscopy level NAAT platforms

Lab-on-a-chip

From macrofluidics to microfluidics

With most efficient isothermal amplification! Sample volume
Combine most accurate markers with best performing POC technology

**Biomarkers**
- Antigen
- Antibody
- VOCs
- DNA / RNA
- The “omics”
- Host markers

**Technologies**
- LFI with new labeling technologies & handheld readers
- Label-free platforms
- Spectrometric methods
- Microfluidics
TB biomarker research -
*Leaving the shallow end of the biomarker pool*

- Systematic approaches
- Large sample repositories
- Much more resources

2x10^4 genes >10^6 mRNAs >10^6 proteins
>10^7 modified proteins 3x10^3 metabolites

Bacterial factors
⇒ Host factors
The new face of TB biomarker discovery
Point-of-care subgroup

- 31 registered subgroup members
- 14 from academia, 10 from MOH/agencies, 7 from industry
- Web forum: share point for members of the subgroup
- Public website: www.tbdiagnostics.org
- Workplan / activities

Thank you for any input & feedback