PROJECT

Supervisor:	Prof. Stefano Crippa
Title:	Development and Clinical Validation of Multi-Omics Biomarkers for Personalized Risk Stratification in Intraductal Papillary Mucinous Neoplasms (IPMNs)
Curriculum:	Experimental and Clinical Medicine
Link to the personal page of the University or relevant hospital site website:	**https://www.unisr.it/docenti/c/crippa-stefano**

Description of the Project (max 3,000 characters including spaces)

Background/gap of knowledge

Pancreatic ductal adenocarcinoma is characterized by an extremely poor prognosis, largely due to late diagnosis and an early propensity for early metastatic dissemination[1]. Intraductal papillary mucinous neoplasms (IPMNs) are recognized precursor lesions of pancreatic cancer, representing a unique opportunity for early intervention and cancer prevention[2]. Current IPMN management relies mainly on the assessment of worrisome features and high-risk stigmata to guide clinical decision-making[3,4]. However, the limited accuracy of these criteria leads to overtreatment in nearly half of patients, who undergo unnecessary or at least premature pancreatic surgery, and undertreatment in approximately one third of patients, in whom invasive carcinoma is already present at the time of surgical resection[5,6]. There is therefore a strong unmet clinical need for improved risk stratification in IPMN management to support more personalized approaches.

Rationale and hypothesis

Emerging evidence suggests that inflammatory, endocrine, and metabolic alterations contribute to the malignant potential of IPMNs and can be feasibly assessed in clinical practice using peripheral blood and cystic fluid biomarkers[7-11]. This PhD project is embedded within one specific aim of a broader ongoing AIRC-funded research focused on the development of multi-omics panels for the identification of malignant IPMNs. The central hypothesis is that the integration of exposome data, radiomics, somatic and germline mutations, and metabolic/proteomic markers will enable the development of a comprehensive biomarker panel, through AI-driven predictive models, to improve discrimination between low-grade dysplasia and high-grade dysplasia/invasive carcinoma.

Objectives and specific aims

The main objective of this PhD project is to contribute to the clinical and translational identification of biomarkers associated with IPMN risk of malignancy. Specific aims are:

1) to prospectively enroll and clinically characterize patients undergoing surgery for IPMN forming the discovery cohort for multi-omics panel development, with structured collection of clinical, radiological, and pathological data;

2) to analyze inflammatory and endocrine biomarkers in peripheral blood and cyst fluid and assess their association with histological outcomes;

3) to contribute to the development and interpretation of multi-omics biomarker panels and machine learning/AI-based models;

4) to participate in the prospective enrollment and longitudinal follow-up of IPMN patients under surveillance (≈500) and surgically resected (≈200) for validation of the identified biomarker panel.

Expected outcomes

This project is expected to identify a comprehensive multi-omics biomarker panel for the accurate identification of high-risk IPMNs. The results may contribute to improving patient selection for surgery and surveillance, promoting a more personalized and evidence-based management of IPMNs.

Skills that the student should acquire (max. 600 characters including spaces):

The project will provide advanced training in basic and translational research applied to pancreatic diseases, including skills in the analysis and interpretation of biomarkers in peripheral blood and cyst fluid. The student will progressively develop autonomy in IPMN patient care by actively overseeing longitudinal follow-up. The project will also offer structured exposure to machine learning and AI-based risk stratification models, with a strong focus on clinical applicability and translational impact.

References (max. 15)

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10. Kannan A, Murimwa GZ, Mansour JC, et al. Molecular Analysis of Mixed-Type and Branch-Duct Intraductal Papillary Mucinous Neoplasms. JAMA Surg. 2026;161(2):171. doi:10.1001/jamasurg.2025.5692

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