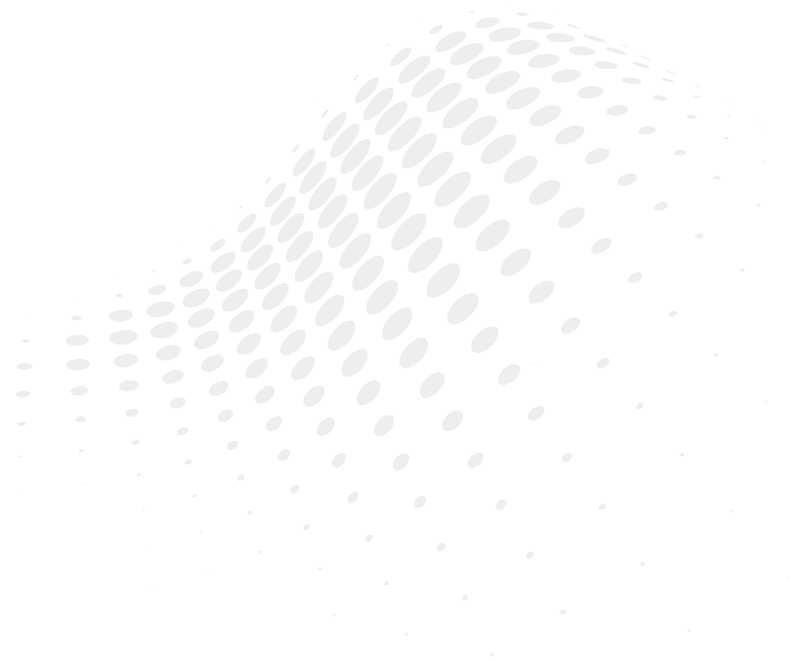


White paper

Improved early-stage diagnosis of pancreatic cancer offers a major opportunity to improve overall survival



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Improved early-stage diagnosis of pancreatic cancer offers a major opportunity to improve overall survival

by Immunovia AB, Lund Sweden (www.immunovia.com)

Abstract

Pancreatic cancer (PC) has one of the worst survival rates of the most common cancers with only 4-6% surviving five years after they are diagnosed. The mortality is expected to increase further over the coming years. PC thus remains a highly fatal disease. Today, complete surgical resection (removal of the pancreas) is the only potentially curative modality of treatment available. Detecting PC lesions early enough to perform this procedure is, however beset with difficulties. Nevertheless, the timeline of progression from low grade precursor lesions to invasive cancer does offer a window of opportunity to detect the disease earlier than it is currently possible. This in turn, should radically improve overall survival in PC by making far more patients eligible for resection. By providing physicians with actionable information early enough for the cancer to be removed surgically, the overall 5 year PC patient survival rate could increase from 4-6% to approximately 60%.

This white paper presents IMMray™ PanCan-d, a blood test developed for early stage diagnosis of pancreatic cancer. Based on recent results from retrospective studies, that are now under publication, IMMray™ PanCan-d is able to differentiate with 96% accuracy the early resectable stages of pancreatic cancer, stage I and II, from the healthy controls. When analyzing all stages of pancreatic cancer in retrospective studies covering more than 3000 blood samples, the accuracy of IMMray™ PanCan-d is reported as high as 98%. To complete the validation of the test, Immunovia plans to perform additional retrospective studies and implement a prospective study involving 1000 risk group individuals at five different centers in the US and Europe.

The in-house skills are outlined in the white paper with particular focus on the antibody microarray production and the test methodology to derive unique serum biomarker signatures through state-of-the-art bioinformatics algorithms and software. Immunovia's own laboratory service for IMMray™ PanCan-d testing, that is currently undergoing accreditation, is introduced in this paper for the first time.

As IMMray™, creates a biological snapshot of an individual's immune response by analysing serum proteins that change as a sign of disease, the white paper describes the partnership opportunities not only for early diagnosis, but also for following disease progression, therapy monitoring and patient classification, both for cancers and auto-immune diseases.

Reference:

Small carcinoma of the pancreas is curable: new computed tomography finding, pathological study and postoperative results from a single institute. *Shimizu Y et al. J Gastroenterol Hepatol. 2005 Oct;20(10):1591-4.*

1. Problems and opportunities in pancreatic cancer

The pancreas, a pear-shaped gland about 6 inches long located behind the stomach and in front of the spine, has two basic functions. It produces digestive enzymes or juices that are secreted into the small intestine to help break down and digest food. This function is performed by the gland's exocrine cells. The pancreas also produces hormones that regulate blood sugar levels, a task performed by its endocrine cells.

Pancreatic cancer is a disease in which malignant (cancer) cells appear in the pancreas. Approximately 90 to 95% of pancreatic cancers begin in the exocrine cells and are known as pancreatic ductal adenocarcinomas (PDAC), here referred to simply as PC.

The lack of early-stage symptoms, combined with the gland's placement deep within the abdomen, make pancreatic cancer difficult to detect and diagnose before it has progressed to a serious health concern. Furthermore, symptoms tend to be similar to other illnesses, rather than pointing specifically toward PC.

Mortality rates have not improved

PC is thus a highly fatal disease and recent clinical developments have not resulted in improved survival; overall mortality rates have changed very little throughout the past three decades. Worldwide, PC is the eighth leading cause of cancer deaths in men (138,100 deaths annually) and the ninth in women (127,900 deaths). In the United States, it affects over 42,000 people and is the second leading cause of cancer death.

Furthermore, PC is usually only diagnosed at an advanced stage. Almost all patients presenting with the disease die from it; its 5-year survival rate is less than 4%. Fewer than 20% of patients are eligible for surgical resection (the removal of all demonstrable PC). This procedure generally improves survival benefit, but in the majority of cases does not translate into long-term 5-year survival. In other words, resection is rarely curative.

May become the second leading cause of US cancer deaths

The annual number of new PC cases in the United States is estimated to double from 43,000 to 88,000 between 2010 and 2030, and the adjusted number of deaths due to PC in that time period is expected to increase from 36,888 to 63,000. Because of rising incidence and poor survival, PC will probably become the second leading cause of cancer deaths in the United States by 2020. Radical improvement in 5-year PC survival is unlikely without a better means of earlier stage detection (and thus improved resectability rates) plus the development of more effective chemotherapeutic agents to prolong survival following resection.

The potential to improve overall survival via earlier detection of PC is thus clear. Moreover, the period between the appearance of detectable cancer lesions and the development of metastatic disease seems to offer the best window of opportunity for detection screening. For example, the median of two months between symptoms and diagnosis could be the difference between disease stages II and III (see below) and thereby result in significantly improved survival. Since the size of the primary lesion appears to correlate with long-term survival, diagnosis as early as possible in the tumour progression could reveal a lesion that is 100% curable. Furthermore, the introduction of a diagnostic test that is less invasive and less costly than the expensive imaging-based methodolo-

gies commonly used today offers additional opportunities to extend testing to a broader risk group population.

2. Disease pathology and staging

As noted earlier, the term 'pancreatic cancer' usually refers to a ductal adenocarcinoma of the pancreas. This represents the vast majority of all pancreatic neoplasms and most affected patients share a similar poor long-term prognosis. The more inclusive term 'exocrine pancreatic neoplasms' includes all tumours that are related to the pancreatic ductal and acinar cells and their stem cells. Approximately 95% of malignant neoplasms of the pancreas arise from the exocrine elements. Accordingly, neoplasms arising from the endocrine pancreas (i.e. pancreatic neuroendocrine tumours) comprise no more than 5% of pancreatic neoplasms.

Precursor lesions to symptomatic pancreatic cancer

A number of stages in the progression from precursor lesions to symptomatic PC are recognised. Pancreatic intraepithelial neoplasia (PanIN), regarded as the precursor lesion for PC, progresses from PanIN-1 (hyperplastic and benign) through PanIN-2 (low-grade dysplasia) to PanIN-3 (high-grade dysplasia or carcinoma in situ). PanIN-3 is synonymous with carcinoma in situ in the TNM (tumour-node-metastasis) classification of solid tumour development used by the Union for International Cancer Control (UICC) and the American Joint Committee on Cancer (AJCC).

