Instituto de Medicina Molecular João Lobo Antunes

Master Project Proposal

Title: Crosstalk between PLCγ1 and Estrogen Receptor Modulates the Prognosis and Therapy Resistance of Luminal Breast Cancer

Synopsis: PLCγ1 is a direct downstream effector of receptor and non-receptor tyrosine kinases which catalyses the hydrolysis of the membrane phospholipid phosphatidylinositol 4,5-bisphosphate (PIP2) into diacylglycerol (DAG) and inositol 1,4,5-trisphosphate (IP3) (1). PLCγ1 is involved in the tumorigenesis and progression of different types of cancer, including breast cancer (BC) (2). Previous studies showed that PLCγ1 downregulation in BC cell lines resulted in a strong inhibition of metastasis formation in nude mice (2). Additionally, overexpression of PLCγ1 is a risk factor for distant relapse in early luminal A and B breast cancer patients (3). Our previous work showed that PLCγ1 induces cetuximab resistance in metastatic colorectal cancer by activating ERK and AKT pathways (4). In this project, we aim to understand the link between PLCγ1 and Estrogen Receptor signalling and how it impacts the prognosis and therapy of luminal breast cancer. To answer that question, we will use both human samples available in our biobank and *in vitro* models of breast cancer cell lines depleted (knockout) or overexpressing PLCγ1 in several cellular assays such as: cell viability, drug resistance, apoptosis, invasion and signalling.

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