Serum Biomarker Signature-based Liquid Biopsy for Diagnosis of Early-Stage Pancreatic Cancer

Linda D. Mellby[a], Andreas P. Nyberg[a] , Julia S. Johansen[b], Christer Wingren[c], Børge G. Nordestgaard[d], Stig E. Bojesen[d], Breeana I. Mitchell[e], Brett C. Sheppard[e], Rosalie C. Sears[e], Carl A.K. Borrebaeck[c]

[a]Immunovia AB, Medicon Village, Lund, Sweden; [b]University of Copenhagen, Copenhagen, Denmark; [c]Lund University, Lund, Sweden; [d]Copenhagen University Hospital, Herlev, Denmark; [e]Oregon Health and Science University, Portland, Oregon, USA.

Introduction

Pancreatic ductal adenocarcinoma (PDAC) has a very poor 5-year survival rate of less than 10%. By resecting more tumors when they are still confined to the pancreas, the overall 5-year PDAC patient survival rate would increase significantly. In an effort to achieve reliable early detection we have developed IMMray™ PanCan-d, a microarray-based blood test for diagnosis of PDAC patients.

Objective

The purpose of this study is to derive a novel biomarker signature of early-stage PDAC from a large patient cohort and to subsequently validate the derived biomarker signature in an independent study cohort.

CONCLUSIONS

- PDAC stage I and II patients were detected with **96% accurcy*** and validated with a distinct patient cohort.
- PDAC stage I to IV patients were detected with **98% accuracy*** and validated with a distinct patient cohort.
- Chronic pancreatitis was discriminated from PDAC with an accuracy* of **84%**.
- Malignant IPMNs were correctly classified as PDAC.

Results

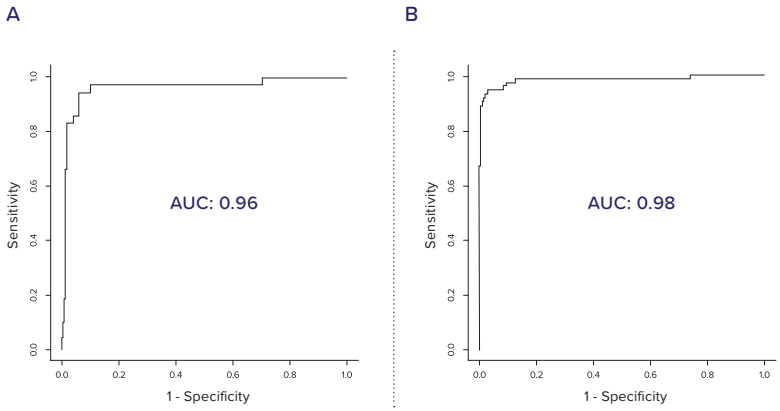

Fig 1. Classification of pancreatic ductal carcinoma stages in the Scandinavian cohort, using biomarker signatures.

Using data from the Scandinavian study, predictive models that were based on frozen support vector machine were built. Two biomarker signatures were defined, using the backward elimination algorithm, for classification of (A) normal control (NC) samples from pancreatic ductal adenocarcinoma (PDAC) stage I and II, and (B) PDAC stage III and IV, respectively. The results are presented as receiver operating characteristic curves and their corresponding area under the curve (AUC) values.

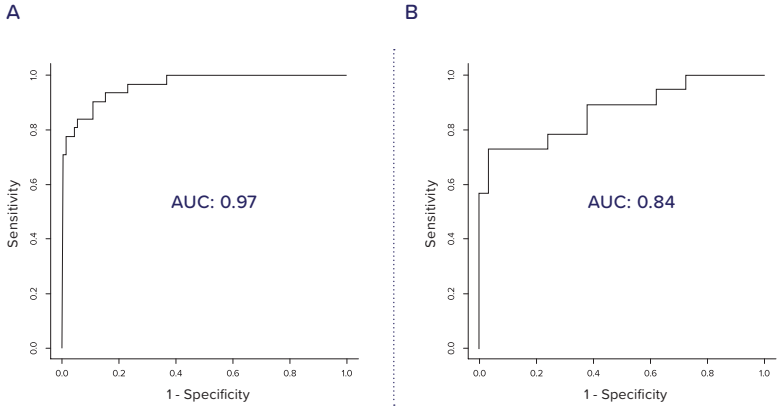

Fig 2. Validation of the consensus signature in stage I and II pancreatic ductal carcinoma from the United States cohort.

