The scope of the research carried out by the Genetic and Molecular Epidemiology Group (GMEG) ranges from the identification of aetiological agents and genetic pathways, 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, including omics data, to better characterise exposures, genetic susceptibility patterns, and cancer outcomes. While omics data provide a unique opportunity in this regard, its integration with non-omics data poses important challenges, and GMEG explores this methodological field 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 and course of patients with cancer by integrating epidemiological and clinical data with omics information.

→ Assess clinical and public health strategies for cancer control using newly developed biomarkers and algorithms.

“The integrative effort of the epidemiology, statistics, bioinformatics, and molecular biology fields has allowed us to gain additional insight into the inherited basis of pancreatic cancer.”
Regarding bladder cancer (BC), GMEG participated in a European-based effort to subclassify non-muscle-invasive bladder cancer (NMIBC) through a large integrative multi-omics analysis including gene expression, chromosomal instability, and spatial proteomics. The integrated classifier had independent prognostic value beyond established prognostic clinicopathological parameters. Under the umbrella of the AECC muscle-invasive bladder cancer (MIBC) study, we reported that patients with BASQ-like tumours have a higher likelihood of experiencing a pathologic complete response non-adjacent chemotherapy. In addition, through an international collaboration, we observed that FGFRF3 plays a functional role distinct from FGFR from overexpression, pointing to the possibility that patients with FGFRF3 mutations may be more likely to benefit from anti-FGFR therapy than patients with over-expression only.

Methodological Contributions
GMEG continued to explore the analytic strategies and tools to integrate omics and non-omics data into the cancer risk models, and started considering the integration of medical image information (radiomics and digital pathology) through an H2020-funded project (PanCaim).

Translational Activities
GMEG actively provides support in several clinical trials on immunotherapy and vitamin D in BC at the methodological level. We continue to sustain the Spanish Familial PC Registry (PanCan-FAM) and the European Registry of PC (PancreOS). We launched a PC research platform (PC-CAM) to accelerate the translation of research results into the clinical domain. We lead the Research Work Stream of the Pancreatic Cancer Europe (PCE) multi-stakeholder platform and we moved forward in increasing awareness of PC among health policy makers by translating the urgent need to invest on PC research by joining efforts with EC IPAAC Joint Action and with EAPM.

Figure 1: Pancreatic Cancer GWAS Study Flowchart: overview of the complementary approaches

Figure 2: DAs showing results from causal mediation analyses within 2,289 cases and 1,540 controls evaluating mediator effects of obesity or T2DM on PC risk associations by T2DM subtype. The natural indirect (NIE), direct (NDE) and total (TE) effects of the associations were shown. A and B for LSDM or obesity (mediators) in association analyses between obesity or T2DM and PC risk, respectively. C and D for LSDM or obesity (mediators) in association analyses between overweight/obesity and NDM and PC risk, respectively.

**Databases**
- Pancreatic Cancer Genome Atlas (PCGA)
- Pancreatic Cancer Genome Map (PCGM)
- PanCan-FAM
- Pancreatic Cancer Europe (PCE)
- Human Cancer Genomics Programme (HCGP)
- Human Cancer Genetics Programme (HCGP)
- European Cancer Genome-phenome Atlas (ECAAtlas)

**Awards and Recognition**
- Member of the working group of experts to evaluate the carcinogenicity of opium consumption, IARC Monographs Vol 112, 2016.