A Field-deployable Platform for Diagnostic Hepatocellular Carcinoma Screening in Low-resource Settings

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Hepatocellular Carcinoma (HCC) in Mongolia

- Patient survival is compounded by the lack of and geographic access to preventative care.
- Nearly all diagnosed HCC cases in Mongolia are referred to the National Cancer Center of Mongolia (NCCM), located in the capital city of Ulaanbaatar.
- Unfortunately, ~90% of patients seeking HCC treatment at NCCM are late stage (i.e. tumors >2cm) and are not eligible for resection or other curative treatments.

Development of a HCC Marker Panel

Table 1. Serum markers of HCC and Infectious Disease That Increase HCC Risk

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>Abbreviation</th>
<th>Function</th>
<th>Target Levels for Risk Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alphafetoprotein</td>
<td>AFP</td>
<td>fetal glycoprotein that is increased in HCC</td>
<td>≥10 ng/mL</td>
</tr>
<tr>
<td>Lens-culinaris agglutinin binding Alphafetoprotein</td>
<td>AFP-L3</td>
<td>fucosylated variant of AFP that has a high affinity to Lens culinarius produced by malignant hepatocytes</td>
<td>&gt;10% of total AFP (1 ng/mL)</td>
</tr>
<tr>
<td>Des-Gamma-Carboxy Prothrombin</td>
<td>DCP</td>
<td>arises from an acquired defect in post-translational carboxylation of the prothrombin precursor in malignant hepatocytes</td>
<td>≥10 ng/mL</td>
</tr>
<tr>
<td>Core Antibodies to Hepatitis B Virus</td>
<td>HBV</td>
<td>small enveloped DNA virus that can lead to HCC</td>
<td>5 ng/mL</td>
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<tr>
<td>Core Antibodies to Hepatitis C Virus</td>
<td>HCV</td>
<td>small enveloped DNA virus that can lead to HCC</td>
<td>5 ng/mL</td>
</tr>
</tbody>
</table>

Detection of Alphafetoprotein in Serum

- Digital Image of Membrane
- 0.1 µg/mL
- 100 µg/mL
- 2000 cts/s
- 1500 cts/s
- 10000 cts/s
- 1236 cm⁻¹
- 8800 cts/s
- 15000 cts/s
- 10000 cts/s
- Raman Shift (cm⁻¹)
- 1350 cm⁻¹

Effect of Blocking Agent on Performance

- Blocking Agent: 10 ng/mL AFP
- Blank (serum)
- 1% Bovine Serum Albumin
- Phosphate Buffered Saline
- 0.1% Tween 20
- Calibration Plot for AFP using 1% BSA to block membranes
- LOD reduced to ~3 pg/mL

Conclusions and Future Directions

- A PON assay for AFP has been successfully developed for AFP with a LOD ~3 pg/mL, which is over 3000x lower than the proposed clinical value of 10 ng/mL.
- We are actively working towards multiplexed detection of the markers in Table 1.

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