Heat map visualization of the diagnostic biomarkers that overlap between Pancreatic cancer and other indications; Analysis using GOBIOM data

Sreeni Devidas, Ramadevi Sanam, Sreenivasa Rao Guggilla, Vijaya Rao Pidugu, Pavan Kumar Reddy Patlolla, Srikanth Yinala, Rajkumar Kommalapati, Suman Challa, Ayyappa Chaturvedula

Background

Pancreatic cancer, a leading cause of cancer death, is one of the most aggressive diseases where 80% of the patients show an advanced tumor at the time of diagnosis with an overall 5-year survival rate of less than 5%. Despite marked improvement in the new therapies, the major reasons for the poor survival rate is lack of early detection of pancreatic cancer and rapid metastasis with profound resistance to both chemo- and radiotherapy. Early detection process can become more sensitive and specific if we focus on a panel of markers instead of a single analyte. The evaluation of serum biomarker levels in patients diagnosed with pancreatic cancer and their overlap with other diseases provides evidence for the emerging role of blood-based screening in the clinical management of various diseases. These findings not only helps us in the identification of multimarker panels capable of detecting pancreatic cancer, but also offer improved insight into the complex network of factors involved in tumorigenesis and discover new biomarker patterns across multiple therapeutic indications.

Objective

The aim of this study is :

a: To analyze the candidate blood-based diagnostic biochemical markers that are reported for pancreatic cancer and explore for the possibility of developing a diagnostic panel that can increase the sensitivity of the disease detection.

b: To see if there are any serum diagnostic markers that are common between Pancreatic cancer and other oncological, metabolic and cardiovascular indications.

c: To explore the probable role of common diagnostic markers reported in multiple indications which will enable in understanding the complex biological system and cellular networks in a disease development.

GOBIOM Database

GVK BIO Online Biomarker Database (GOBIOM) is a comprehensive database of validated and putative biomarkers providing insights into relationship between biomarker and disease. The user friendly interface facilitates analyzing and visualizing the biomarker data, which can aid in better understanding of biological processes involved in specific pathology, identification of new drug targets and accelerated drug discovery, development of personalized medicine strategies utilizing companion diagnostics, development/validation of diagnostic assay kits and monitoring the safety of experimental or marketed drugs. GOBIOM in a single platform provides clinical and preclinical information on biochemical, genomic, imaging, metabolite, clinical scoring scales and cellular markers spanning over 18 different therapeutic areas, covering 1064 therapeutic indications with its reported utilities like diagnosis, prognosis, monitoring disease progression, treatment response, surrogate, efficacy and toxicity.

Data is manually curated from

∠ Clinical trials and their results ✓ Scientific meetings ∠ Patents Regulatory approved documents

Approved Assays from 510K and PMA database Peer-reviewed journals ∠ Other relevant web resources



Database is developed in collaboration with a big pharma and USFDA.

A proprietary tetrahedron model is adopted in the framework of database by linking biomarkers, indication, drug, target and study population. This model simplifies the process of biomarker data analysis using GOBIOM

GOBIOM Statistics

Therapeutic Area	# Biomarkers	# Indications
Oncology	20186	241
Diseases of the circulatory system	3660	189
Endocrine, nutritional and metabolic diseases	3058	146
Diseases of the musculoskeletal	2859	62
system & connective tissue		
Diseases of the nervous system	2338	95
Infectious and parasitic diseases	1745	83
Diseases of the digestive system	1732	73
Mental and behavioral disorders	1595	61
Others	1503	1
Diseases of the genitourinary system	1309	50
Diseases of the respiratory system	1273	42
Diseases of the skin and subcutaneous tissue	829	26
Injury, poisoning	691	25
Diseases of the blood	383	42
Diseases of the eye and adnexa	372	42
Congenital malformations	251	59
Diseases of the ear and mastoid process	149	7
Certain conditions originating in the perinatal period	10	5
Total :	43943	1249

Methodology

Following steps are carried out in the analysis;

Entire published literature on diagnostic markers of Pancreatic cancer and other indications is taken from GOBIOM database and looked for common biomarkers.



The Proprietary Tetrahedron database model evolved in onjunction with relevant ndustry participants, allows the user in understanding the complexity of the process volved in biomarkers discovery and validation.