Pancreatic cystic neoplasms (PCN) are common diseases with an estimated prevalence in the general population of approximately 20%. A wide range of different cystic tumors has been described, but IPMN and MCN seem to be the most prone to undergo malignant transformation. Furthermore, the incidence of IPMN appears to be high in individuals with a familial risk for PC and, conversely, a positive family history for PC is a risk factor for IPMN development. The risk of cancer in IPMN patients ranges from 24% in IPMN involving the branch ducts to over 60% in lesions involving the main pancreatic duct. For this reason, follow-up or preventive surgery of these neoplasms is recommended.

References:

Early detection and prevention of pancreatic cancer: Is it really possible today? *Del Chiaro M et al. World J Gastroenterol. 2014 Sep 14; 20(34): 12118–12131*

Pancreatic cancer staging

All pancreatic cancers, i.e. both exocrine and neuroendocrine, are classified according to the TNM system. Intended to delineate the extent of disease spread and identify patients who are eligible for resection with curative intent, this scale distinguishes four main disease stages. Stages I and II (both sub-divided into A and B) are considered the early stages of PC. In stages III and IV, the cancer has spread. These four stages, and their potential for treatment, are briefly summarised below.

- **Stage I:** Lesions are confined to the pancreas. In stage IA, the tumour may be small (less than 2 cm). In stage IB, it may be larger than 2 cm but still not spread to nearby organs. Stage I tumours are resectable; the disease has not spread into the body and the patient can undergo surgery.
- **Stage II:** Lesions have extended beyond the pancreas to nearby tissue and organs. In stage IIA, without lymph node involvement, in Stage IIB with lymph node involvement. Stage II tumours are also resectable.
- **Stage III:** The disease has spread to adjacent major blood vessels. Although some cases may be borderline resectable, the majority are regarded as unresectable.
- **Stage IV:** Tumours may be any size and the disease has spread to both nearby and distant organs, such as the lung, liver and peritoneal cavity. These distant metastases render the cancer unresectable, regardless of the feasibility of local resection.

3. Treatment options

Stages I and II

The PC is amenable to local surgical resection. Approximately 20% of patients present in this way and complete resection can yield 5-year survival rates of 18% to 24%. However, ultimate control remains poor because of the high incidence of both local and distant tumour recurrence. Furthermore, the role of post-operative therapy

(chemotherapy with or without chemoradiation therapy [CRT]) in PC management remains unclear.

A number of phase III trials have examined the potential overall survival benefit of post-operative adjuvant 5-fluorouracil (5-FU)-based CRT, as well as 5-FU plus infusional 5-FU and concurrent radiation, or the adjuvant gemcitabine (a nucleoside analogue) plus infusional 5-FU and concurrent radiation. However, much of the randomised clinical trial data generated are statistically underpowered and the results conflicting. Today, there is no consensus regarding the overall optimal management of patients after resection of an exocrine PC, and the approach is different in Europe and in the United States. Nevertheless, some results suggest that a gemcitabine-containing regimen represents an appropriate choice for current management of patients with resected PC and may thus be considered as an acceptable standard.

Stage III

Stage III PC patients have tumours that are technically unresectable because of local vessel impingement or invasion by the tumour. Some do have PCs regarded as borderline resectable (usually based on simple anatomic considerations only), but aggressive tumour biology and/or the patient's physical inability to undergo both surgery and perioperative chemoradiation therapy could negate any survival benefit of PC resection.

Trials attempting to examine combined modality therapy versus radiation therapy alone have again suffered from substantial deficiencies in design or analysis. One study evaluating the role of radiation therapy with concurrent gemcitabine compared with gemcitabine alone in patients with localised unresectable pancreatic cancer has demonstrated improved overall survival with acceptable toxicity for the former regime. This can therefore be considered as the current standard therapy for Stage III PC. Note however, that promising response rates with FOLFIRINOX chemotherapy (a combination of leucovorin calcium, fluorouracil, irinotecan hydrochloride and oxaliplatin agents) in the metastatic setting have encouraged oncologists to use this regime instead of gemcitabine in younger patients with good performance status.

Stage IV

Stage IV cancers are not considered for resection. Furthermore, current chemotherapy in newly diagnosed patients with stage IV PC is characterised by a low response rate and lack of survival benefit.

Nevertheless, occasional patients have palliation of symptoms when treated by chemotherapy with well-tested older drugs such as 5-FU. Gemcitabine has also demonstrated activity in stage IV patients and is a useful palliative agent. Improvements in survival are, however, often modest or not significant and may be achieved at the cost of increased toxicity and poor quality of life. In patients with metastatic PC with good performance status, the current standard treatment option would include FOLFIRINOX combination chemotherapy, while Gemcitabine-based chemotherapy remains the treatment of choice for most other patients. Supportive palliative care plays a crucial role in this group.

In summary, the lack of effective systemic therapies, particularly in the later stages of PC, suggests that earlier detection to allow down-staging of locally unresectable disease (thereby permitting surgical resection) has the greatest potential to reduce the risk of metastatic disease and radically improve survival.

4. Challenges in early detection

The possibility of early detection (and the increased rate of surgically resectable tumours that will result) is enticing but not without its challenges, as the following examples illustrate.

Lack of clinical symptoms and poor detection

Cancer-specific symptoms are largely associated with advanced PC (disease stages III and IV), whereas earlier stage PC lacks clinical symptoms. Thus, detecting resectable PC will require screening asymptomatic subjects. In addition, the incidence of PC in the general population is relatively low (approx. 10/100,000). Even in subjects of 50 years or older, the age-adjusted incidence of PC is only 38/100,000. Screening such unselected populations for asymptomatic PC is not feasible; due to reasons of cost and complexity, none of the current detection technologies are suitable for this task. Furthermore, early PC is not detectable by routine cross-sectional imaging.

For example, computed tomography lacks the sensitivity to detect small pancreatic lesions, not to mention precursor PanIN lesions. Based on available technology, therefore, detection of early lesions will require innovative non-invasive imaging or invasive testing, such as molecular endoscopic ultrasound (EUS). Unfortunately, abnormalities on EUS are not specific for lesions of early PC.

In contrast to the general population, groups with a moderate to high risk of developing PC, e.g. those with family history of PC or possessing certain genotypes, would likely benefit from improved detection. To be effective, however, this approach still needs a method based on inexpensive screening technology able to accurately detect early stage lesions.

Lack of biomarkers

Biomarkers that identify advanced but pre-cancerous lesions to achieve early-stage differential diagnosis thus have the potential to overcome many or all of the drawbacks noted above. Until now, however, there have been no validated biomarkers of early PC.

None of the candidate biomarkers available today possess sufficiently high accuracy or specificity to be implemented for screening, even in high-risk patients. For example, the carbohydrate antigen 19-9 (CA-19-9), currently used as the benchmark for following up patients with a PC diagnosis during treatment, may also be positive in patients with non-malignant diseases, including liver cirrhosis, chronic pancreatitis and other gastrointestinal cancers.

Taking all the issues discussed above into account, it is clear that early detection will have a great impact on improving survival in pancreatic cancer by making more cases amenable to curative treatment. In addition, it can be stated that:

- There is a relatively wide window of opportunity for early-stage detection.
- Current imaging technologies are cost-prohibitive and difficult to apply.
- An ideal screening biomarker should be universally present in curable-stage PC, but absent in cancer-free individuals.
- The assays should be rapid, inexpensive and practical to perform, as well as highly sensitive and specific.

Further information on pancreatic cancer

The following publications provide excellent reviews of pancreatic cancer and discuss many of the issues raised in Sections 1 to 5 in greater depth.

