COVID-19 antibody tests and the UK Rapid Testing Consortium

June 18, 2020

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CEO Blue Earth Diagnostics
Chairman Polarean Imaging plc.
Chairman UK Rapid Test Consortium
And now for something completely different ..

- Blue Earth Diagnostics*
  - Robust portfolio of approved and investigational PET diagnostic/therapeutic compounds for prostate cancer and brain metastases
- Polarean Imaging*
  - Hyperpolarized gas MRI imaging of lungs

*Blue Earth Diagnostics and Polarean Imaging are not connected to the UK Rapid Test Consortium

My normal job

COVID

Professor Sir John Bell (Oxford) “Your Country Needs You”!
UK government 5 pillar plan for COVID-19 testing

Our National Testing Strategy

Pillars 1, 2: Antigen tests for virus; Pillar 3: Antibody (to SARS-CoV-2) testing
COVID-19 testing

Antigen testing

- Detecting SARS-CoV-2 viral RNA in nasal swabs, etc..
- RT PCR
  (Reverse Transcription Polymerase Chain Reaction)

Antibody testing

- Detecting antibodies to SARS-CoV-2 in blood
- ELISA and other Lab-based tests
- Lateral Flow Tests (decentralized & home use)
Immune response to SARS-CoV-2 infection

A: viral infection

SARS-CoV-2
single stranded RNA genome
~30kB

trimeric
spike protein

antibody response to
viral spike protein

B: antibody response

- IgM - acute phase
- IgG - convalescent phase

Antibody concentration

Infection (day 0)  Acute sample (eg day 7-10)  Convalescent sample (eg day 28-35)

Long(er) term immunity?

Antibody tests need a good Antigen

SARS-CoV-2
single stranded RNA genome
~30kB

RNA sequence

Spike protein code

Insert into Mammalian cells

Bioreactor

Antigen (Spike protein)

0.5 ug / assay

Trimeric S protein

Purification

An alternative antigen used in some Antibody tests is the Nucleocapsid (N) protein
ELISA
Enzyme-linked Immunosorbent Assay

• Once you have a good antigen, you can use it to detect the Neutralizing Antibodies to the antigen in a sample

• The “Gold Standard” method employs the ELISA technique

• There are multiple ELISA techniques for COVID IgG

• The Oxford ELISA seems to be a very good one
Evolution of IgG over time (Oxford ELISA)

Lateral Flow Tests (LFTs)

- Point of care / Home use
- Fast ~ 20 minutes
- Cheap ~ $10-20
- Essential .. UK lacks extensive testing lab infrastructure

For detection of IgG

Optimal characteristics for any COVID Antibody test (including LFT)

- Need very high Specificity
- Don’t want FalsePositives

- Need high Sensitivity
- False negatives less risky, but not helpful

Ideal characteristics

<table>
<thead>
<tr>
<th>Specificity</th>
<th>Sensitivity</th>
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<tbody>
<tr>
<td>&gt; 99%</td>
<td>&gt; 95%</td>
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</table>
9 LFTs tested against Oxford ELISA

• 9 Commercially available LFTs were compared to Oxford ELSIA

Performance of 9 COVID-19 LFTs in detail

<table>
<thead>
<tr>
<th>Assay</th>
<th>RT-PCR positive</th>
<th>Pre-pandemic control</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>True positive</td>
<td>False positive</td>
<td>True negative</td>
<td>False negative</td>
</tr>
<tr>
<td>ELISA</td>
<td>34</td>
<td>6</td>
<td>50</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td>18</td>
<td>15</td>
<td>60</td>
<td>0</td>
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<td>2</td>
<td>23</td>
<td>15</td>
<td>90</td>
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<td>21</td>
<td>12</td>
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<tr>
<td>9</td>
<td>22</td>
<td>18</td>
<td>138</td>
<td>4</td>
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</table>

9 LFTs performance characteristics

<table>
<thead>
<tr>
<th>Specificity</th>
<th>Sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>93%-100% (point 98%)</td>
<td>65-85% (ideal ~ 90%)</td>
</tr>
</tbody>
</table>

Most COVID-19 Lateral Flow Antibody Tests don’t work that well
Everyone wanted COVID LFTs ..

- Lots of tests approved on very small (carefully chosen) data sets
- Need to be very careful if you use/buy them ..

**U.K. Paid $20 Million for New Coronavirus Tests. They Didn’t Work.**

Facing a global scramble for materials, British officials bought millions of unproven kits from China in a gamble that became an embarrassment.

**FINANCIAL TIMES**

*myFT Daily Digest*

**Health sector**

Delay and confusion about finding a reliable antibody test in the UK

**JUNE 18, 2020**

**MedTech**

**FDA names 28 antibody tests to be taken off the market**

by Conor Hale | May 22, 2020 10:40am
Can we make a better LFT for COVID?
Formation of UK Rapid Test Consortium (RTC)

• Why UK focus?
• Life Science capability
• Security of supply
• Major COVID shortages of medical equipment, PPE, etc.
• Return of the Nation state..
RTC objectives
My role as Chairman

RTC objectives:
• Perform an 8-month development project in 25% of the time
• Develop Phone App to read test
• Scale up to manufacture later in 2020

My role as Chairman
• Wikipedia “research” on LFTs
• Independent of the companies involved
• Promote trust and cooperation
• Provide moral support when working with UK Department of Health & Social Care, NHS, UK Treasury
• Forming, Norming, Storming, Performing in real time
RTC challenges

Macro
• COVID-19 is a new disease, not fully understood
• Government strategy being developed at pace
• The situation changed on a weekly / daily basis
• Interfacing between 4 small companies and DHSC / Treasury

Micro
• Supply of key materials (antigen, lancets, nitrocellulose, …)
• Finding enough blood samples with appropriate ethics for testing
• Developing user instructions that work for the whole population

• Everyone I know wants a free test
Almost there ... !

• LFT developed and optimized
• Modification of existing Phone App to work with new test and interface to NHSx (Digital)
• Development of Regulatory strategy and collaboration with MHRA
• Transition to large scale manufacture for more widespread evaluation & distribution

ELISA negative
Specificity
Close to optimal

ELISA positive
Sensitivity
Close to optimal
How’s it different to PET radiopharmaceuticals?

• Very rapid development!
• Not a lot of IP hurdles
• You can do a clinical trial with 100s of samples in a day!
• Simpler Regulatory environment
• Very low cost
• Very high volume

• I need to come back to PET for a rest
Thank you!