S6: Ageing and Sustainability– Health Diagnosis

Applied Models in Cancer Research

Cancer is a chronic disease that has been increasing in developed countries. An important reason for this increase is the aging population. The screening and early diagnosis are necessary instruments for appropriate patient treatment and to improve the patient prognosis.

Nowadays, there are several strategies for cancer study including the identification of biomarkers for screening and early detection of cancer as well as biomarkers for targeted therapy.

In this symposium we will show retrospective studies identifying potential biomarkers for screening and diagnosis of cancer and for targeted therapy. Some functional studies in cell lines and some in vivo models will be presented as tools for the validation of the biomarkers. We will also show innovative technologies as the next-generation sequencing and CRISPR-Cas9 gene editing which have been revolutionizing the field of cancer research.

Moderador: Regina A. Silva (ESTSP.IPP)

Studies to identify potential biomarkers for screening, diagnosis and therapy: breast cancer model

Diana Martins[1,2], Fernando Schmitt[2]

[1]Department of Pathological, Cytological and Thanatological Anatomy, School of Allied Health Technologies, Polytechnic Institute of Porto, Vila Nova de Gaia, Portugal
[2]Institute of Molecular Pathology and Immunology of the University of Porto, Porto, Portugal

Introduction: The Introduction of high-throughput technologies in breast cancer enabled the recognition of groups with prognostic value, in which target-therapies can be applied. However, a relevant percentage of patients show no clinical benefit. A possible solution could be the inhibition of pathways that are common in all tumor subtypes. Alterations of the serine-threonine kinase mammalian target of rapamycin (mTOR) signaling pathway are common in cancer and thus mTOR is being pursued as a therapeutic agent.

Objectives: We proposed to evaluate the expression of activated mTOR and its association with the main molecular subtypes of breast carcinoma. We also aimed to evaluate the ability of Everolimus, a rapamycin analog, to inhibit mTOR expression and function in breast cancer cells.

Materials and Methods: Large series of invasive breast carcinoma samples and cell lines.

Results and Discussion: Considering the molecular subtypes of breast carcinomas, p-mTOR was more frequently observed in basal-like breast carcinomas (80.6%). All breast cancer cell lines, representative of distinct molecular subtypes, showed expression of total and activated mTOR. These cells have been treated with Everolimus, in order to assess their sensitivity to this drug, and all cell lines showed a

decrease of p-mTOR expression after everolimus treatment. Due to the higher prevalence of p-mTOR in basal-like tumors, we treated three basal-like cell lines with Everolimus to assess the effects on cell invasion and aggregation. Cell invasion was significantly inhibited in response to Everolimus. Conslusion: The results revealed that there is a significant higher frequency of p-mTOR in basal-like tumors, compared with the other subtypes. In addition, Everolimus is able to significantly decrease mTOR expression and activity, inhibiting invasion capacity of basal-like breast cancer cells emphasizing the antitumour activity of mTOR inhibitors in breast cancer models.

In vivo models in cancer research

Madalena Costa[1,2], Filipa Quintela, Vilela [1,3] and Regina A. Silva[1]

[1]Department of of Pathological, Cytological and Thanatological Anatomy, School of Allied Health Technologies, Polytechnic Institute of Porto, Vila Nova de Gaia, Portugal
[2]Abel Salazar Biomedical Sciences Institute, University of Porto, Porto, Portugal
[3]Cancer Biology and Epigenetics Group –Research Center, Portuguese Oncology Institute – Porto, Porto, Portugal

Cancers figure among the leading causes of morbidity and mortality worldwide. Over the last decade there has been an extraordinary increase in our knowledge of the fundamental molecular processes that are involved in the development of cancer and its response to treatment. Studies in tissue culture have multiplied our acquaintance of cancer cell pathophysiology, mechanisms of transformation and strategies of survival of cancer cell lines, revealing therapeutically exploitable differences to normal cells. However, tumors are heterogeneous, structurally complex and result from an evolving crosstalk between different cell types and its surrounding tissue. A full elucidation of events occurring inside the cancer microenvironment is fundamental more effective therapies. Experiment in vivo models remains essential to understand the fundamental mechanisms underpinning malignancy and to discover improved methods to prevent, diagnose and treat cancer. This presentation will summarize currently available in vivo models of cancer, define the limitations and advantages of each modeling option and suggest the basis with which particular models should be used to answer a specific scientific question.