



## **Tumor evolution in an ecological context: How genetic and microenvironmental factors shape the pathogenesis of pancreatic cancer**

Giulia Girolimetti<sup>1</sup>, Grazia Bramato<sup>2</sup>, Alessandro Fiore<sup>2,\*</sup>, Roberta Romano<sup>1</sup>, Flora Guerra<sup>2</sup>, Cecilia Bucci<sup>1</sup>, Alberto Basset<sup>2,3</sup>

\*lead presenter: [alessandro.fiore1@unisalento.it](mailto:alessandro.fiore1@unisalento.it)

1 University of Salento, Department of Experimental Medicine

2 University of Salento, Department of Biological and Environmental Sciences and Technologies (DiSTeBA)

3 Italian National Research Council (CNR), Institute for Research on Terrestrial Ecosystems (IRET)

Pancreatic ductal adenocarcinoma (PDAC) is an aggressive cancer with a dismal prognosis and a growing global incidence. Despite its clinical relevance, the processes driving PDAC tumorigenesis and progression remain poorly understood, challenging traditional molecular models. Here, we address the biological and evolutionary mechanisms underpinning PDAC development and growth, integrating cellular and molecular aspects with an ecological perspective. This multidisciplinary approach offers broader insights into the analysis of PDAC pathogenesis—from precancerous lesions to metastatic spread—by viewing cancer cells as dynamic entities influenced by evolutionary pressures similarly to individuals, populations, and species in nature. Genetic and epigenetic changes form the foundation for intratumoral heterogeneity, contributing to progression and metastasis. These processes are governed by clonal expansion and the ecological fitness of neoplastic cells within their microenvironmental niches. By recognizing cancer as an evolving system of interdependent “cell individuals” and “clone populations,” we obtain new insights into how tumors develop and spread. This research emphasizes a holistic perspective and underlines the importance of the intrapopulation biological diversity of cancer cell clones for guiding future scientific inquiry.