1. **Carcinoma of the Pancreas and Stereotactic Radiosurgery.** *White Paper January 2013.*
The Radiosurgery Society San Mateo, CA, USA.
www.therss.org
A general review of pancreatic cancer including coverage of incidence, prognosis, staging and treatment options.
2. **Early Detection of Sporadic Pancreatic Cancer: Summative Review.** *Suresh T. Chari et al. Pancreas, Vol. 44, No. 5, July 2015.*
An in-depth summary of current efforts in the field, including challenges that exist in early detection.

5. IMMray™ PanCan-d test for early detection of pancreatic cancer

IMMray™ PanCan-d is a blood-based screening test for the early detection of stage I and II PC when the cancer is still resectable. Now being commercialised by Immunovia, it is based on the company's antibody microarray technology platform IMMray™. Immunovia will offer the test as an in-house laboratory service.

IMMray™ combines many years of leading-edge clinical immunoproteomics research, the development of unique serum biomarker signatures, and a state-of-the-art bioinformatics algorithm and software to interpret clinical test data from a variety of major diseases. Each blood sample is analyzed and characterized using a disease-specific antibody microarray targeting a multiplex panel of biomarkers. A simple blood test thus could provide all the necessary information for enabling early diagnosis, as well as for following disease progression, and/or therapy monitoring. Several proof-of-concept studies on other cancer forms are summarised in Section 10.

In PC, IMMray™ PanCan-d overcomes the lack of a validated serum biomarker of sufficient accuracy and specificity for early-stage screening by employing a (frequently) <25-serum biomarker signature able to discriminate PC from the combined group of pancreatitis diseases and healthy controls (N). Of particular importance is that this signature has been identified through a stepwise

biomarker/analyte selection process; one biomarker is excluded at a time in an iteration process that adopts Immunovia's in-house backward elimination algorithm. Based on a support vector machine (SVM) classification, this algorithm generates the combination of biomarkers that shows the highest discriminatory power between healthy and disease states.

The IMMray™ PanCan-d test thus has a high diagnostic potential and several pre-validation studies have already demonstrated its value in PC (see Section 11). In addition to differentiating healthy vs. PC vs. pancreatitis at different disease stages, the test has also proven to be robust and to work on genetically different populations.

The technology platform, biomarker discovery, test methodology, proof-of-concept studies on other cancer forms as well as clinical validation studies on PC are described in more detail in the following sections.

6. Antibody-based microarrays – the IMMray™ technology platform

Using conventional proteomic technologies in the search for candidate biomarker signatures has proven to be a challenge. Recombinant antibody-based microarrays now offer a more promising approach, providing miniaturised set-ups capable of profiling numerous protein analytes in a sensitive and selective manner suitable for disease diagnostics and prognostics. By transforming the microarray patterns generated into molecular fingerprints and applying advanced bioinformatics, biomarker signatures can be de-convoluted and tested for clinical applicability, with the ultimate goal of transferring them into clinical practice.

In brief, minimal amounts of individual antibodies with the desired specificity are applied in discrete positions in an ordered pattern onto a solid support. This 'antibody printing' creates the array. The arrays are then exposed to small amounts of non-fractionated proteomes, e.g. serum or plasma, and specifically-bound analytes are detected and quantified. The array images are then transformed into protein expression profiles. Finally, bioinformatics are applied to define differences and similarities in these profiles between the sample cohorts, e.g. healthy vs. cancer. Figure 1 outlines this process.

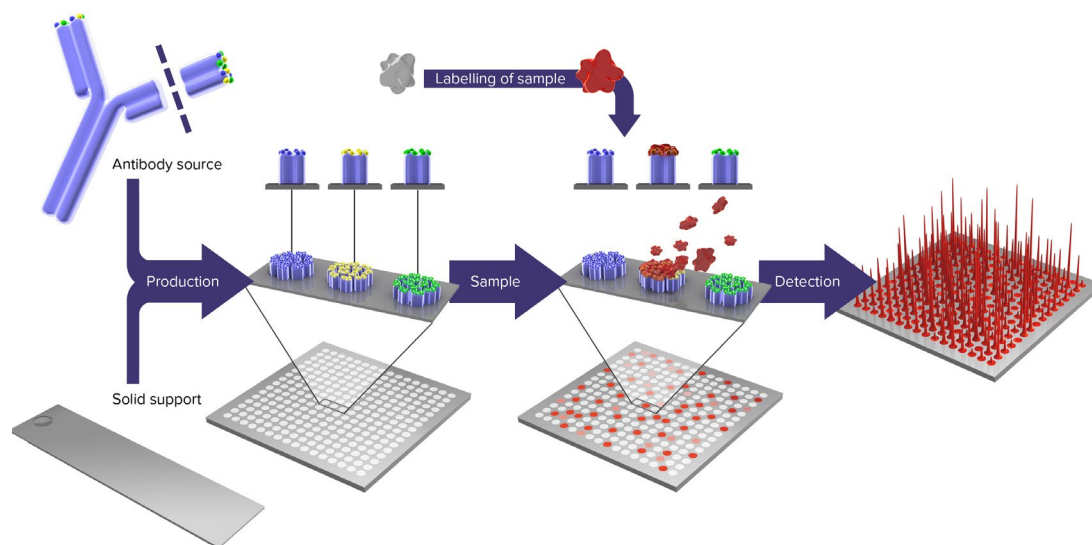


Fig. 1. Miniaturized microarrays are printed with antibodies carrying desired specificities. Small amounts of sample are added and specifically-bound analytes detected and quantified. The array images generated are converted into protein expression profiles, thus revealing the detailed composition of the sample. Finally advanced bioinformatics are applied. As well as disease diagnostics, the results can be applied in biomarker discovery, disease proteomics, and patient stratification.

7. Biomarker discovery exploits the diagnostic power of the immune system

Immunovia's approach to biomarker discovery harnesses the diagnostic/prognostic power of the immune system to target various indications, primarily cancer (as described in this White Paper) and autoimmunity. It is based on the fact that the immune system is very sensitive to changes in an individual's state of health; during disease, for example, the system registers this alteration via fluctuations in the levels of various analytes, in particular immunoregulatory analytes.

The company has thus designed a recombinant antibody microarray technology platform that mainly targets immunoregulatory proteins. These 'immunosignatures' can be seen as snapshots of the immune system's activity in a patient at the time of the test. This view (or fingerprint) provides a unique read-out reflecting what is going on inside the patient.

The fingerprints reflect a combination of direct and indirect (systemic) effects in response to diseases like cancer and can collectively be exploited as candidate classifiers for a specific disease. Disease-associated candidate biomarker signatures that display high diagnostic and prognostic power have been deciphered, thereby demonstrating the strength of the technology.

Further information on the microarray technology platform

The microarray technology platform developed and used by Immunovia is described in a number of publications, several of which are listed below.

1. **Detection of pancreatic cancer using antibody microarray-based serum protein profiling.** *Ingvarsson J et al. Proteomics 2008, 8, 2211–2219.* Describes an affinity proteomic attempt to explore differences in serum protein content in cancer patients versus healthy subjects based on a recombinant antibody microarray containing array adapted single-chain fragment variable (scFv) fragments.
2. **Antibody-Based Microarrays.** *Wingren and Borrebaeck. In Microchip Methods in Diagnostics, Ursula Bilitewski (ed.), Vol. 509, Humana Press, New York, USA, 2008.* This review describes the antibody-based microarray technology, highlighting its applications within disease proteomics, biomarker discovery, disease diagnostics, and patient stratification.
3. **Developing and applying recombinant antibody microarrays for high-throughput disease proteomics.** *Borrebaeck C and Wingren C. European Pharmaceutical Review, Issue 6, 2010.*

This mini-review discusses selected steps in the process of developing and applying recombinant antibody microarrays for high-throughput disease proteomics, as well as addressing the issue of transferring proteomic discoveries into clinical practice.

4. **Serum proteome profiling of pancreatitis using recombinant antibody microarrays reveals disease-associated biomarker signatures.**

Sandström A et al. Proteomics Clin Appl, 2012 6, (9-10):486-96.