Analysis: Biochemical Blood Based Biomarkers



Pancreatic Cancer Vs Other Oncological Indications

50% of the markers overlap between Pancreatic, Ovarian and Prostate cancers

Serum inflammatory markers, IL-6, CRP, TNF-ALPHA, modulated in multiple cancers including Pancreatic, Ovarian, Prostate, Breast, Colorectal, Melanoma, Lung cancer, Lymphoma and Multiple Myeloma suggesting that malignant transformation is closely associated with chronic inflammation.

CA125, CA19.9, CEA, Osteopontin can be used as a panel of non-specific tumor markers for screening high-risk population.

Combination of non-specific tumor markers and the markers only modulated in Pancreatic cancer like Pancreatic elastase-1, Regenerating protein 1 alpha, Laminin gamma 2, Mucin 4 can increase the sensitivity of disease detection.

Analysis: All Specimen (Biochemical and Genomic)



Pancreatic Cancer Vs Other Indications (Biochemical)

Proinflammatory cytokines play a major role in diverse diseases.

Modulation of IL6, CRP and TNF alpha is associated not only with inflammatory K-ras, p53, p16, EGFR, PTEN, PIK3CA and microRNA remain the most significant and disorders but also with multiple cancers, diabetes, cardiovascular and neurological strategic cancer biomarkers disorders





Pancreatic Cancer Vs Metabolic Disorders

Diagnostic serum markers, CRP, Adiponectin, Glucose, Insulin, IL-6 show close association with Pancreatic cancer, Diabetes type 2 mellitus, Obesity and Dyslipidemia strongly suggesting that there is a high risk of Pancreatic malignancy in diabetic and obese patients.

Data suggests that screening for Pancreatic cancer should be performed in patients with new-onset hyperglycemia and diabetes.

Such biomarker profiles should help us in identifying the onset of Pancreatic cancer in chronic diabetic patients.

Pancreatic Cancer Vs Cardiovascular indications

Modulation of inflammatory cytokines and adiponectin shows the importance of inflammation, insulin resistance and diabetes in the development of Pancreatic cancer.

More specific biomarkers of inflammation should be investigated to understand the biological mechanism underlying Pancreatic cancer.



Pancreatic Cancer Vs Other Indications (Genomic)

Dysregulation of microRNA is observed in multiple cancers.

Conclusions:

The overlapping diagnostic biomarkers between pancreatic cancer and other indications suggests that inflammation, diabetes, insulin resistance, dyslipidemia, are the major risk factors for the disease development.

Combination of non-specific tumor marker like CA19.9 with Pancreatic cancer specific biomarkers may provide a powerful and reliable diagnostic method for pancreatic cancer with a high sensitivity and specificity.

Further focused studies should help us in identifying more robust panels for both screening and differential diagnosis of Pancreatic cancer thus decreasing unnecessary invasive procedures, and potentially avoiding unnecessary health care costs.

Focused biomarker databases like GOBIOM can be a very useful resource to perform such large scale studies and identify the hidden patterns in the published literature.

Acknowledgements:

We are thankful to Karthik Lingineni, Amarnath Reddy Nelaturi, Anil Kumar Manchala and Raju Sarvasiddi for their support in this study.



Gradient represents the number of patients analyzed.

GOBIOM Strengths

Data Content

*∝*Biomarker nature

- Therapeutic indication
- ∠ Utilities of biomarker
- SFDA/EMEA approval data for biomarkers and associated assay methodologies
- Analytical and Clinical qualification
- ✓Drugs/Intervention details
- *∝*Endpoints observed
- Efficacy and Safety characteristics
- Clinical and Preclinical qualification
- Study population
- Drug-Induced organ toxicities
- ∠ Drug resistance

Data Features

- Web-enabled search application for quick and easy access
- Controlled vocabulary through out
- ✓Instant generation of `biomarker report'
- ✓Data export options in custom format to Excel, XML and PDF
- Intuitive User Interface with comprehensive search features
- "Alert a Colleague" option to share the data with other users
- ∠ Biweekly update with auto alert function
- Custom alert by therapeutic area and biomarker name
- A dedicated server located in USA with backup server in
- Provision of user-required data in their own formats
- Easy integration with client proprietary data
- Alert service on new marker addition or updates of existing markers
- Condemand service for any biomarker addition into the database
- Competitive intelligence analysis
- ✓On-demand training sessions

Contact Information Sreeni Devidas, Ph.D GVK Biosciences Inc., 245 First Street, Riverview II, 18th Floor, Cambridge, Massachusetts, 02142 Tel: 001 858 405 2125