How can we accelerate the translation of early detection biomarkers into the clinic? Do we have good *in vitro* models mimicking early-stage human disease?

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The Pereira/Acedo Lab

- Multidisciplinary team formed by basic and clinical scientists
- Research aim: to impact patient outcomes

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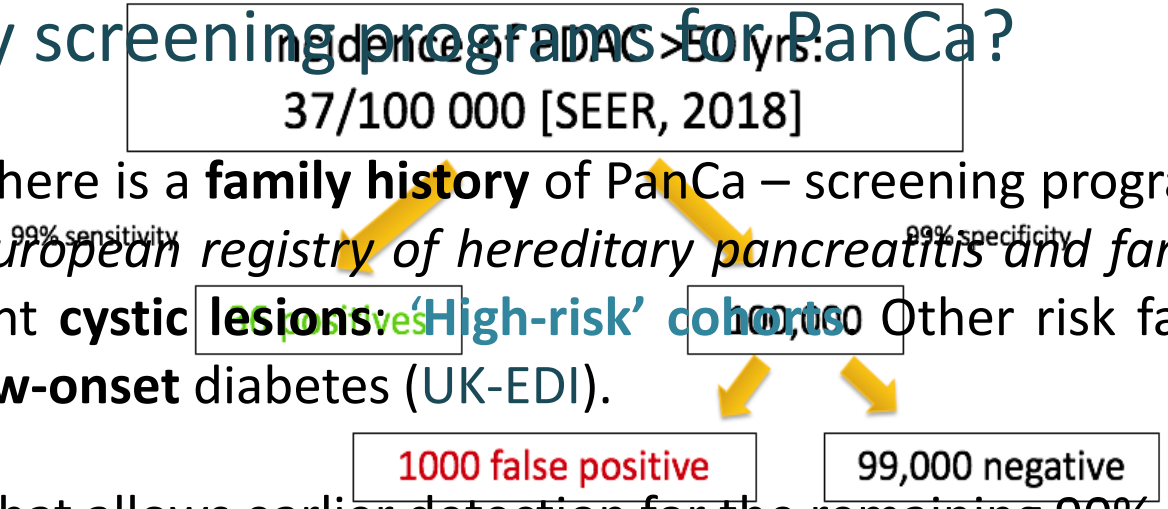
Population screening for Pancreatic Cancer is not feasible

- Screening for PanCa in average risk individuals will fail due to low cancer prevalence
- Use of an “almost perfect test” with a 99% sensitivity and a 99% specificity for PDAC

Are there any screening programs for PanCa?



- In 10% of cases there is a **family history** of PanCa – screening programs are available (e.g. EUROPAC: *The European registry of hereditary pancreatitis and familial PanCa).* Patients with premalignant **cystic lesions**. ‘High-risk’ cohorts. Other risk factors currently under investigation: **new-onset** diabetes (UK-EDI).
- There is **no test** that allows earlier detection for the remaining 90% of cases (**sporadic** pancreatic cancer).

Hart & Chari *Clin Gastro Hep* 2018

Our research question in Early Detection

HOW CAN WE IMPROVE THE EARLY DETECTION OF PANCREATIC CANCER?

