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Title: Pancreatic cancer: ontogeny, molecular subtyping and drug repurposing

Pancreatic cancer has a dismal prognosis with an overall survival rate of less than 10%, and with few improvements in the last 50 years, partly due to a lack of in-depth knowledge of pancreas (cancer) biology.

We have developed four broad themes of research: i) study of normal cell differentiation and loss thereof as a first step facilitating tumour development, in particular pancreatic exocrine cell dedifferentiation, ii) profiling of pancreatic tumours in the context of molecular subtypes, using in situ RNA detection and studying spatial heterogeneity within the tumours and among different subtypes, iii) studies on the biology of axon guidance genes in pancreatic cancer, following its first discovery in pancreatic cancer in 2012 based on whole exome sequencing analysis, iv) repurposing of non-cancer drugs for pancreatic cancer.

A lot of efforts go into finding new genes and pathways that are aberrantly expressed in pancreatic cell dedifferentiation and tumour development (hypothesis driven approach and unbiased integrative –omics analyses). For obtaining spatial resolution of -omics datasets, an extended RNA analysis (ERA) platform is available in the lab whereby RNAscope/BaseScope technology is combined antibody-based cell profiling and digital scanning of whole tissue slides (e.g. Zeiss Axio Scan.Z1) followed by AI-based quantitative image analysis. Research projects start from observations in human material, including patient samples and primary human cell cultures (normal human cells, tumour-derived organoids), Further investments are made in 3D imaging of cleared whole or scalable organ samples using lightsheet microscopy.

Significant new insights in pancreas (tumour) biology will drive the development of improved detection methods and therapeutic strategies for pancreatic cancer, leading to better outcomes for patients.

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