Translation of a blood-based biomarker strategy for the early detection of lung cancer to a CLIA laboratory

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At-a-glance

New Assay method for blood biomarker detection applied to a known candidate biomarker improves cancer/benign prediction.

Translation of CYFRA 21-1 FSA assay to a CLIA clinical setting can improve early diagnosis of lung cancer in at-risk patients with pulmonary nodules.

Introduction

The management of indeterminate pulmonary nodules (IPNs) remains a challenging problem. Our new assay methodology, the Free Solution Assay (FSA), measured by the Compensated Interferometric Reader (CIR), consisting of a diode laser, capacitor, and CCD, provides high sensitivity quantification of CYFRA 21-1 protein in patient serum at a LOQ of 8.1 pg/mL.

Mix-and-Read Assay Method

Target analyte is quantified by measuring the difference in response between sample (serum incubated with probe antibody) and reference (serum incubated with control). Comparison of the binding and reference samples enables quantification of the target analyte in complex matrices.

The Compensated Interferometric Reader consists of an interferometer, a droplet generator for sample introduction and a pump. A capillary is interfaced to the droplet generator, which produces 0.75 µL sample droplets separated by 40 µL oil droplets.

Calibration curves are prepared by spiking CYFRA 21-1 into serum. Limit of quantification is calculated as 3σ/slope, where σ is the standard deviation of replicate measurements.

Clinical Performance: Risk prediction in relevant cohort (N = 225)

Conclusions

• In a clinically relevant cohort (N = 225), measurement of CYFRA 21-1 using FSA enabled improved quantification of the biomarker and improvement of diagnostic power when combined with the Mayo Risk model for prediction of lung cancer.

• Translating the CYFRA 21-1 FSA-CIR assay to a CLIA laboratory will allow the diagnostic performance of the test in a true prospective clinical setting.

• The results suggest that CYFRA 21-1 represents a strong candidate biomarker for risk stratification of patients with IPNs.

References

Acknowledgements

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Biomarkers for clinical management

The incidentally detected IPN population: roughly 1.2 million per year

Clinical Risk Model

Follow up

Combined Biomarker Model

Lower rate of unnecessary biopsy/thoracotomy/PET

Patient Cohort (N = 225)

<table>
<thead>
<tr>
<th>Age (mean ± SD)</th>
<th>No cancer</th>
<th>ADC</th>
<th>SCC</th>
<th>SCLC</th>
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<tbody>
<tr>
<td>N (75)</td>
<td>39.5 ± 12.7</td>
<td>65.2 ± 8.0</td>
<td>65.4 ± 7.8</td>
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<tr>
<td>Male</td>
<td>40 (53)</td>
<td>26 (56)</td>
<td>29 (66)</td>
<td>36 (59)</td>
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<tr>
<td>Female</td>
<td>35 (47)</td>
<td>19 (42)</td>
<td>15 (34)</td>
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<td>15 (34)</td>
<td>25 (41)</td>
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<td>Smoking (%)</td>
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<td>11 (25)</td>
<td>20 (33)</td>
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<tr>
<td>Ex</td>
<td>54 (72)</td>
<td>38 (84)</td>
<td>37 (85)</td>
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<td>Current</td>
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<td>1 (2)</td>
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<td>Pack Years</td>
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<td>50.1 ± 21.3</td>
<td>56.9 ± 23.5</td>
<td>63.7 ± 32.8</td>
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<td>Nodule Size (cm)</td>
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<td>2.7 ± 1.7</td>
<td>2.7 ± 2.0</td>
<td>3.6 ± 1.2</td>
</tr>
</tbody>
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Figure 1: Development of CYFRA 21-1 FSA. (A) Measurement of CYFRA 21-1 by FSA-CIR across individuals with benign lung nodules (benign), adenocarcinomas (ADCs), stage 1 and 2 lung squamous cell carcinomas (SCCs), and all stage small cell lung cancers (SCLCs). (B) ROC curve illustrating added value of FSA-CIR over clinical parameters and nodule size (the Mayo risk model) for the diagnosis of IPNs. N = 225.

References

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