1. Identifying accurate and cost-effective biomarkers for ED in high-risk populations

2. Modelling *in vitro* models mimicking human disease

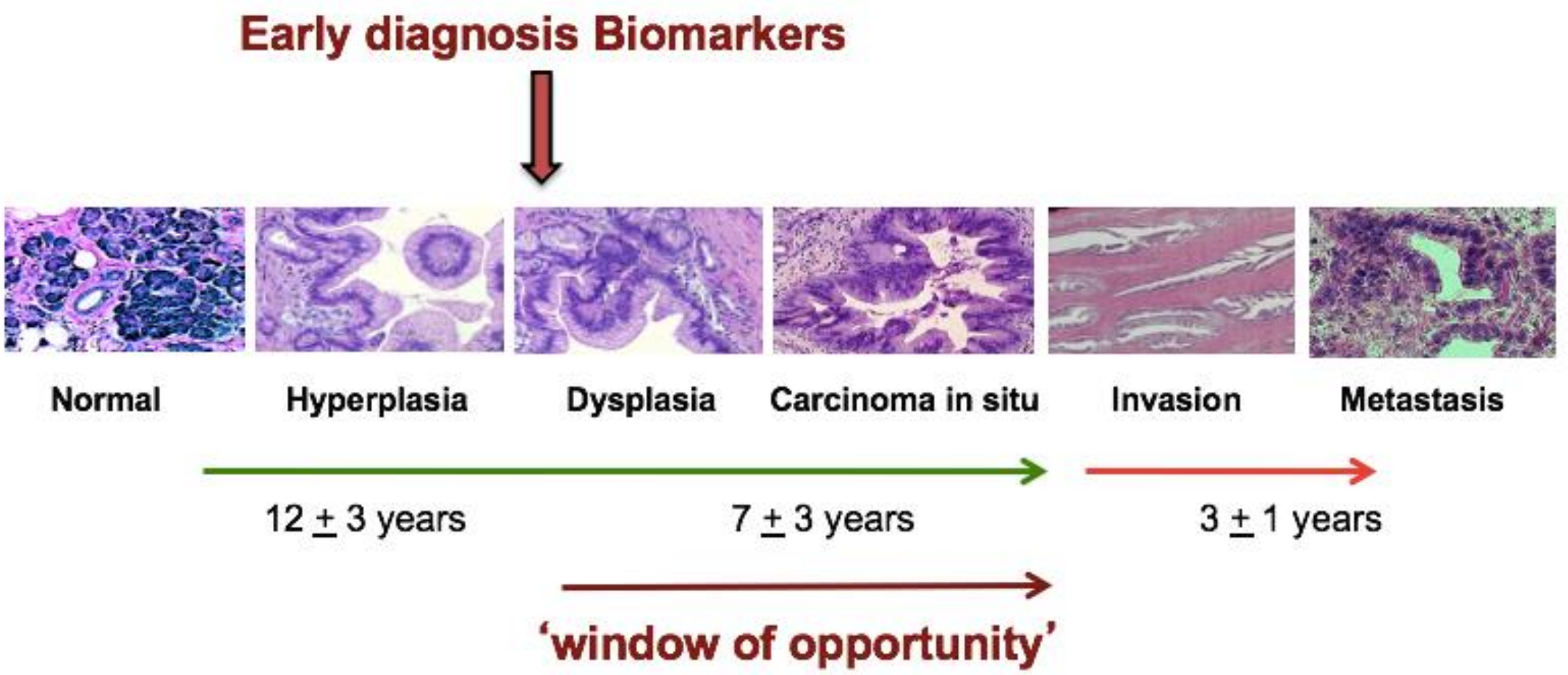
3. Developing biomarker platforms for implementation in the clinical setting

1. Discovery of biomarkers for early detection

Pancreatic Cancer UK

Early Diagnosis Research Alliance

When can we detect PDAC?



The ADEPTS study: **A**ccelerated **D**iagnosis of neuro**E**ndocrine and **P**ancreatic **T**umour**S**