This study demonstrates the potential of the antibody microarray approach for stratification of pancreatitis and demonstrates its potential for multiplexed affinity proteomics in disease stratification.

5. **Identification of Serum Biomarker Signatures Associated with Pancreatic Cancer.** *Wingren C et al. Cancer Res. 2012 15;72(10):2481-90.*

Describes the first pre-validated, multiplexed serum biomarker signature for diagnosis of pancreatic cancer with the potential to improve diagnosis and prevention in premalignant diseases and in screening of high-risk individuals.

8. IMMray™ immunoproteomics technology in practice

Immunovia exploits the immune system as an early, specific and sensitive sensor for disease. scFv Antibodies are generated towards clinically-relevant immunoregulatory proteins. The antibodies are arranged on miniaturized arrays (smaller than 1 cm²) ranging in density from a few antibodies to several thousand. These are then incubated with minute amounts (µL scale) of labelled non-fractionated biological sample, e.g. patient serum. Next, specifically-bound proteins are detected and quantified, using fluorescence as the mode of detection. Finally, the microarray images are transformed into protein expression profiles to reveal the composition of the patient sample at the molecular level.

Using the state-of-the-art bioinformatics mentioned earlier, this information is then used to decipher condensed protein signatures (frequently < 25) or molecular fingerprints that reflect the target disease. Measuring the delineated biomarker panels can ultimately provide clinicians with actionable information that enables early and specific diagnosis, prognosis and classification. Monitor-

ing patients for factors such as risk of relapse and response to treatment are further applications of great potential clinical merit. Figure 2 illustrates the planarwell array in close up.

The platform's combination of sensitive, clinically-relevant biomarkers and advanced in-house bioinformatics thus leads to a clear, easy-to-interpret answer per patient sample. Its key operational benefits include:

Blood-based assay

- Uses standard serum and plasma patient samples

Highly specific and sensitive

- Recombinant scFv antibody library
- Measures patients' immune response
- Discovery chip with up to 500 antibodies, IVD chip with 25 clinically-relevant biomarkers

Robust and reproducible

- 3 x 10¹⁰ recombinant scFv library microarray adapted by molecular design

Rapid and easy to perform

- ELISA assay time
- Fluorescent-based read-out system

Automated data analysis

- Advanced bioinformatics provide one simple answer to the clinician

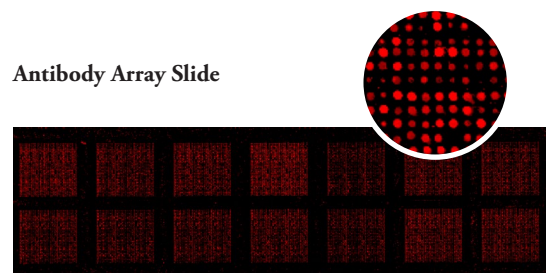


Fig. 2. The planarwell array with the bound clinically-relevant biomarkers for discovery projects.

Note: For commercial application the IVD chip will have 20-30 clinically-relevant biomarkers.

HIGH-THROUGHPUT PROTEIN EXPRESSION PROFILING

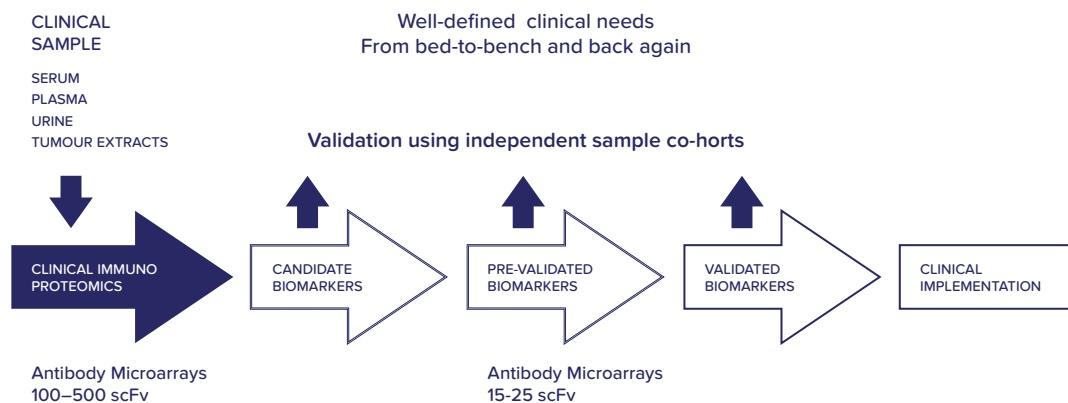


Fig. 3. The overall biomarker development approach is based on high-throughput protein expression profiling. Reference: Wingren and Borrebaeck, *Exp. Rev. Mol. Diag.* 2007, 7, 673-686. Wingren and Borrebaeck, *DDT*, 2007, 12, 813-819. Borrebaeck and Wingren, *J Proteomics* 2009, 72, 928-. Borrebaeck and Wingren, *J Exp. Rew. Proteomics*, 2009, 6, 11-13.

9. Biomarker development – proof-of-concept discovery studies

This overall biomarker development approach, on which IMMray™ PanCan-d is based, is illustrated in Figure 3. It meets well-defined clinical needs and is characterised by a bed-to-bench and back again workflow, i.e. from serum sample via an antibody microarray assay to clinical implementation.

As part of the work to test the overall viability of this approach, a number of proof-of-concept discovery studies in breast cancer and glioblastoma multiforme based on this strategy have been performed. These are outlined below.

A. Predicting the development of distant metastases in primary breast cancer using IMMray™ molecular serum profiling

An IMMray™ recombinant antibody microarray platform containing 135 antibodies against 65 mainly immunoregulatory proteins was used to screen 240 sera from 64 patients with primary breast cancer collected between 0 and 36 months after the primary operation. Leave-one-out cross-validation together with a backward elimination strategy in a training cohort enabled the identification of a 21-protein signature. Testing and subsequent evaluation of this signature in an independent test cohort

showed that patients could be classified into high versus low-risk groups for developing metastatic breast cancer (ROC AUC = 0.85) (Fig. 4). More importantly, it was demonstrated that the IMMray™ protein signature provided added value compared with just conventional clinical parameters (AUC = 0.90). The candidate serum biomarker signature presented was thus able to classify patients with primary breast cancer according to their risk of developing distant recurrence with an accuracy that outperformed currently available procedures.

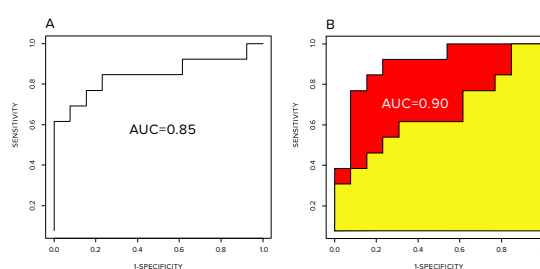


Fig. 4. The IMMray™ protein signature classified breast cancer patients into high versus low-risk groups and provided added clinical value.

Reference

Molecular serum portraits in patients with primary breast cancer predict the development of distant metastases. Carlsson A et al. *PNAS* 2011 108(34):14252-7.

B: IMMray™ based biomarker signatures can improve the classification and selection of patients for personalized therapy against glioblastoma multiforme

This study investigated the applicability of large-scale recombinant antibody-based microarrays based on IMMray™ biomarker signatures for the sensitive and selective plasma protein profiling of glioblastoma multiforme (GBM) patients undergoing immunotherapy with autologous IFN-γ transfected glioma cells. It demonstrated that the candidate plasma protein signatures associated with GBM could be used for GBM classification and monitoring the effects of the immunotherapy, as well as for pre-operatively stratifying patients according to the beneficial effect of the adopted immunotherapy.

