PROJECT 1

DoS: Cristina Scielzo

Title: 3D modelling of non-functioning neuroendocrine pancreatic neoplasms for personalized medicine

Curriculum: Basic and Applied Immunology and Oncology

Link to OSR: /UniSR personal page:
https://research.hsr.it/en/divisions/experimental-oncology/units/malignant-b-cells-biology-and-3D-modelling/cristina-scielzo.html

Project description (*Number of characters*, *including spaces*: 2.000 - 3.000):

Pancreatic Neuroendocrine Neoplasms (PanNENs) are rare neoplasms characterized by a highly heterogenous biological behavior. Although PanNENs are often indolent in nature, 40-45% of patients have distant metastases at diagnosis[1] and up to 20-30% of patients develop recurrence after surgical resection[2]. Personalized therapies according to patients and tumors' characteristics are still laking. Preclinical models are essential tools for developing a precision medicine approach also in the management of PanNENs. However, the current available models[3–8] present several limitations and are unable to recapitulate accurately the biology and the physiology of the original tissue. Recently, promising results have been shown by the development of patient-derived PanNENs tumoroids[9], however they are unable to replicate tumor vascularization and its microenvironment that are critical elements of these tumors.

Taking advantage of our recognized expertise in cancer 3D modelling[10–12] and 3D bioprinting[10] the aim of the project is to overcome the limit presented by state of the art models by developing a personalized 3D model of PanNEN by: 1) developing a novel patient-specific 3D bioprinted model recapitulating the biological features of PanNENs and reflecting the tumor microenvironment, 2) exploiting the 3D bioprinted model for testing response of specific treatments to be correlated with predictive factors on the original tissue.

The project will be conducted in strict collaboration with the Pancreatic Surgery. In our Hospital, each year approximately 50 patients affected by PanNEN undergo surgical resection and are charachterized for both radiological and biological features.

PanNENs cell lines will be initially exploited to reflect cancer heterogeneity and once the model will be optimized and validated, they will be substituted with patient-derived cells. For the project, a vascular network and a stromal compartment will be included into the scaffold. The ultimate endpoint of our project will be to generate a 3D bioprinted model exclusively employing autologous cells, retrieved from surgical specimens (i.e., tumor cells, endothelial cells, stromal cells). Furthermore, tumor responsiveness to drugs will be tested in our system, under controlled perfusion in bioreactors to better mimic the physiological settings. Finally, drug response *in vitro* will be compared to patients' response *in vivo*, to validate the predictive value of the model.

Skills to be acquired by the student (*Number of characters*, *including spaces*: max 600):

The student will be part of a multidisciplinary team acquiring the skills to interact with biologist, clinician, physicist and bioengineers. He/she will acquire skills in cellular and molecular biology, will handle cell lines and primary cells derived from PanNENs and other cells from the tumor microenvironment. He/she will use new

advanced 3D culture systems including 3D bioprinting and dynamic growth in bioreactors. He/she will mainly adopt imaging strategies (e.g. IHC, confocal microscopy), flow cytometry and RnaSeq analysis.

References (max. 15)

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