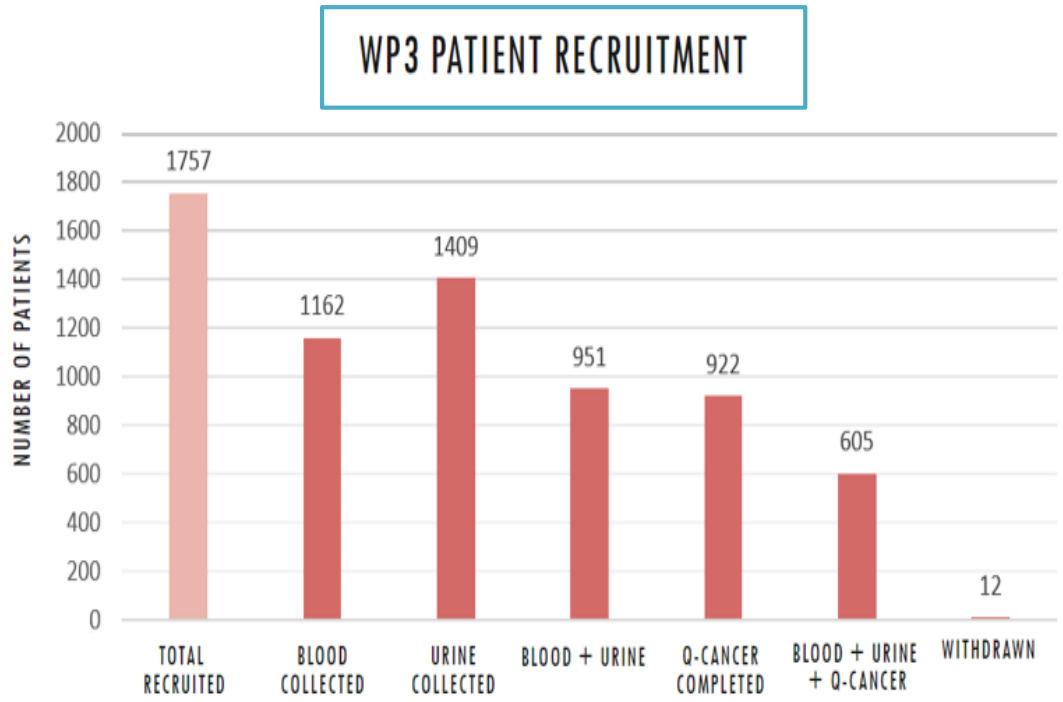
AIM: **i)** To identify symptoms earlier (risk stratification), and **ii)** to develop new tests to diagnose pancreaticobiliary cancers at an early stage; less invasive diagnosis.

- **Creating a bank of samples from people with vague symptoms** similar to those diagnosed with PanCa (OUR CURRENT TARGET GROUPS: HIGH-RISK GROUPS)

