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Diagnosis of early stage pancreatic ductal adenocarcinoma using a serum biomarker signature

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Introduction

Pancreatic ductal adenocarcinoma (PDAC) shows a very poor survival rate with less than 7% 5-year survival. 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 the IMMray™ PanCan-d microarray-based test is to detect both early and late stage PDAC from a blood sample. The purpose of the IMMray™ PanCan-d microarray-based test is to detect serum biomarkers associated with PDAC.

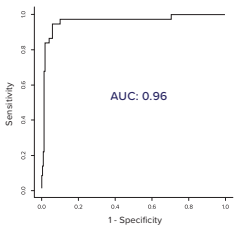
Conclusions

- 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 **83%**.
- IPMN samples of all grades were classified as positives.
- Six studies covering 2482 samples demonstrated robustness and high accuracy of the IMMray™ PanCan-d platform.

Results

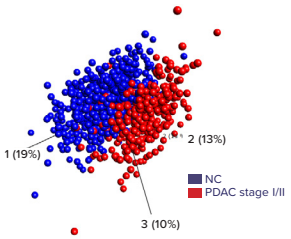
Discovery: In a retrospective study on a South Scandinavian cohort, 1355 blood samples were analyzed.

NC vs. PDAC stage I/II



The IMMray™ PanCan-d signature discriminated 148 patients in PDAC stage I and II from 888 healthy controls very accurately.

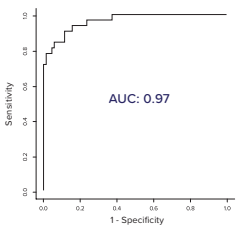
NC vs. PDAC stage I/II



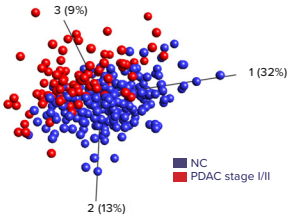
The signature discriminated 148 patients in PDAC stage I and II from 888 healthy controls with an accuracy* of 96%.

Validation: In a retrospective study on a North American cohort, 429 blood samples were analyzed.

NC vs. PDAC stage I/II



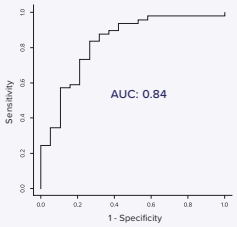
NC vs. PDAC stage I/II



The IMMray™ PanCan-d signature discriminated 90 patients in PDAC stage I and II patients from 219 healthy controls very accurately.

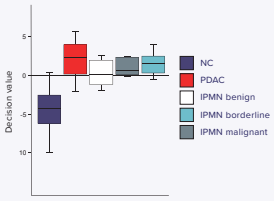
Chronic pancreatitis and IPMN

CP vs. PDAC stage I/II



Fiftyseven CP samples were included in the validation cohort. The IMMray™ PanCan-d signature discriminated them from PDAC stage I and II very accurately.

NC vs. IPMN



Twenty IPMN samples were included in the validation cohort. The IMMray™ PanCan-d signature classified a majority of them as positives.

Studies performed on the IMMray™ PanCan-d platform

STUDY	NO. OF SUBJECTS	AUC**
Ingvarsson *et al.* 2008[1]	44	1
Wingren *et al.* 2012[2]	103	0.95
Gerdtsson *et al.* 2015[3]	338	0.98
Gerdtsson et al. 2016[4]	213	0.96
South Scandinavian[5]	1355	0.98
North American[5]	429	0.96
Total no. of subjects	2482	

Analyses of pancreatic cancers in several retrospective studies proved that the test could classify the samples consistently and with a ROC-AUC of ≥ 95%.

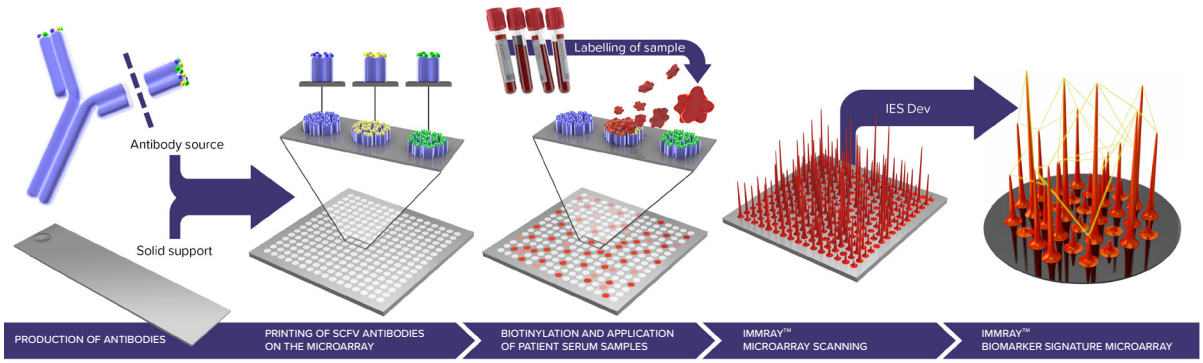
**Based on specificity and sensitivity values generated by the classification model. **Healthy controls vs PDAC patients.*

Ref: *1. Ingvarsson J et al. Proteomics 2008 8(11):2211-9. 2. Wingren et al. Cancer Res. 2012 15;72(10):2481-90. 3. Gerdtsson et al. Int Journal of Proteomics 2015;2015:587250. 4. Gerdtsson et al. Mol Oncol. 2016 Oct;10(8):1305-16. 5. Mellby et al. Manuscript submitted April 2018 in collaboration with OHSU Knight Cancer Institute and the Brenden-Colson Center for Pancreatic Care.*

Methods

Antibody microarray 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



- 1010 scFv antibodies in library
- In-house production of antibodies
- Optimized microarray surface for binding scFv

- Fully automated high throughput robot printer
- One antibody per spot
- Discovery format >400 antibodies

- Patient serum < 100µl
- Biotinylation pretreatment of serum
- Apply serum to IMMray™ microarray

- IMMray™ microarray scanned with standard fluorescence scanner
- Signal intensity from each spot corresponds to analyte concentration

- IMMray™ Evaluation Software Dev (IES Dev) translate scanned image to a biomarker signature
- Industry Standard Format
- Commercial 10-35 Abs in the signature
- 14 samples per microarray

Fig 1. *IMMray™ Microarray Technology*

References

1. Ingvarsson J et al. Proteomics 2008 8(11):2211-9. 2. Wingren et al. Cancer Res. 2012 15;72(10):2481-90. 3. Gerdtsson et al. Int Journal of Proteomics 2015;2015:587250. 4. Gerdtsson et al. Mol Oncol. 2016 Oct;10(8):1305-16. 5. Mellby et al. Manuscript submitted April 2018 in collaboration with OHSU Knight Cancer Institute and the Brenden-Colson Center for Pancreatic Care.