Instituto de Medicina Molecular João Lobo Antunes

Master Project Proposal

Title: Antigen-driven T cell responses during gastric cancer initiation

Synopsis: Common Variable Immunodeficiency (CVID) is the most common symptomatic primary immunodeficiency worldwide. It is defined as a defective B-cell differentiation into memory B cells and IgG-secreating plasma cells. Despite the therapeutic management of the disease with the administration of IgG, CVID patients have a high prevalence of gastrointestinal infections, including *Helicobacter pylori.*
H. pylori is a bacteria that colonizes the human stomach and is the strongest risk factor for the development of gastric cancer. *H. pylori* disrupts the normal epithelial structure, promotes inflammation and induces genomic instability. Accordingly, CVID patients have a high prevalence of *H. pylori* infection and a 10- to 47-fold increase in gastric cancer incidence. Gastric tissue from CVID patients has a characteristic exacerbated T cell infiltration, and an accelerated process of carcinogenesis. CVID patients, are thus excellent models to dissect T cell responses during gastric cancer initiation.
The aim of the proposed project is to identify *H. pylori*-specific and/or gastric cancer-specific T cells and their cognate antigens. Identification of pathogen-specific and cancer-specific T cell antigens is the basis for the development of vaccines and immunotherapies against cancer.

The Master student will characterize the T cell receptor (TCR) repertoire of gastric tissue-infiltrating T cells, in CVID blood and gastric specimens. Single cell transcriptomics and bioinformatics approaches will be applied, as well as cellular biology techniques, namely T cell stimulation assays and flow cytometry. The opportunity to perform part of the project at the University of Oxford will be discussed with the student.

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Bibliography:

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