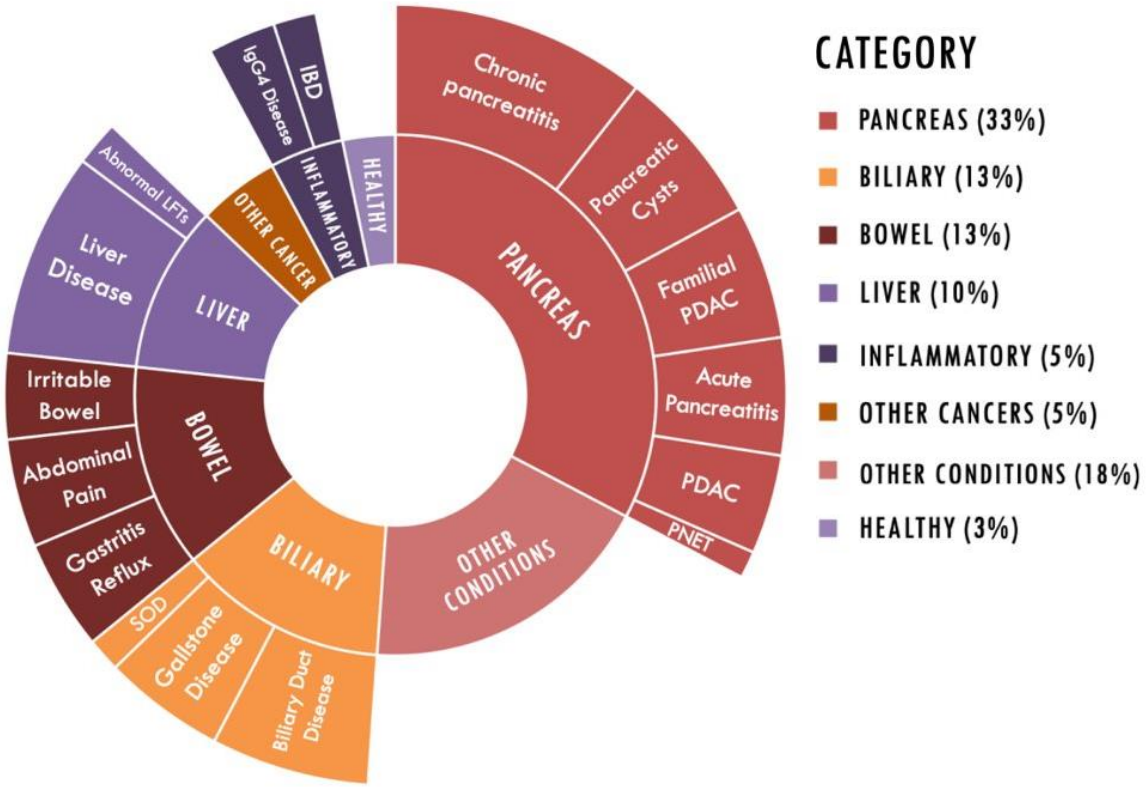
> 1,000 samples collected

Pancreatic Cancer UK

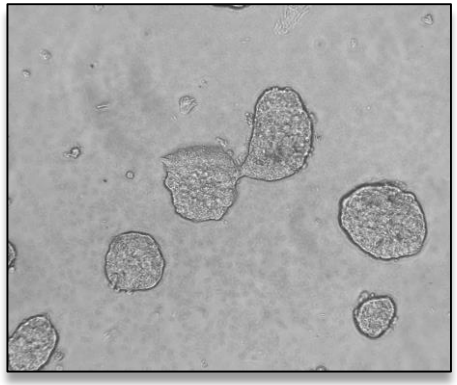
The ADEPTS study:



Diagnosis breakdown



2. Establishment of patient-derived models



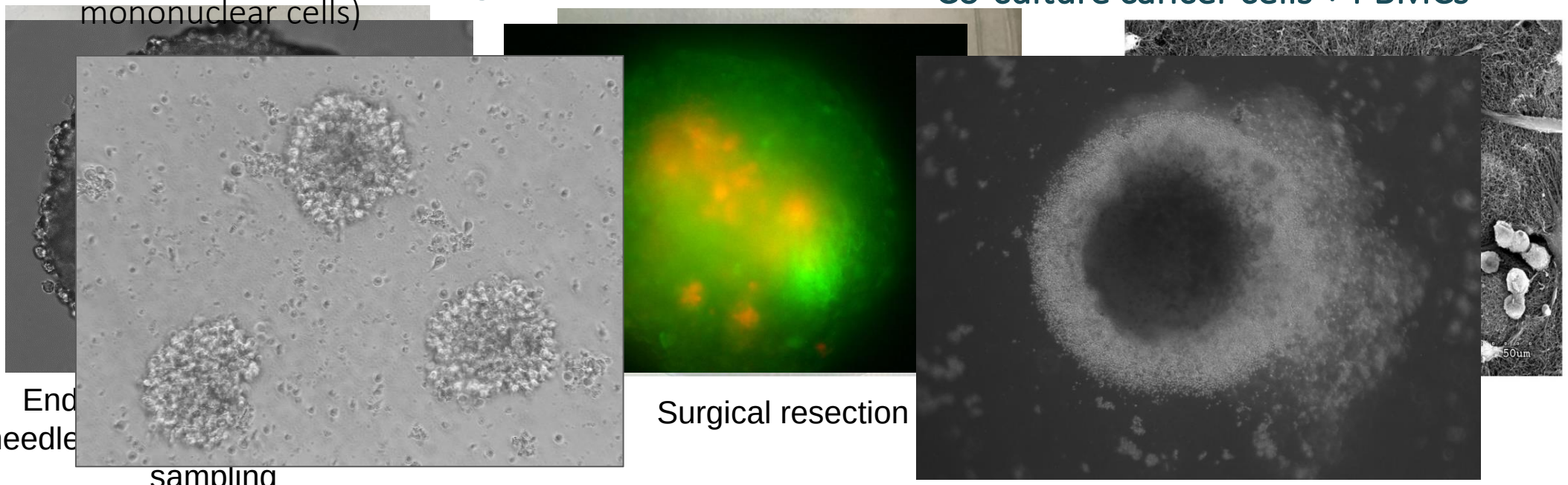
Organoids and Spheroids…the challenge of early-stage disease