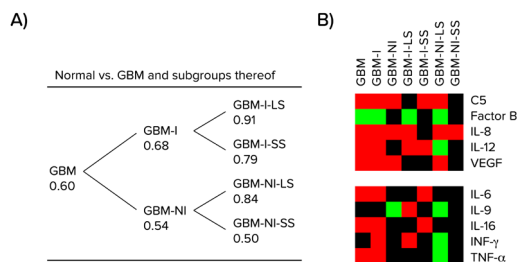


Fig. 5. The IMMray™ protein signature proved capable of classifying, monitoring and stratifying glioblastoma multiforme patients pre-operatively.

Reference

Plasma proteome profiling reveals biomarker patterns associated with prognosis and therapy selection in glioblastoma multiforme patients. *Carlsson A et al. Proteomics Clin Appl. 2010 4(6-7):591-602.*

Summary

The two discovery studies highlighted above confirm the suitability of the IMMray™ immunoproteomics technology for generating accurate clinical data that will improve the classification, discrimination and selection of cancer patients for therapeutic procedures. In particular, it was able to:

- Improve the classification of patients with primary breast cancer according to their risk of developing distant recurrence.

- Discriminate between histological grades 1, 2, and 3 of breast cancer tumours with high accuracy.
- Profile GBM patients, monitor immunotherapy and pre-operatively stratify patients.

10. Pre-validation studies in pancreatic cancer

The driving force behind oncoproteomics is to identify protein biomarkers that are associated with a particular malignancy. This White Paper focuses on Immunovia's work to define and apply recombinant scFv antibody microarrays to classify PC patients versus healthy subjects. To achieve this goal and thereby significantly improving the potential for treatment and survival, the company has conducted a number of pre-validation studies. These studies, as well as work planned, are outlined in this paper.

As can be seen below, the microarray technology platform and the number of antibodies were refined during development to achieve optimum robustness and quality. Today, Immunovia is in a phase where the validation necessary from quality and regulatory perspectives can be implemented to achieve a product approved for clinical use. This product will be designated the IMMray™ PanCan-d test.

A. Differentiation of healthy controls vs. stage 3 and 4 pancreatic cancer patients

The first retrospective study, published in 2008, was designed to show whether a particular patient serum signature could distinguish PC patients from patients without the disease. It also aimed to demonstrate the ability to distinguish PC patients with a survival prognosis of over 24 months from those with a survival prognosis of less than 12 months. Forty-four serum samples collected at two Swedish hospitals were analysed; 24 from PC patients with already established diagnosis that had not undergone therapy treatment and 20 from healthy individuals.

An antibody microarray with approximately 130 human recombinant scFv antibodies was used to analyse the samples. Twenty-eight samples (18 from cancer patients, 10 from healthy individuals) were used to identify a serum signature. The rest were used to verify this signature. (Fig. 6).

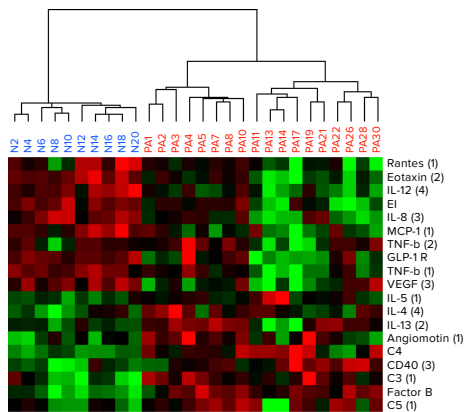


Fig. 6. Results showed that a serum signature of 19 scFv antibodies could distinguish stage III and IV pancreatic cancer patients from healthy individuals.

Reference

Detection of pancreatic cancer using antibody microarray-based serum protein profiling. *Ingvansson J et al. Proteomics 2008 8(11):2211-9.*

B. Identification of serum biomarker signatures associated with pancreatic cancer.

This retrospective study, aimed to distinguish PC patients from healthy controls (N), patients with chronic pancreatitis (CP), and patients with autoimmune pancreatitis (AIP). To this end, samples from 34 PC patients, 30 healthy individuals, 16 with chronic pancreatitis and 23 AIP patients collected at two different sites were analyzed on a microarray comprising 121 different scFv antibodies.

To demonstrate that PC patients could be distinguished from healthy control patients based on a biomarker signature, the sample cohort was divided into training set (64 samples) and validation set (45 samples). Based on the training set, a condensed biomarker signature composed of 18 relevant antibodies was identified using a backward elimination variable selection strategy. The signature was applied on the independent validation set, and the result showed that it was possible to classify PC patients from healthy controls with AUC value of 0.95 (Figure 7 A).

Next, the classification power of PC patients vs. benign conditions and healthy individuals was investigated using all antibodies, i.e. unfiltered data. The results showed that it was possible to distinguish PC patients from AIP (AUC 0.99), CP (AUC 0.86) and the combined group of CP, AIP and N (AUC 0.85) (Fig. 7 B).

Figure title: Differentiation of healthy controls vs. cancer vs. pancreatitis

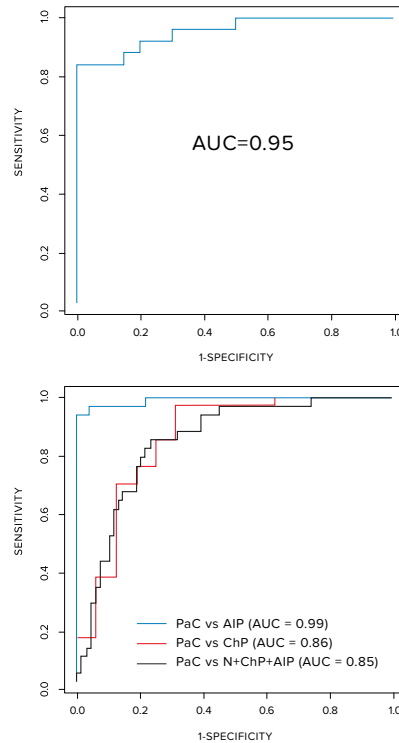


Fig. 7. (A) PC patients could be discriminated from healthy individuals (AUC 0.95) based on an 18 antibody signature. (B) Discrimination of PC patients against AIP (AUC 0.99), CP (AUC 0.86) and the combined group of AIP, CP and N (AUC 0.85).

To further test the discriminative power of PC patients from the combined group of benign conditions (CP and AIP) and healthy individuals, a condensed biomarker signature composed of 25 antibodies was identified using training set. When applied on the independent validation set, the result showed that PC could be classified with AUC value of 0.88.

Importantly, PC patients could be distinguished from healthy control individuals and the combination of benign conditions and healthy individuals using serum biomarker signatures exhibiting high diagnostic potential. This study thus presents evidence for the first pre-validated, multiplexed serum biomarker signatures able to diagnose pancreatic cancer, and with the potential to improve diagnosis and prevention in premalignant diseases and in screening high-risk individuals.

Reference

Identification of serum biomarker signatures associated with pancreatic cancer. *Wingren C et al. Cancer Res. 2012 15;72(10):2481-90.*

C. Serum proteome differentiation of pancreatitis from healthy controls

Pancreatitis is an inflammatory condition of the pancreas that mainly appears in acute (AcP) and chronic (ChP) manifestations. Over the past couple of decades, autoimmune pancreatitis (AIP), a chronic, heterogeneous disorder, has emerged as a separate clinical pancreatitis entity. Since it will be important to differentiate between pancreatitis and PC, as well as between PC and healthy individuals when attempting to detect early-stage disease, a retrospective study was performed to evaluate the use of affinity oncoproteomics for identifying potential markers of pancreatitis and for stratifying its different subtypes.

One hundred and thirteen serum samples comprising normal controls (N, n = 30), ChP patients (n = 16), AIP patients (n = 23) and AcP (n = 44) patients were collected from two hospitals. High-content, recombinant antibody microarrays with 121 human recombinant scFv antibody fragments targeting 57 serum analytes were applied. The sample groups were compared using supervised classification based on support vector machine (SVM) analysis.

