Instituto de Medicina Molecular

Master Project Proposal

What we are looking for:
An ambitious MSc student with background/studies in bioinformatics/computational biology-related areas

Title: Dissecting the impact of IL-7/IL-7R-mediated signaling networks in cancer

Synopsis:
IL-7 and its receptor (IL7R) are absolutely essential for normal T-cell development and function. However, they can also promote autoimmunity, chronic inflammation and cancer. For more than 10 years, we have been studying a very aggressive blood cancer, with high prevalence in children: T-cell acute lymphoblastic leukemia (T-ALL). We have characterized some of the signaling mechanisms by which IL-7 and IL-7R can promote T-cell leukemia in vitro and in vivo (e.g. Barata et al, *Blood* 2004; Barata et al, *J. Exp. Med* 2004; Silva et al, *Leukemia* 2011; Silva et al, *Cancer Research* 2011; Melão et al *Haematologica* 2016), and showed that T-cell acute lymphoblastic leukemia (T-ALL) patients can display IL7R gain-of-function mutations leading to constitutive signaling and cell transformation (Zenatti el at, *Nature Genetics* 2011).

We now want to take our understanding of **how IL-7/IL-7R-mediated signaling promotes cancer** to a whole new level. We will compare physiological, IL-7-dependent signaling in normal versus leukemia cells, versus the signaling elicited by mutational activation of IL-7R (which does not require IL-7) which occurs only in leukemia cells, and characterize their differences. This will be done by comparing (phospho)proteomics, transcriptomics (RNA-seq) and chemical genomics datasets experimentally generated by our lab. We will also analyze whole exome datasets from T-ALL cell lines and patients and cross them with the remaining data. In turn, we will be able to 1) identify new genes and functional pathways associated with IL-7/IL-7R signaling; and 2) develop an unbiased and systematic view of the signaling landscape downstream from both physiological as well as mutant IL-7R activation.

The MSc student selected for this project will be involved mainly in the RNA-seq and whole exome-seq dataset analyses. Depending on the student's performance, commitment, interest and ambition, inclusion in the team for a subsequent PhD may be contemplated. The student will be integrated in a highly dynamic, productive, easy-going but internationally-competitive team, supported by a prestigious ERC grant (**"IL7SigNETnure - IL-7/IL-7R signaling networks in health and malignancy" (ERC CoG-648455)**). We want to recruit a top quality student with the same spirit as the remaining team. Of note, our institute provides an excellent working environment that integrates both "wet lab" biologists and bioinformaticians. The student will count on the direct supervision of a senior computational biologist: Dra. Ana Rita Grosso. In addition, Dr. Aviv Regev (Broad Institute, Cambridge, MA, USA) and Dr. Nuno Barbosa-Morais (iMM) will act as consultants to the project.

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Webpage of the group: https://imm.medicina.ulisboa.pt/en/investigacao/labs/barata-joao-t-lab/