Activated PBMCs (peripheral blood mononuclear cells)

Co-culture: cancer cells (green) + stromal cells (red)

Co-culture cancer cells + PBMCs

Patient-derived organoids



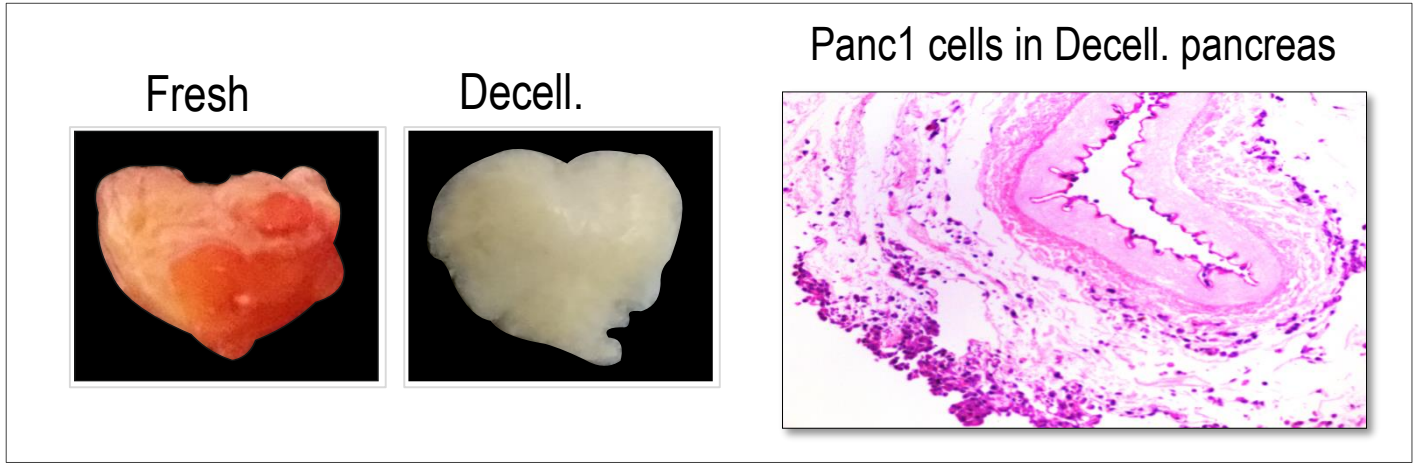
End
needle

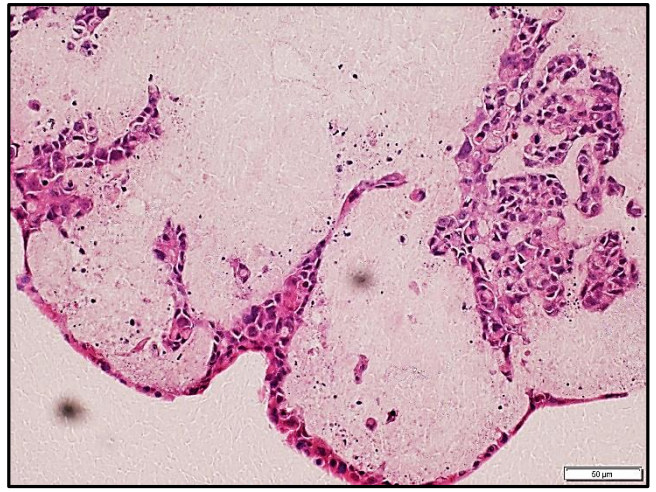
sampling

Surgical resection

Blast cell formation

Human Pancreas ECM Scaffolds





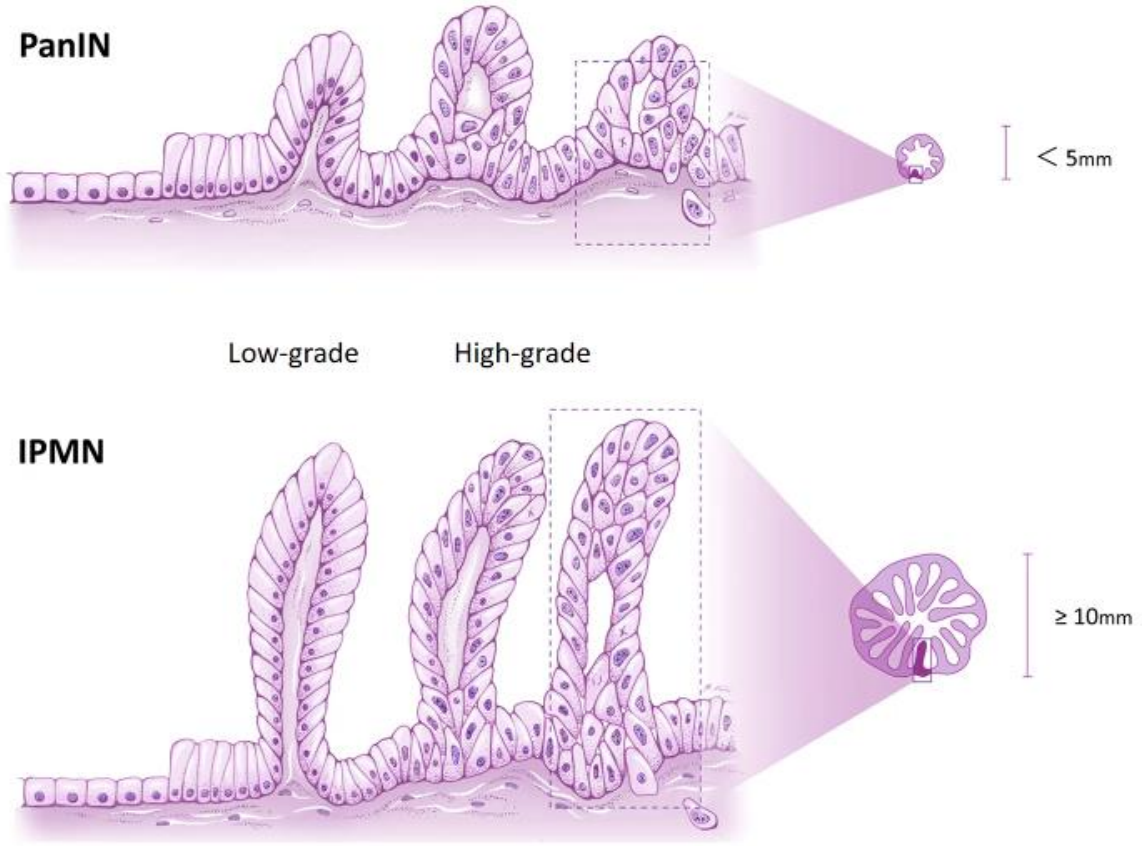
Patient-derived cells growing into a decellularised human pancreas scaffold

Collab. Prof Pinzani and Dr Mazza

Manuscript under review: *"Tissue-specific human extracellular matrix scaffolds promote pancreatic tumor progression and chemotherapy resistance"*

A lot of studies focus on advanced pancreatic cancer…..

- What is the best strategy to understand the initiation and progression in pancreatic tumorigenesis?
- How can these findings improve care of early-stage pancreatic cancer patients?



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