Universitat Pompeu Fabra Barcelona | Master in Bioinformatics for Health Sciences

Master project 2021-2022

Personal Information

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Project

Computational genomics

Project Title:

Epigenetic role in aromatase inhibitor resistant breast cancer

Keywords:

Breast cancer, epigenetics, ATAC-seq, machine learning, transcription signatures

Summary:

Hormone receptor positive breast cancer patients has improved largely their outcome over the last decades, mainly due to efficacy of hormone receptor treatments (HRTx). However, some of these patients relapse after several years. In the MSK-Impact metastatic breast cancer study, authors identify some mechanism of HRTx, however mechanism affecting around 60% of metastatic breast cancer are still unknown (Razavi et al. Cancer Cell 2018). We have identified some subgroups that are more likely to relapse after 10 years (Rueda et al. Nature 2019), and we think that some epigenetic related mechanism could be affecting at least one of these subtypes. In this project we will leverage the dataset from (Selli et al. Breast Cancer Research 2019) in order to find the patterns that distinguish dormant from resistant tumors. We will investigate the epigenetic enrichments on these patterns. Then we will develop a signature to identify these dormant tumors in other datasets, including TCGA. We will use the TCGA ATAC-seq data to identify peak and motifs that are associated with dormancy based on our signature. Finally, we will correlate the tumors identified by our signature with time to relapse and with current breast cancer subtypes.

References:

Razavi, P., Chang, M. T., Xu, G., Bandlamudi, C., Ross, D. S., Vasan, N., ... & Baselga, J. (2018). The genomic landscape of endocrine-resistant advanced breast cancers. Cancer cell, 34(3), 427-438. Rueda, O. M., Sammut, S. J., Seoane, J. A., Chin, S. F., Caswell-Jin, J. L., Callari, M., ... & Curtis, C. (2019). Dynamics of breast-cancer relapse reveal late-recurring ER-positive genomic subgroups. Nature, 567(7748), 399-404. Selli, C., Turnbull, A. K., Pearce, D. A., Li, A., Fernando, A., Wills, J., ... & Sims, A. H. (2019). Molecular changes during extended neoadjuvant letrozole treatment of breast cancer: distinguishing acquired resistance from dormant tumours. Breast Cancer Research, 21(1), 1-15.

Expected skills::

Differential expression analysis, pathway enrichment, machine learning, ATAC-seq differential peak and motif enrichment.

Possibility of funding::

No

Possible continuity with PhD: :

To be discussed

Comments:

There will be funding for one PhD position associated with this project.