To assess the predictive power of the antibody microarrays, the serum protein expression profile of the combined pancreatitis cohorts was first compared to that of normal controls. An SVM classification based on a leave-one-out cross-validation showed that all samples could be correctly classified with high AUC values (0.96–1.00), i.e. up to 100% specificity and sensitivity (Fig. 8).

Moreover, characteristic protein patterns and AUC values in the range of 0.69–0.95 were observed for the individual pancreatitis entities when compared to each other, and to all other samples combined.

Differentiation of healthy controls vs. individual pancreatitis entities

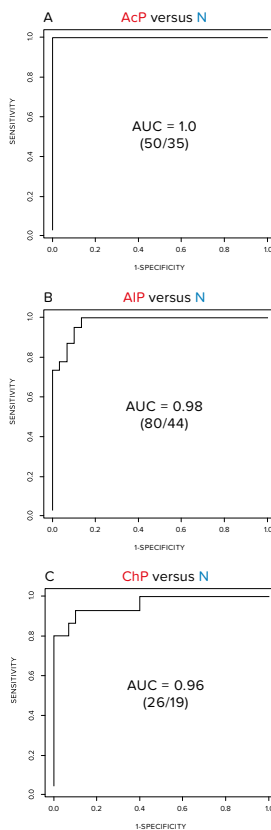


Fig. 8. Prediction and protein profiling of individual pancreatitis groups vs. controls. The number of antibodies/analytes showing statistical significance ($p < 0.05$) are given within brackets. (A) ROC curve for AcP versus N. (B) ChP versus N. (C) AIP versus N.

This study shows by applying the antibody microarray approach, the information content in a simple blood sample is able to differentiate between healthy individuals versus those with pancreatitis. What's more, its demonstration of distinct multiplex serum biomarker signatures for chronic, acute, and autoimmune pancreatitis further emphasises the suitability of affinity proteomics as an important tool for both screening and diagnosis.

Reference

Serum proteome profiling of pancreatitis using recombinant antibody microarrays reveals disease-associated biomarker signatures. *Sandström et al. Proteomics Clin. Appl. 2012, 6, 486–496.*

D. Robust pancreatic cancer diagnosis in a multi-centre trial

In the studies summarised above, all samples were collected from a limited number of hospitals. To broaden the test's reliability and credibility, a multicentre retrospective study was initiated and carried out in collaboration with a number of centres in Spain. Its specific aim was to identify a robust, diagnostic serum protein signature associated with stage III and IV PC at the time of clinical diagnosis.

The study analyzed 338 serum samples from patients with stage III and IV PC (n=156), other pancreatic disease (OPD) (n=152) and controls (NPC) (n=30) collected at five different hospitals in Spain. Patients with suspicion of PC were included. A panel of experts validated by consensus the final diagnosis of all patients through a careful revision of clinical and pathological records and follow-up information. Samples (one per patient) were collected before any treatment was given.

The antibody microarrays contained 293 human recombinant scFv antibodies, the majority selected against immunoregulatory proteins and with previously demonstrated robust on-chip functionality. Microarrays were produced using a non-contact printer with thirteen identical subarrays on each slide.

Serum samples were added and the slides analyzed using a confocal microarray scanner. After local background subtraction, intensity values were used for data analysis. Data acquisition was performed by a trained member of the research team and blinded to the sample classification and clinical data.

The approach used to identify the optimal combination of biomarkers was a supervised model based on Support Vector Machine (SVM) analysis in combination with a Backward Elimination algorithm. Data were subdivided into training sets, from which biomarker signatures were identified. The classification power of these signatures was subsequently evaluated in separate test sets of the remaining samples using the area under the ROC-curve (AUC) to obtain accuracy of classification performance.

Results suggested that up to ten protein markers were sufficient for a highly accurate discrimination of PC vs. NPC controls, while an average of 67 antibodies was necessary for optimal classification of PC vs. OPD, the

latter reflecting the challenge in distinguishing PC from symptomatically-related benign conditions. When the top 25 antibodies from each elimination process were selected, the AUC values generated as a measure of classification accuracy reached 0.98 (PC vs. NPC).

The serum signatures identified from all five hospitals were robust enough to contribute to the development of a multiplexed biomarker immunoassay for improved PC diagnosis with high sensitivities and specificities.

A further interesting discovery indicated that it should be possible to distinguish whether the PC is localized in the head or the body-tail of the pancreas. This observation has important clinical implications since the prognosis for a head-located cancer appears worse compared with a tail location.

Robust and accurate diagnosis of PC in a multi-centre trial

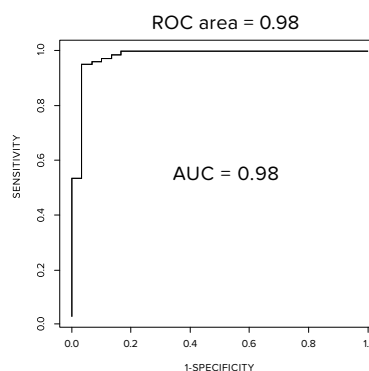


Fig. 9. Patient samples (n=338) collected from five study sites showed that a condensed 25-antibody biomarker panel test set had a high power of classification accuracy (0.98) and could successfully discriminate PC patients from controls.

Reference

A multicenter trial defining a serum protein signature associated with pancreatic ductal adenocarcinoma. *Sandström Gerdtsen A et al. Int Journal of Proteomics. 2015*

E. Successful early diagnosis of PC in genetically different populations, including discrimination of stage I/II and stage III/IV cancers from healthy patients.

The four studies summarized above have clearly demonstrated the accuracy (ROC AUC > 0.90) that multiplexed analyses display when discriminating PC vs. controls and PC vs. pancreatitis. They were, however, conducted on Caucasian individuals, essentially from a Swedish population.

To test whether the antibody microarray blood-based screening test is equally applicable on a different genetic population, collaboration with clinical researchers and laboratory staff at the Tianjin Medical University Cancer Institute and Hospital (TMUCIH) in China was initiated. Performing the tests on Chinese soil using Chinese equipment would also be a good indication of how robust the test is when applied outside of Immunovia's own laboratories.

Equally important to note is that the China study cohort was grouped according to PC stage, i.e. resectable disease (stage I/II), locally advanced (stage III) and metastatic disease (stage IV). In other words, it offered the opportunity to assess whether stage I/II tumours could be discriminated from controls with accuracy sufficient to permit early diagnosis and thereby increase the detection rate of surgically resectable tumours.

A total of 213 plasma samples were used for this study. Enrolled PC patients (n=118) were all Chinese Han ethnicity and treated at TMUCIH. None had received chemotherapy or radiotherapy at the time the samples were taken. All PC samples were confirmed by cytology.

Data on tumour stage and size at diagnosis and tumour location within the pancreas were based on clinical pathology. Normal control (NC) samples (n=95) were collected from healthy inhabitants of Tianjin at their routine physical examination at TMUCIH, and were genetically unrelated to the PC patients.

The antibody microarrays contained 350 human recombinant scFv antibodies, most of which had previously been used in array applications and also validated. Sample and variable distribution was analyzed and visualized and the performance of individual markers was evaluated. Separation of different subgroups within the data was assessed using a support vector machine (SVM) function. Models for discriminating groups were created using a leave-one-out cross validation procedure.

A high initial level of differentiation between PC and controls (AUC 0.88 based on unfiltered data) motivated further in-depth data processing for generating a PC-associated protein signature. By repeating the backward antibody elimination process, a signature of 23 markers able to deliver an optimal discrimination of PC vs. NC could be defined. Moreover, this signature overlaps significantly with those derived from Caucasian patient cohorts.

The results clearly show that despite differences in ethnicity and experimental / bioinformatic processes, Immunovia's antibody microarray blood-based screening test does not show any significant differences in signatures or disease discrimination between a Chinese and a European population with regard to pancreatic cancer patients and healthy individuals.

