Master's project: Pan-cancer discovery of RNA-editing-derived neoantigens for cancer immunotherapy

Project description

Personalised cancer immunotherapy aims to direct T-cell responses against tumour-specific antigens that are present in cancer cells but absent from healthy tissues. Most current neoantigen discovery approaches focus on classical DNA-level mutations, such as single-nucleotide variants and short indels. However, cancer cells may also generate tumour-specific antigens through non-canonical mechanisms.

One particularly interesting source is **RNA editing**: post-transcriptional nucleotide changes that alter RNA sequences without changing the underlying DNA. If such edited transcripts are translated, they may generate altered protein sequences that can be presented on HLA molecules and recognised by T cells, as they are, similarly to viral proteins, represent a non-self sequence. These RNA-editing-derived peptides could therefore represent a new class of targets for personalised cancer vaccines or T-cell-based therapies.

RNA-editing-derived neoantigens remain largely unexplored, and in many ways this area is still a **black box** in the field. It is not yet clear how common these candidates are across cancer types, how patient-specific they are, whether they recur across tumours, or how safe they are as therapeutic targets. This makes the project exploratory, but also high-potential: systematic analysis across large cancer cohorts could reveal an underused source of tumour antigens, especially in cancers where classical mutation-derived neoantigens are limited.

In our group, we have drafted a computational pipeline for identifying RNA-editing-derived neoantigen candidates. The goal of this master's project is to apply and further develop this pipeline across multiple cancer types from TCGA, and potentially compare the results against normal tissue datasets such as GTEx. The central question is whether RNA-editing-derived peptides can provide safe and tumour-specific for future cancer vaccines.

Main aims

The student will investigate:

1. Which cancer types show the highest burden of RNA-editing-derived neoantigen candidates and whether they can be used to apply immunotherapy in patients with low canonical tumor-mutational burden.
2. Which RNA-editing events private to individual patients or recurrent across patients and cancer types. Recurrent variants are good off-the-shelf vaccine targets.
3. Which RNA-editing events are not present in healthy tissues, and therefore make a safe vaccinable target.

Student tasks

The student will:

- Run and update the somatic variant calling and neoantigen prediction pipeline.
- Analyse large-scale cancer datasets, primarily from TCGA.
- Integrate normal tissue data, for example, from GTEx, to assess tumour specificity.
- Summarise results across patients and cancer types.
- Generate statistical analyses and publication-quality visualisations.
- Help improve pipeline automation, reproducibility, and documentation.

Hard skills the student will learn

This project is a strong opportunity to gain practical experience in computational cancer genomics with immunotherapy applications and large-scale bioinformatics. Along the way, the student will learn about:

- Bioinformatics pipeline development and automation. Nextflow workflow management.
- Linux-based high-performance computing.
- Statistical analysis of patient-level and cancer-type-level data.
- Version control with Git.
- Biological principles of T-cell-based cancer immunotherapy.

Expected student background

The project is suitable for a motivated master's student with an interest in cancer genomics and immunotherapy. The student is expected to have:

- Basic Python and/or R skills.
- Basic Linux command-line literacy.
- Basic understandings of cancer genomics and adaptive immunology.

Prior experience with Nextflow, high-performance computing, or version control is not required.

Expected outcome

The project will produce a pan-cancer overview of RNA-editing-derived neoantigen candidates and assess their potential as safe T-cell targets. The results may help identify cancer types where RNA editing provides a promising source of non-canonical antigens and will contribute to a future publication.