upf. Universitat Pompeu Fabra *Barcelona*

Master in Bioinformatics for Health Sciences

Master project 2024-2025

Personal Information

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Project

Computational genomics

Project Title:

Single cell mapping of tumor-immune coevolution in organ-specific breast cancer metastasis

Keywords:

Metastasis, Tumor immunology, Coevolution, Breast Cancer, clinical data

Summary:

Metastasis is a dynamic complex process that accounts for most of cancer related deaths. During metastasis, most of the disseminated tumor cells fail to adapt to new tissue conditions and die, resulting in a selection of the fittest cells. The immune system's anti-tumor activity is one of the main barriers of metastatic colonization. We hypothesize that metastatic colonization is the result of a coevolutionary process of tumor cells and immune cells in the distant organs, the product of organ-specific immune pressure and fittest cancer clones. Each organ in our body is populated by a unique immune repertoire of cells, which may exert selective pressure into metastatic clones. Yet, the spatiotemporal map of clonal events is difficult to resolve because current approaches have omitted mutual interdependency between immune and tumor compartments. Simultaneous tracing of tumor and immune cells will allow to follow the coevolutive chronicle of tumor-immune clonal events and transcriptomic states across different organs at the single-cell level. For instance, breast cancer phenotypic heterogeneity, including cancer stem cells, epithelial to mesenchymal transition states, and other phenotypes will be traced alongside the myeloid and lymphoid immune lineages sculping them in the different organs. Using computational methods the TFM candidate will learn how to study tumor-immune coevolution from experimental data to computational validations using large clinical RNA-seq and single cell RNA-seq datasets. This project will reveal unprecedented tumor-immune coevolutionary events underlying metastasis in different organs and will add a new dimension of knowledge for innovative immunotherapeutic strategies.

References:

I. Pérez-Núñez; C. Rozalén; J.A. Palomeque; et al; (31/31) T. Celià-Terrassa (AC). 2022. LCOR mediates interferon-independent tumor immunogenicity and responsiveness to immune-checkpoint blockade in triple negative breast cancer. Nature Cancer. https://doi.org/10.1038/s43018-022-00339-4 Von Locquenghien M, Rozalen C, Celià-Terrassa T (AC). (2021) Interferons in cancer immunoediting: sculpting metastasis and immunotherapy response. Review in The Journal of Clinical Investigation. https://doi.org/10.1172/JCI143296 Celià-Terrassa T.; Caleb Bastian; Daniel Liu; et al; Yibin Kang. (1/14) 2018. Hysteresis control of epithelial-mesenchymal transition dynamics conveys a distinct program with enhanced metastatic ability. Nature Communications. https://doi.org/10.1038/s41467-018-07538-7 Celià Terrassa, T.; Liu, DD.; Choudhury, A.; et al; Kang, Y. (1/15). 2017. Normal and cancerous mammary stem cells evade interferon-induced constraint through the miR-199a-LCOR axis. Nature cell biology. https://doi.org/10.1038/ncb3533

Expected skills:

RNA-seq analysis; GSEA, GSVA, single-cell RNA-seq analysis

Possibility of funding:

Yes

Possible continuity with PhD:

To be discussed

Comments:

NO remuneration/contract for TFM students. After TFM completion, possibility to extend the project with a competitive contract and remuneration.