The consensus signature generated from the Scandinavian cohort was validated in the independent cohort in the United States by classifying (A) normal controls (NC) v patients with pancreatic ductal adenocarcinoma (PDAC) stage I and II, and (B) patients with PDAC stage I and II v patients with chronic pancreatitis (CP). The results are presented as representative receiver operating characteristic curves and their corresponding area under the curve (AUC) values.

Methods

Antibody micorarray slides are printed and incubated with biotinylated patient serum. Levels of bound antigens are detected by fluorescence scanning. State-of-the-art machine learning algorithms were employed in the development of the IMMray™ PanCan-d signature. Hundreds of analytes were thus reduced to generate a comprehensive signature capable of distinguishing PDAC from controls.

IMMray™ Microarray technology

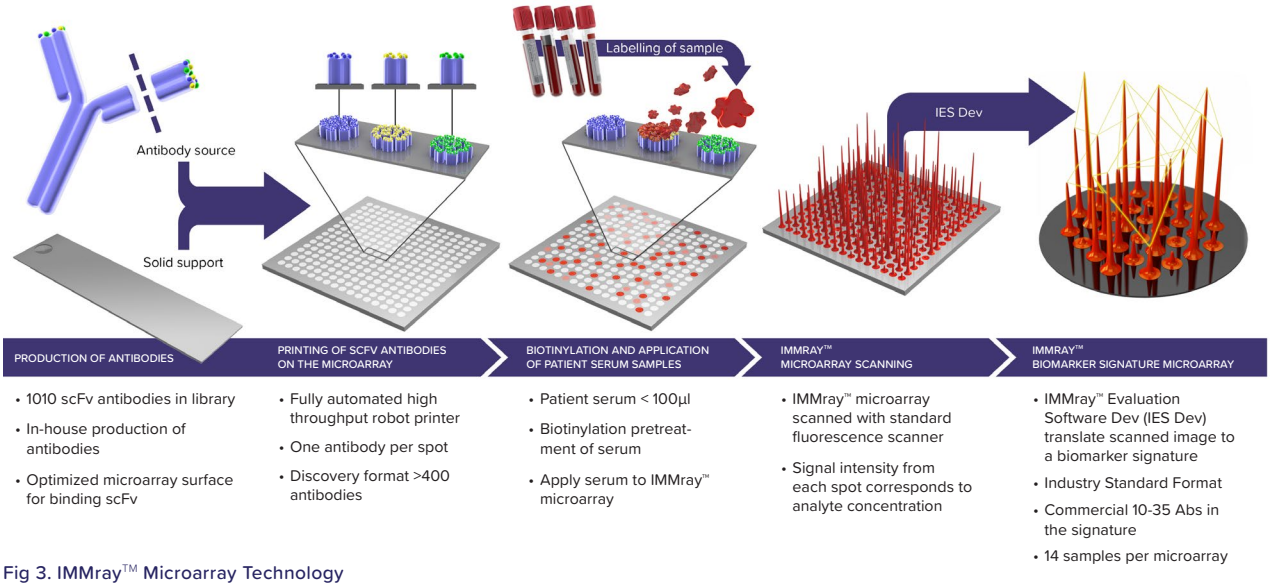

Fig 3. IMMray™ Microarray Technology

References

Mellby LD, Nyberg AP, Johansen JS, et al. Serum Biomarker Signature-Based Liquid Biopsy for Diagnosis of Early-Stage Pancreatic Cancer. Journal of Clinical Oncology. August 2018. doi: 10.1200/JCO.2017.77.6658