Development of a Sustainable Diagnostic Toolbox for Detection of West African Infectious Diseases

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Global Distribution of Emerging Infectious Diseases

Diagnostic Window

Acquired immune response (late)

Innate Immune Response (early)
Antigen/ Nucleic Acid
Antigen-Specific IgM
Antigen-Specific IgG

Clinical Disease

Time (days)

Diagnostic Direction

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# Diagnostic Toolbox

<table>
<thead>
<tr>
<th>Technique</th>
<th>Biomolecule Detected</th>
<th>Expertise Needed</th>
<th>Cost</th>
<th>Time Needed</th>
<th>Limit of Detection</th>
<th>Multiplex?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pathogen Isolation</td>
<td>Whole Pathogen</td>
<td>Yes</td>
<td>$$$</td>
<td>1-2 weeks</td>
<td>+++</td>
<td>N/A</td>
</tr>
<tr>
<td>PCR</td>
<td>Nucleic Acid</td>
<td>Yes</td>
<td>$$$</td>
<td>1 day</td>
<td>+++</td>
<td>Yes</td>
</tr>
<tr>
<td>ELISA</td>
<td>Antigen/IgG/IgM</td>
<td>Yes</td>
<td>$$</td>
<td>1-2 days</td>
<td>++</td>
<td>No</td>
</tr>
<tr>
<td>RDT</td>
<td>Antigen/IgG/IgM</td>
<td>No</td>
<td>$</td>
<td>10-30 minutes</td>
<td>+</td>
<td>Yes (3-4 plex)</td>
</tr>
<tr>
<td>Magpix</td>
<td>Antigen/IgG/IgM</td>
<td>Yes</td>
<td>$$</td>
<td>120-240 minutes</td>
<td>++/+++</td>
<td>Yes (10+ plex)</td>
</tr>
</tbody>
</table>
Integrated and Sustainable Diagnostics

Integrated: Tests are statistically independent or non-overlapping but, in combination, provide a higher degree of certainty of the final result.

Sustainable: All assay components are easily produced, stable, and safe to use (monoclonal antibodies, recombinant antigens, synthetic primers and probes).

Real-time PCR

ELISA/MAGPIX®
Customizable Multiplex Panels

- Individual assays are developed, optimized, and validated
- Panels are established based on regional or syndromic needs
- All assays designed using sustainable reagents

Assay Target Identified
- Source existing assay reagents (1-4 weeks) OR
- Custom reagent development (3-4 months)

Assay Development
- Downselect best antibody pairs (1-2 days)
- Dynamic Range and LOD testing (1-2 days)
- Inclusivity/Exclusivity (2-4 days)

Assay Validation
- LOD with live agent (1-2 days)
- Inclusivity/Exclusivity (2-4 days)
- Reproducibility/Repeatibility (3 days)
Joint West Africa Research Group (JWARG)

- Consortium to build surveillance capability
  - MHRP, NMRC, NAMRU-3, and USAMRIID
  - Nigeria, Ghana, and Liberia
- Integrated approach
  - MAGPIX Multiplex immunoassays
  - Real-time RT-PCR
- Acute febrile illness study

**Tier 1: West African Panel**
- Magpix assays to be run on all Day 0 samples
- EBOV GP and VP40
- MARV GP and VP40
- LASV GP and NP
- CCHF NP
- RVFV NP
- pan-alpha E
- pan-flavi E

**Tier 2: Species/Strain specific PCR**
- Given results of T1 assays, proceed to T2 assays for confirmation

**Tier 3: Virus Isolation, IgM/IgG detection, Sequencing at USAMRIID**

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Have MAGPIX. Will Travel.

Nigeria Serosurveillance

<table>
<thead>
<tr>
<th>Target</th>
<th>% Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>RVFV</td>
<td>43%</td>
</tr>
<tr>
<td>Alphavirus</td>
<td>43%</td>
</tr>
<tr>
<td>Flavivirus</td>
<td>72%</td>
</tr>
<tr>
<td>MARV</td>
<td>2%</td>
</tr>
<tr>
<td>EBOV</td>
<td>9%</td>
</tr>
<tr>
<td>LASV</td>
<td>30%</td>
</tr>
<tr>
<td>CCHFV</td>
<td>62%</td>
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</table>

Accra, Ghana

Lagos, Nigeria
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**United States Army Medical Research Institute of Infectious Diseases**
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Disclaimers

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