Propuesta de Trabajo Fin de Máster
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Máster en Métodos Computacionales en Ciencias

Proyecto Nº 14

Título: *Statistical inference of clonal mutation and the impact of Clonal neoantigen burden in the immune response*

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Resumen

Intratumour heterogeneity (ITH) is observed across many cancer types. While ITH can have an impact on patient response to targeted therapies, their impact on antitumour immunity and sensitivity to immunotherapy is not well established. Recently, it has been shown that patients with a high clonal neoantigen burden and low level of neoantigen ITH exhibited a better response to immunotherapy than those with low clonal neoantigen burden or a high level of neoantigen ITH (1). In addition, in a recent study in patients with gastrointestinal cancers, neoantigen-reactive tumor-infiltrating lymphocytes mainly recognized clonal somatic mutations (2). These findings suggest that neoantigen clonality may play a role in response to immunotherapy and could help select the best neoantigen candidate for personalized medicine, such as vaccine. Due to the current methods of molecular analysis where a mixed population of cancer cells are lysed and sequenced, heterogeneity within the tumour cell population is under-detected. This results in a lack of information on the clonal composition of cancer tumours. Recently a novel statistical method, PyClone, has been developed for inference of clonal population structures in cancers (3). PyClone is a Bayesian clustering method for grouping sets of deeply sequenced somatic mutations into putative clonal clusters while estimating their cellular prevalence and accounting for allelic imbalances introduced by segmental copy number changes and normal cell contamination. We propose to explore neoantigen heterogeneity and the relevance of clonal neoantigen burden in response to immunotherapy, using cancer patients included in The Cancer Genome Atlas (TCGA) project that have been classified as responders or non-responders to immunotherapies treatments.

It is not necessary for the student to know about advanced statistics. The student will have the opportunity to learn programming in R, working with the cluster and several algorithms ready to use in the cluster. We will guide and help the student in all the processes.

1. *McGranahan N et al. Clonal neoantigens elicit T cell immunoreactivity and sensitivity to immune checkpoint blockade.Science. 2016 Mar 25; 351(6280):1463-9.*
2. *Parkhurst MR et al. Unique Neoantigens Arise from Somatic Mutations in Patients with Gastrointestinal Cancers. Cancer Discov. 2019 Aug;9(8):1022-1035*
3. *Roth A et al. PyClone: statistical inference of clonal population structure in cancer.Nat Methods. 2014 Apr;11(4):396-8.*