Comparison	AUC-value
Stage I and II vs Healthy	0.80
Stage III and IV vs Healthy	0.96
Stage I vs Healthy	0.71
Stage II vs Healthy	0.86
Stage III vs Healthy	0.90
Stage IV vs Healthy	0.93

Fig. 10. Discrimination of pancreatic cancer stage I-IV vs healthy individuals, based on leave-one-out cross validation procedure using unfiltered data.

Moreover, the testing performed in Tianjin showed that early-stage confined disease (stage I/II) and late-stage invasive disease (stage III/IV) groups could be discriminated, based on unfiltered data, from NC with AUC values of 0.80 (early stage) and 0.96 (late stage) (Fig. 10)

This is the first time that patients with resectable stage I/II PC tumours could be distinguished from controls with high accuracy, in strong contrast to previous samples where the majority of the differentiated PC patients were in the later stage III or stage IV, and thus had a much worse forecast.

Reference

Re-submitted. Plasma protein profiling of stage defined pancreatic cancer cohorts - implications for early diagnosis. *Sandström Gerdtsen A et al. Accepted Sept. 2015.*

Summary

The results of these retrospective studies indicate that the serum-based test developed by Immunovia for early detection of pancreatic cancer has a solid clinical background to build on. In particular, the test was able to:

- Distinguish stage III and IV pancreatic cancer patients from healthy individuals.
- Distinguish PC patients from healthy controls (N), patients with chronic pancreatitis, and patients with autoimmune pancreatitis.
- Distinguish healthy controls from patients with pancreatitis and differentiate individual pancreatitis entities.
- Distinguish healthy individuals from III and IV PC patients at multiple centres with no difference in results.
- Distinguish resectable stage I/II PC tumours from controls despite differences in genetic populations and experimental / bioinformatic processes.

These results have formed the basis for ongoing and future clinical trials, as summarised below.

F. Studies in progress and planned

The study performed in China at Tianjin Hospital and Cancer Institute provided a strong indication that the IMMray™ PanCan-d test can identify asymptomatic PC patients as early as stage I or stage II.

As a result, Immunovia in collaboration with CREATE Health Translational Cancer Centre in Lund, Sweden initiated a retrospective study comprising blood samples from Scandinavian patient cohorts of all stages of pancreatic cancer as well as healthy individuals. The study covered 1400 blood samples, making it the largest study for diagnosing pancreatic cancer in all stages.

The results of the study that are now under publication, show that IMMray™ PanCan-d is able to differentiate 149 blood samples of the early resectable stages of pancreatic cancer, stage I and II, from the 700 matched healthy controls with 96% accuracy.

When analyzing all stages of cancer, 448 samples and 966 matched controls, the accuracy of IMMray™ PanCan-d is reported as high as 98% confirming the findings in the previous studies.

The number of stage I and II cases is sufficiently large to provide a statistically relevant biomarker signature that can detect the early stages of pancreatic cancer.

To complete the validation of the IMMray™ PanCan-d biomarker signature, Immunovia plans to perform additional retrospective studies. One study will be in partnership with Oregon Health & Science University (OHSU), Portland, Oregon with the aims to demonstrate that the validated and finalised IMMray™ PanCan-d test platform can be established outside of Immunovia's own laboratories, and partly to show that it will perform reliably within the US clinical community. The sample cohort also contains a substantial number of stage I and II samples (139) that can further verify that IMMray™ PanCan-d biomarker signature can detect even the early stages of pancreatic cancer.

The need for prospective studies has also increased significantly in recent years since healthcare systems began to set higher standards for test usefulness and economic benefits. Individual countries may also place increased demands for studies to be implemented in order to gain market acceptance there.

Immunovia therefore is planning for a prospective observational study for early detection of pancreatic cancer with a three-year duration involving approximately 1000 risk group individuals from at least 3 different centers: Oregon Health and Science University (OHSU) in Portland, USA, Mount Sinai Hospital, New York, USA and Liverpool University Hospital in the UK. The aim with the study is to generate data that can support approval for reimbursement of the test.

Study results will also be used to conduct a dialogue on the level of compensation payers believe is most appropriate. They will also comprise part of a regulatory dossier to be submitted to the FDA.

When this study is completed and the test validated in clinical laboratories, its use can be expanded to include the testing of a greater number of at-risk groups than is possible today. These groups include, for example, patients with newly-diagnosed Type II diabetes as well as other pancreas-related disorders with increased risk of developing PC.

11. Key benefits of IMMray™ PanCan-d

A. Technology platform offers a specific and sensitive marker for disease

As a technology platform, IMMray™ PanCan-d delivers many practical advantages, especially regarding handling, which is both efficient and economical. Serum sampling is non-invasive and only requires low microliter amounts of material. Reagent consumption is equally low. Sensitivity and specificity are high and the test's multiplex capability measures numerous proteins at the same time.

Assays can be performed using existing laboratory hardware and times are rapid (very similar to conventional ELISA) so fast answers are easy to obtain. Finally, by measuring antibody signatures in microarrays and exploiting the immune system as a specific, sensitive and early marker for disease, the test platform is highly suitable for high-throughput protein expression profiling of complex proteomes.

B. Patients, physicians and policymakers gain across-the-board benefits

Even though several clinical evidence studies are still ongoing, IMMray™ PanCan-d is already able to demonstrate a wide range of tangible benefits. As noted above, patients will appreciate the non-invasive diagnostic procedure as opposed to a CT scan or biopsy. Their major benefit naturally comes from the test's ability to detect early-stage PC (stage I and II) in risk-group individuals even before symptoms are discovered, and the consequent increase in 5-year survivability due to the tumours' amenability to complete resection.

Physicians win access to a simple yet reliable diagnostic tool that delivers answers at a disease stage where no equivalent tools are currently available. In addition, the blood test result can motivate the use of more expensive diagnostic procedures.

Policymakers gain a new possibility to introduce procedures for screening high-risk groups for a common form of cancer, as well as a concrete tool for implementing personalized medicine policies. Moreover, IMMray™ PanCan-d supports the implementation of the In Vitro Diagnostic Medical Devices Directive 98/79/EC (IVD Directive) and the US Recalcitrant Act.

C. Health economics data show QALY cost below European Willingness-to-Pay threshold

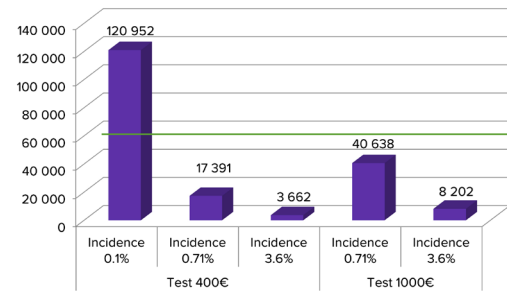
A health economic study on the early detection of PC, performed on the independent initiative of the Swedish Institute for Health Economics and published in the International Journal of Cancer, has shown that screening high-risk patients for PC using IMMray™ PanCan-d results in a cost for a QALY (Quality Adjusted Life Year) that is well below the Willingness-to-Pay (WTP) threshold in Europe. Figure 11 illustrates this finding.

WTP per QALY, the threshold where the payers of European health systems consider it health economically sound to introduce a new tool, varies between countries. The horizontal red line at 50k EUR indicates the average figure in Europe. A cost below this line thus shows that introducing such a test would be justified from a health economic point of view.

The graph illustrates the cost per QALY for different screening groups. The first bar (screening all the population over 60) shows, not surprisingly, that testing in this manner is not health economically justifiable due to the low incidence rate of PC (0.1%).

Bars two and three show the middle-aged, newly-onset diabetes risk group (incidence 0.71%) and the hereditary risk group (incidence 3.6%) respectively at a price per test of 400 Euro. Bars four and five show the same groups with a sensitivity analysis using a price of 1000 Euro per test. Even at this higher price, the cost per QALY is still in the WTP range. Full details are available in the publication.

Incremental cost-effectiveness ratio (ICER) (€/QALY gained)



Incidence - men aged 60-74: 97/100,000 inhabitants (0.1%)
 Incidence - newly diagnosed diabetics: 0.71%; Hereditary pancreatitis: 3.6%
 Willingness to Pay (WTP) per QALY is ca. €50,000/QALY gained, in Europe

Fig. 11. Health economics data show QALY cost below European Willingness-to-Pay threshold.

