Plano de trabalhos para tese de Mestrado 2016/2017

Patient-derived tumour cell models in stirred-tank bioreactors

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Duração: 1 ano lectivo

Sumário:

Epithelial tumours – carcinomas – are the most frequent type of tumours in adults, accounting for 85% of the total worldwide**.** The current view is that these are complex and heterogeneous organ-like structures - the tumour microenvironment is composed by a network of fibroblasts, vascular & immune cells, and secreted vesicles, soluble factors & extracellular matrix molecules. Tumour stroma is highly (re)active as the organization, phenotype and molecular wiring of these cells change during tumour progression; the stroma is associated with the sequence of tumour-related events such as inflammation, angiogenesis and metabolic reprogramming. Ultimately, these lead to disease progression via primary tumour invasion and metastization. The major challenge in studying these mechanisms is the lack of human cell models in which the crosstalk between the different cell types and consequent tumour microenvironment remodelling during disease progression can be recapitulated *in vitro.*

At the Advanced Cell Models Lab of the Animal Cell Technology Unit our research is focused on assessing the role of tissue microenvironment in disease progression and biopharmaceutical response, developing and employing advanced cell-based disease models. We have been working on the establishment of novel cancer cell models that retain key features of tumour microenvironment. We have recently showed that tumour progression events can be recapitulated *in vitro* by combining bioreactor technology with 3D co-culture of cancer cell lines & stroma cells. We've observed phenotypic alterations typical of advanced breast cancer stages & accumulation of extracellular components along one month of culture.

Based on these developments, we are now implementing patient-derived cultures of several carcinomas, in collaboration with clinical groups at IPOLFG. The specific objective of this research project is to implement, characterize and validate novel patient-derived tumour cell models.

Task 1. Bioreactor culture conditions (dissolved oxygen concentration, pH, agitation rate, perfusion rate, etc.) will be optimized to favour long-term cell viability, cell proliferation and maintenance of cell phenotype. Cultures will be characterized phenotypically and in terms of gene expression.

Task 2. Validation of the models with standard of care compounds used in the clinic (mostly chemotherapeutic agents). Optimization of read-outs; implementation of improved cell-based assays.

Task 3. Thesis writing.