An integrated European platform for pancreas cancer research: from basic science to clinical and public health interventions for a rare disease

COST Action (BM1204)

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The Action aims to unite groups across Europe interested in pancreas cancer research and provides an innovative and unique platform for collaborating and sharing information, ideas and experience.

185 multidisciplinary members from:
22 EU countries
5 EU gov & non-gov institutions
3 Biotech companies (SME)
1 Pharma company

Grant Period – 14 December 2012 to 13 December 2016
1st Grant Period – 31 May 2014
2nd Grant Period – 1 June 2015
3rd Grant Period – 1 June 2016

www.eupancreas.com
Scientific scope: Pancreas cancer

Pancreas cancer “rare disease”

World (2012) 337,872 new cases (rate 4.2 per 10^5 p-y)
EURO (2012) 110,499 new cases (rate 6.5 per 10^5 p-y)
111,029 deaths (rate 6.4 per 10^5 p-y)

Death rates from pancreatic cancer are rising while rates for all other cancers continue to fall in Europe

In US, PDAC is projected to become the second leading cause of cancer-related deaths by 2025 (Rahib 2014).

Pancreas cancer Clinical challenges

- Silent disease: Unspecific symptoms
- Diagnosis done too late: a 2cm tumour is metastatic
  High percentage of misdiagnosed patients
- No efficient treatment:
  Only 15-20% of patients undergo major surgery: radical resection?
  Chemotherapy resistant: slightly improves survival
  Evidence-based personalized treatment
- No progress in the recent decades
- Fatal disease: Diagnosis = Death (6 months mean survival)
- Difficult disease & patient & family management
- Nihilism in the medical community
- No survivors = no pressure → ORPHAN DISEASE

Pancreas cancer Prevention challenges

Primary Prevention
- Complex aetiology: Chronic inflammatory related disease
- Risk factors - largely unknown

PANCREAS CANCER: A chronic inflammation-related disease

[Diagram showing various factors such as Vitamin D, Helicobacter pylori, Selenium, Metals (Cd, As, Pb), Alcohol, Statins, Allergy/Asthma, Chronic pancreatitis, Diabetes, Obesity, Tobacco, Blood group, Periodontitis, and genome blood (SNP, CNV, Rare variants).]
Genetics of pancreas cancer

Asthma/Allergy

Alcohol

Type 2 diabetes

Obesity/OW

Genetics of pancreas cancer and co-morbidities

Apo, ANXA3 - FAM91A1, ARAC - HSP48P10, BACH1, BID1, CLPTM11, CRBN - LRRN1, DAB2, DEC1, DPP6, FAM19A5, FAM204A - PRLHR, FOXQ1 - FOXF2, GUS3 - SLC1A1, GRID1, GTF2H1, HNRNPA3P5 - MIR548X2, IRX4 - IRX2, KRT18P32 - MIPEP2, LDRAD4, MYO1D, NDFIP2 - SPRY2, NCO3 - MIR1202, NR5A2, NUMIP2 - BAI3, PARK2, RNF49, RNF43, RNF5P1 - TACC1, RNY1P1 - MARK2P12, RPL3AP27 - HMG1P3, RPL3AP28 - OR7E156P, SBF2, SDHAP1 - TFC, TFF2 - TFF1, TVP235 - PRPSAP2, UBBP1 - THSD7B

Relative risk

Allele frequency
Pancreas cancer Prevention challenges

Primary Prevention
- Complex aetiology: Chronic inflammatory related disease
- Risk factors - largely unknown
  Prevalent in the population & Highly correlated
  Small risk
  Explain little

Pancreas cancer RESEARCH challenges

- Small incidence and no prevalence → underpowered studies
- High percentage of misdiagnosed patients → misclassification
- Patients too sick to participate → biases
- <20% of patients undergo surgery → lack of tumor tissue
- Tumour surrounded by a fibrotic mass → lack of tumor tissue
- High levels of RNAses → inappropriate sample
- Little funding
Defined as a “recalcitrant cancer” by the U.S. Congress leading to the implementation of a 5-year effective Pancreatic Cancer Research and Education Act involving research for biomarkers of early detection.

The Recalcitrant Cancer Research Act:
An Important step toward improving pancreatic cancer survival

The statute has created a path for progress in pancreatic cancer research.

The scientific framework for pancreatic cancer built upon a report the NCI released in June 2013 called “Pancreatic Cancer: Scanning the Horizon for Focused Interventions.” The Horizon Scan report proposed four specific initiatives for advancing pancreatic cancer research. The scientific framework expands on these recommendations by providing specific suggestions for moving forward for each one.