Reference:

Modelling the benefits of early diagnosis of pancreatic cancer using a biomarker signature. *The Swedish Institute for Health Economics*. Ghatnekar O. et al. *International Journal of Cancer*, 2013.

12. About Immunovia

Immunovia was founded in 2007 by investigators from the Department of Immunotechnology at Lund University and CREATE Health, the Center for Translational Cancer Research in Lund, Sweden. Its strategy is to decipher the wealth of information in blood and translate it into clinically useful tools to diagnose complex diseases earlier and more accurately than previously possible.

The company's main tool for achieving this goal is IMMray™, its core technology platform based on antibody microarray analysis developed following decades of clinical immunoproteomics research. Briefly, this solution combines a single-chain fragment variable (scFv) antibody library arranged as an array-based set-up, antibody biomarker signatures, and an advanced, in-house developed clinical algorithm and software for interpreting the data.

A. Capabilities

The company has its own antibody library, antibody production and purification as well as its own chip/array production. Clinical laboratory services are now undergoing validation for ISO accreditation.

In-house production

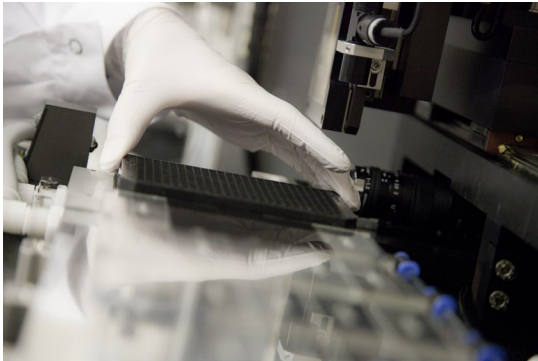
High-quality recombinant antibodies, produced and purified in-house using robotic systems and high-throughput processes, are used for microarray fabrication. The renewable monoclonal source of antibodies, which uses recombinant human antibody libraries specifically designed on a molecular level for optimal on-chip functionality, is a key element in ensuring high-performing microarray tests.

Recombinant antibody microarrays are produced using a state-of-the-art, non-contact dispensing (robotic) system, that spots ultra-low volumes (picoliters) of antibodies onto a solid support in a high-throughput manner.

Bioinformatics

Advanced bioinformatics is a key Immunovia strength. It applies front-edge bioinformatic workflows and tools to analyze microarray data, including data handling, normalization, biomarker signature identification and classification. The data generated is used to build Immunovia's own predictive model based on biomarker signatures and the support vector machine (SVM) classification algorithm.

Biomarker signatures able to accurately classify/distinguish a disease state are then identified through a stepwise biomarker/analyte selection process. One biomarker is excluded at a time in an iteration process that adopts the company's in-house developed backward elimination



approach. The backward elimination algorithm, based on SVM classification, generates the combination of biomarkers showing the highest classification power between healthy and disease states.

Operation as a service laboratory

Immunovia is developing an in-house laboratory service offering clinical testing for early diagnosis of PC. Patient serum samples are analyzed on in-house produced antibody microarrays. Each microarray generates protein expression profiles (molecular fingerprints) that are evaluated for PC using Immunovia's classification software algorithm.

The company's quality system meets the following general regulatory requirements: ISO/IEC 17025 and EN ISO 13485.

An application to SWEDAC (the Swedish Board for Accreditation and Conformity Assessment) for ISO/IEC 17025 accreditation is planned during 2016.

B. Mission and vision

Immunovia's mission is to establish its blood-based test for early diagnosis of PC as a standard amongst pancretologists and diabetes physicians worldwide for detecting PC in high-risk groups much earlier than is possible today. Ultimately, the company's vision is to significantly improve the survival rates, choice of treatment and life quality of other patients and their families by targeting a broader range of cancers (e.g. prostate cancer and breast cancer) as well as autoimmune diseases such as Systemic Lupus Erythematosus (SLE), a severe chronic autoimmune connective tissue disease.

In 2015, Immunovia received approval of a € 4.2 million grant from Horizon 2020, the EU Framework

Programme for Research and Innovation, for the clinical validation of the first blood based test for early detection of PC. At the same time, a large financial contribution was secured from Vinnova, The Swedish National Innovation Agency, for the development and commercialisation of an SLE biomarker signature test for differential diagnosis and monitoring.

C. Partnering opportunities

Immunovia is currently collaborating with several reference laboratories, as well as with academic medical centers in different parts of the world, to help implement the IMMray™ PanCan-d test.

Specific agreements have already been signed with the Knight Cancer Institute at Oregon Health and Science University (OHSU) in Portland, USA and the Mt Sinai Cancer Center, NY, USA. Other agreements are pending such as Liverpool University Hospital in UK and others.

The company has ongoing discussions with biotech companies that have identified the IMMray™ technology platform to enable them to select specific biomarker signatures for cancer and autoimmune diseases. As both a discovery chip and an IVD chip, IMMray™ offers many partnership opportunities for reference laboratories as well as pharma and biotech companies in several key collaboration areas, including early detection of disease, patient monitoring and Companion Diagnostics.

For more information on partnership and collaboration opportunities, contact Immunovia (info@immunovia.com).

13. Summary

- Immunovia translates the wealth of information in blood into clinically useful tools to diagnose disease earlier and more accurately than previously possible.
- Based on recent retrospective studies, IMMray™ PanCan-d is able to differentiate with 96% accuracy the early resectable stages of pancreatic cancer, stage I and II, from the healthy controls.
- When analysing all stages of pancreatic cancer in retrospective studies covering more than 3000 blood samples, the accuracy of IMMray™ PanCan-d is 98%.
- When the validation is completed, IMMray™ PanCan-d could be the first blood-based test available for early and specific diagnosis of pancreatic cancer.
- In-house skills include antibody microarray production, advanced bioinformatics know-how and laboratory testing for early diagnosis of pancreatic cancer.
- Partnership opportunities exist for reference laboratories, pharma and biotech in key collaboration areas spanning cancer and autoimmune diseases.

14. Appendix – links to support organisations in pancreatic cancer

Pancreatic cancer is a challenging disease for patients, family members and healthcare professionals. A number of groups whose activities encompass support, education and fundraising exist, including the following:

Pancreatic Cancer Action Network (PANCAN)

<http://www.pancan.org/index.php>

The Pancreatic Cancer Action Network is a US network of people dedicated to working together to advance research, support patients and create hope for those affected by pancreatic cancer.

National Pancreas Foundation

<http://pancreasfoundation.org/>

The National Pancreas Foundation supports the research of diseases of the pancreas and provides information and humanitarian services to those people who are suffering from such illnesses (both non-cancer and cancer).

Lustgarten Foundation

<http://www.lustgarten.org/>

The mission of the Lustgarten Foundation is to advance scientific and medical research related to the diagnosis, treatment, cure and prevention of pancreatic cancer.

Pancreatic Cancer Alliance

<http://www.pancreaticalliance.org/pancal/support.html>

The Pancreatic Cancer Alliance supports the efforts of the medical and research communities as well as patients and their loved ones in the battle against pancreatic cancer.

<http://www.esmo.org/Patients/Patient-Guides/Pancreatic-Cancer>

The European Society for Medical Oncology provides Guides for Patients, designed to assist patients, their relatives and caregivers to better understand the nature of different types of cancer and evaluate the best available treatment choices.

<http://www.cancerresearchuk.org/cancer-info/cancerstats/types/pancreas/incidence/uk-pancreatic-cancer-incidence-statistics>

Cancer Research UK organization contains useful information about the incidence, prevalence, diagnosis and treatment of pancreatic cancer in the UK.

<https://pancreaticcanceraction.org/pancreatic-cancer/>

Pancreatic cancer action focuses on bringing awareness and new info to the public through campaigns and material.



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