Instituto de Medicina Molecular João Lobo Antunes

Master Project Proposal

Title: What can we learn from tumor-resident and gut microbiota about breast cancer progression, dissemination and response to neoadjuvant treatment?

Synopsis:

Breast cancer is the most commonly diagnosed cancer type and the leading cause of cancer-related death in women worldwide. The tumour microenvironment (TME) is an active player in cancer progression, dissemination and response to treatments. Strikingly, a pan-cancer study found that BC has a particularly rich and diverse microbiome compared to other cancer types [1-2]. This suggests that intra-tumoural bacteria exist, are active, and more provocatively that they may play key roles in cancer pathogenesis and response to therapy. The complex interaction between local and gut microbiota, the immune system and malignant cells is still poorly described.

We propose a MSc project to determine the microbiota profiles from over 100 samples of primary and metastatic BC samples at the phylum, class, order, family, genus and species levels. The student will analysed large datasets of full-length 16S rRNA amplicon sequencing obtained from tumour samples. With this project the student will gain experience in microbiome pipelines and analysis, as well as data integration from clinical outcomes. He/She will learn to identify microbiome-based signature associated with BC progression, predisposition to metastasis and response to neoadjuvant therapy.

This project is integrated in the iMM-Laço initiative and the student will join our team and benefit from close interaction and supervision with international and local experts in the field of gut microbiome and its role in remodelling the gut epithelium (Dr *Patrick Varga-Weisz* [3]) and in colorectal cancer (Dr Almeida [4]). In addition, the student will have the possibility to participate in the weekly lab meetings of the "Disease Transcriptomics" lab led by Dr Nuno Morais. Finally, the student will benefit from the collaborative and interdisciplinary environment of iMM and host teams.

Background in bioinformatics, computational biology, computer science, microbiology, R, Python or Unix command-line interfaces will be highly valued.

Supervisor: *Karine Serre, iMM-Laço, karineserre@medicina.ulisboa.pt*
Collaborator international: *Patrick Varga-Weisz,* School of Life Sciences, University of Essex, patrick.varga-weisz@essex.ac.uk
Collaborator from iMM: *Ana Margarida Almeida, anasalmeida@medicina.ulisboa.pt, Nuno Morais, nmorais@medicina.ulisboa.pt*

Webpage(s) group:

https://laco.imm.medicina.ulisboa.pt/
https://imm.medicina.ulisboa.pt/group/distrans/

Bibliography:

[1] Nejman, D. *et al.* The human tumor microbiome is composed of tumor type-specific intracellular bacteria. *Science* **368,** 973–980 (2020).
[2] Yang X, *et al.* Comprehensive analysis of microbiota signature across32 cancer types. *Front.Oncol*. **13**: 1127225.doi: 10.3389/fonc.2023.1127225 (2023).
[3] Corrêa, R. O., *et al.* Inulin diet uncovers complex diet-microbiota-immune cell interactions remodeling the gut epithelium. *Microbiome*, **11**(1), 90. doi: 10.1186/s40168-023-01520-2 (2023).
[4] Almeida, A. S., *et al.* Fiber-associated Lachnospiraceae reduce colon tumorigenesis by modulation of the tumor-immune microenvironment. *BioRxiv*. https://doi.org/10.4049/jimmunol.206.supp.68.14 (2021).