The Pancreatic Cancer Action Network calls on the 113th Congress to give current and future pancreatic cancer patients a fighting chance by:
- Providing $5.26 billion for the National Cancer Institute for FY 2015
- Continuing to include pancreatic cancer in the Department of Defense (DoD) Peer-Reviewed Cancer Research Program (PRCRP) and providing continued funding of at least $25 million for the program
- Ensuring that the provisions of the Recalcitrant Cancer Research Act are fully implemented
- Joining the Congressional Caucus on the Deadliest Cancers

EUPancreas Objectives

1. Integrate knowledge and experience in a multidisciplinary way “from cell to Society”

2. Foster collaborative research to improve our understanding of pancreas cancer and its prevention, early diagnosis and treatment under the Personalized Medicine umbrella

3. Promote the application of uniform study tools and protocols their optimal use by researchers

4. Enhance the mobility and training of researchers

5. Disseminate the results produced to the broader society
Scientific outputs related to (WITHIN and BETWEEN WGs) networking

Pan-Europe Pancreatic Cancer Patient Association
Pancreatic Cancer Action (UK). Ali Stunt, Chief Executive & Founder
Capacity building related to (WITHIN and BEYOND) COST networking

WG1. Harmonization of research tools

WG1-1 Homogenization of the definition of PDAC and establishment of key terminology

WG1-2 Development of protocols for patient enrolment and monitoring and standardization of questionnaires

WG1-3 Development of SOPs for biosample collection, processing, and storage. Establishment of criteria to assess the quality of existing biobanks for PDAC research and interconnection of biorepositories and databases

Irene Esposito (Pathologist - Germany)
Malte Buchholz (Molecular Biologists - Germany)
Eric Duell (Epidemiologist – Spain)
WG1. Harmonization of research tools

Standardized epidemiological questionnaires (available in the web)

Standardized Operating Procedures for tissue collection (in preparation)

Biobanking (negotiating)


Clinical Registry: PancreOS in collaboration with EUMSP-PC, CELGENE, ENCR, EC-ERC

PancreOS

Increase the knowledge base that is used to inform clinical & translational research in pancreatic cancer

• Develop the largest EU-based pancreatic cancer registry
• Gather information relating to all aspects of the management of patients with pancreatic cancer – from initial diagnosis and throughout the treatment continuum
WG2. Integration of “omics” data

WG2-1 Identification of PDAC omics databases (Survey).

WG2-2 Data standardization and optimization and issues related to data sharing

WG2-2 Integrated omics analysis

Kristel Van Steen (Statistician- Belgium)
Núria López-Bigas (Bioinformatician - Spain)
Jörg Hoheisel (Proteomics - Germany)

Survey to identify PDAC omics databases

Common database of pancreas cancer “omics” data using The Pancreatic Expression Database (C. Chelala, UK)


**WG3. Translation Research**

**WG3-1** Initiate a study on “Prospective evaluation of a novel early symptom algorithm and rapid assessment pathway for diagnosis of PDAC in primary care

**WG3-2** Set up a COST initiated European IPMN study group to develop and test risk prediction biomarkers for IPMN

**WG3-3** Set up a prospective multicenter study to collect 10000 early onset diabetes patients

**Stephan Hahn** (Molecular Biologists - Germany)
**Eithne Costello** (Molecular Biologists - UK)
**Chris Michalski** (Surgeon - Germany)

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**WG3. Translation Research**

- Projects
  - Risk Population Subgroup
  - Cystic Tumour Subgroup
  - New Onset Diabetes Collection

- Workshops
WG4. Patient Management

WG4-1 Identification of European centres focused on individualized medicine approaches for PDAC treatment

WG4-2 Establishment of the framework for the development of evidence-based PDAC-best practice guidelines and their translation into the healthcare systems in Europe

Angela Brand (Public Health Genomics - Netherlands)
Denis Horgan (EAPM - Belgium)
Francisco X Real (Molecular Biologists - Spain)


Survey & Report: “Access to Personalised Medicine for PDAC patients”


Clinical Registry: PancreOS
in collaboration with EUMSP-PC, CELGENE, ENCR, EC-ERC

PANCREATIC CANCER WHITE PAPER 2015 (released TODAY!!)

Annual Conference 2015 in Cluj-Napoca, Romania
Carlo La Vecchia (VC)
Irene Esposito (WG1)
Kristel Van Steen (WG2)
Stephan Hahn (WG3)
Angela Brand (WG4)
Filipe Silva (Diss)
Ana Merino (CNIO-GH)