GENETIC AND MOLECULAR EPIDEMIOLOGY GROUP

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OVERVIEW

The scope of the research carried out by our Group ranges from the identification of aetiological agents and mechanisms, to the translation of the findings into the clinical and Public Health domains, focusing on bladder, pancreatic, and breast cancers.

We employ a wide variety of biomarkers to better characterise exposures, genetic susceptibility patterns, and cancer outcomes. *Omics* data provide a unique opportunity in this regard and the Group explores its integration in epidemiologic studies.

The strategic goals of the Group are to:

→ Identify non-genetic and genetic factors, as well as their interactions, associated with cancer development and progression and with its molecular/omics subphenotypes.
→ Develop and apply statistical/informatics tools to model the risk, prediction, and clinical course of patients with cancer by integrating epidemiologic with *omics* information.
→ Assess clinical and public health strategies for cancer control using current genomic tests and data.

"The integration of omics and non-omics data in the same risk models poses several challenges and demands of appropriate analytical strategies. We are contributing to this field towards a personalised prevention of cancer."

RESEARCH HIGHLIGHTS

Research findings

In 2018, the Group mainly focussed its research on pancreatic cancer while building resources for bladder cancer research. For **pancreatic cancer** (PC), we continued exploiting the data generated by the PanGenEU Study to further characterise pancreatic cancer risk. Two main articles exemplify our contributions to this domain. First, by applying complementary analytical approaches we reported that, regardless of non-genetic risk factors, the risk of PC was 2.5 higher among family members with more than 2 relatives affected with PC, with this risk being stronger in current smokers (FIGURE 1). Furthermore, we confirmed that PC was diagnosed at younger ages among those subjects with a family history of PC who smoked than in non-smokers. In the second article, we reported on the underlying genetic basis behind PC and its associated multimorbidities network through a computational approach using the DisGeNET. This strategy allowed us to identify several autoimmune diseases linked to PC and the shared altered genes (FIGURE 2). These associations were subsequently confirmed at the individual level in the PanGenEU study population of 1,705 PC cases and 1,084 controls that resulted in a reduced risk of PC in subjects having ≥2 autoimmune diseases. These findings again pointed to the role of the immunological status in PC carcinogenesis. We also continued to participate in international large-scale investigations to further characterise the genetic susceptibility and somatic alteration landscape of PC. For **bladder cancer** (BC), the Group reported on the inverse association between asthma and BC using the Spanish Bladder Cancer/EPICURO Study resources. This reduced risk of BC was especially observed among aggressive tumours. The Group also participated in the discovery and validation of both urine and tumour prognostic marker combination in large European studies of non-muscle invasive BC. We also

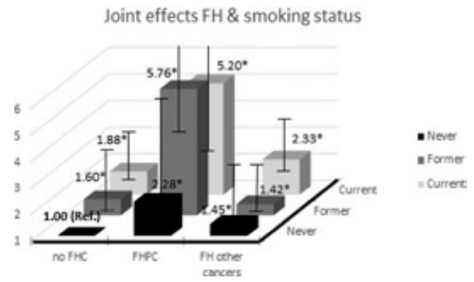

Figure 1 Odd ratios for the joint effect of family history of cancer (FHC) / Family history of pancreatic cancer (FHPC) and smoking on pancreatic cancer risk. PanGenEU case-control study.

performed a review of the genetic susceptibility to BC risk and progression based on GWAS hits. Most of the variants were common and conferred small risk and, therefore, they were not clinically actionable at the individual level.

Methodological contributions

The Group made contributions to both integrative analytic approaches considering omics and non-omics (OnO) data as well as in the nutrition epidemiological filed. Regarding the latter, we compared the antioxidant profiles of 21 a priori-defined Mediterranean diet indexes and reported that the level of dietary antioxidant intake captured through the different indexes differed due to the variation in their construction. As of the data integrative efforts, we observed that only a small number of published studies performed a 'real' integration of OnO data, primarily to predict cancer outcomes. We identified the challenges in OnO data integration and presented, discussed, and proposed integrative analytical strategies towards its integration.

Translational activities

The Group actively provides support in several clinical trials on immunotherapy and vitamin D in bladder cancer at the methodological level. We continue to sustain the Spanish Familial PC Registry (PanGen-FAM) and the establishment of the European Registry of PC (PancreOS). We lead the Research Work Stream of the Pancreatic Cancer Europe (EPC) multistakeholder platform, with who we hosted a session on PC Liquid Biopsy during the 2018 ESMO GI Meeting. To increase awareness of PC among health policy makers and discuss the urgent need to invest in PC research, we participated and co-organised sessions with MEPs at the European Parliament and with delegates at the Annual Meeting of the European Alliance of Personalized Medicine. ■

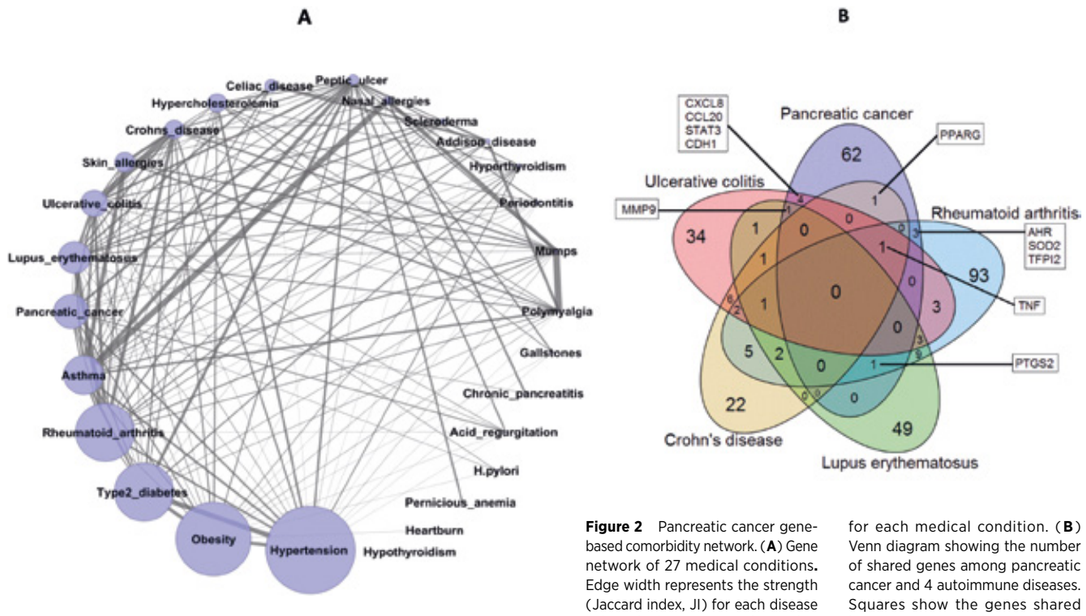

Figure 2 Pancreatic cancer gene-based comorbidity network. (**A**) Gene network of 27 medical conditions. Edge width represents the strength (Jaccard index, JI) for each disease pair. Node size represents the number of genes obtained through DisGeNET for each medical condition. (**B**) Venn diagram showing the number of shared genes among pancreatic cancer and 4 autoimmune diseases. Squares show the genes shared between pancreatic cancer and autoimmune conditions.

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AWARDS AND RECOGNITION

- Member of the jury of the Banco Sabadell Award.