Universitat Pompeu Fabra Barcelona

Master in Bioinformatics for Health Sciences

Master project 2024-2025

Personal Information

Supervisor	Marco Mariotti
Email	marco.mariotti@ub.edu
Institution	Universitat de Barcelona
Website	https://www.mariottigenomicslab.com/
Group	Comparative Genomics of Gene Expression

Project

Computational genomics

Project Title:

An atlas of selenium dependency in cancer

Keywords:

Gene expression, Cancer, Selenium, Genomics

Summary:

Selenium is a trace element that is essential for human health and plays a critical role in various physiological and molecular functions. Selenium exerts its roles in form of selenocysteine (Sec), the 21st amino acid in the genetic code, present in proteins called “selenoproteins” [1]. Unlike other amino acids, Sec is encoded by UGA, normally a stop codon, which is recoded to Sec due to an RNA structure, called the SECIS element, located in selenoprotein mRNAs. Selenoproteins are involved in numerous functions including antioxidant defense, protein folding, thyroid hormone metabolism, and others. A good supply of selenium is considered important for a strong immune response, and has been shown to have cancer preventive properties in certain situations. Recent research has shown that many cancer types heavily depend on selenium, as they overexpress selenium uptake, metabolism, and Sec synthesis [2–4]. We define these cancers as “selenophilic”. This characteristic has been linked to the prevention of ferroptosis, a form of programmed cell death distinct from apoptosis which is triggered by lipid peroxidation. Indeed, the selenoprotein GPx4 prevents lipid oxidation and therefore averts ferroptosis, which is essential for growth of many cancer types. This has brought to a paradigm reversal, as now selenium deficiency (rather than repletion) is being explored as anti-cancer therapy. The objective of this project is to characterize selenium usage across different types of cancers by leveraging publicly available gene expression data, producing an atlas of selenium dependency of cancer. Having this resource may help to recommend selenium-based treatments (based on deficiency or repletion), which may eventually be tested by our and collaborator labs.

References:

[1] V.M. Labunskyy, D.L. Hatfield, V.N. Gladyshev, Selenoproteins: molecular pathways and physiological roles., Physiol Rev. 94 (2014) 739–77. https://doi.org/10.1152/physrev.00039.2013. [2] A.E. Carlisle, N. Lee, A.N. Matthew-Onabanjo, M.E. Spears, S.J. Park, D. Youkana, M.B. Doshi, A. Peppers, R. Li, A.B. Joseph, M. Smith, K. Simin, L.J. Zhu, P.L. Greer, L.M. Shaw, D. Kim, Selenium detoxification is required for cancer-cell survival, Nat Metab. 2 (2020) 603–611. https://doi.org/10.1038/s42255-020-0224-7. [3] K. Eagle, Y. Jiang, X. Shi, M. Li, N.P. Obholzer, T. Hu, M.W. Perez, J.V. Koren, A. Kitano, J.S. Yi, C.Y. Lin, D. Nakada, An oncogenic enhancer encodes selective selenium dependency in AML, Cell Stem Cell. 29 (2022) 386-399.e7. https://doi.org/10.1016/j.stem.2022.01.003. [4] Z. Li, L. Ferguson, K.K. Deol, M.A. Roberts, L. Magtanong, J.M. Hendricks, G.A. Mousa, S. Kilinc, K. Schaefer, J.A. Wells, M.C. Bassik, A. Goga, S.J. Dixon, N.T. Ingolia, J.A. Olzmann, Ribosome stalling during selenoprotein translation exposes a ferroptosis vulnerability, Nature Chemical Biology 2022 18:7. 18 (2022) 751–761. https://doi.org/10.1038/S41589-022-01033-3.

Expected skills:

Python and/or R; High throughput data analysis; Gene expression analysis

Possibility of funding:

To be discussed

Possible continuity with PhD:

To be discussed