Instituto de Medicina Molecular João Lobo Antunes

Master Project Proposal

Title: RANK pathway inhibition as add-on therapy in breast cancer

Synopsis: The receptor activator of the nuclear factor-κB ligand (RANKL)/RANK signaling pathway was identified in the late 1990s and is the key mediator of bone remodeling. Targeting RANKL with the antibody denosumab is part of the standard of care for bone loss diseases, including bone metastases. Over the last decade, evidence has implicated RANKL/RANK pathway in hormone and HER2-driven breast carcinogenesis and in the acquisition of molecular and phenotypic traits associated with breast cancer (BCa) aggressiveness and poor prognosis. This marked a new era in the research of the therapeutic use of RANKL inhibition in BCa. Previous work from the Lab implies RANK signalling in the modulation of hormone receptors in breast cancer, which may have an impact in the efficacy of hormone therapy. We also have extensive data supporting that pharmacological inhibition of RANK pathway may overcome RANK-mediated resistance to therapy. The purpose of the project to be developed by the Master student, who is expected to work full time on the project, is to evaluate the effect of RANK inhibition, using ligand-independent approaches, in response to standard of care therapies. The student will apply several techniques, like RT-qPCR, Western blot, immunocytochemistry and/or flow cytometry, Alamar blue and clonogenic assays, as appropriate. The student is also expected to develop a ligand proximity assay.

Supervisor: Sandra Casimiro, LCosta Lab, scasimiro@medicina.ulisboa.pt
https://orcid.org/0000-0002-6917-4477

Host institution: Luis Costa Lab – Instituto de Medicina Molecular
https://imm.medicina.ulisboa.pt/pt-pt/investigation/laboratories/luis-costa-lab-2/#intro