Can we detect immunotherapy side-effects from a blood test?

Master End Project CS/Nanobiology/LST

Motivation

Immunotherapy is a novel cancer treatment that activates a patient's immune system against the tumor [1] and can be very beneficial against many cancer types, including melanoma (skin cancer) [2]. However, sometimes immunotherapy can have severe side-effects resulting from activation of the immune system towards the patient's own organs such as the intestine. In some cases, if patients experience severe side effects, the treatment has to be stopped [3].

Ideally, we would like to **detect** these **side-effects before a patient develops symptoms**, so we can stop the immunotherapy early and seek alternative treatment. In addition, we want to do so without exposing the patients to invasive procedures, i.e. **from a simple blood test**.

Background

Cells release DNA fragments into the bloodstream, which we call cell-free DNA (**cfDNA**). Disease or injury in a particular tissue/organ leads to increased amount of cfDNA from that tissue [4]. This **cfDNA** maintains its **methylation** which is **tissue-specific** [5] and can be used to **identify the cell type of origin** [6], [7]. We therefore expect that cfDNA from melanoma patients will have a clear "skin" methylation signature as opposed to cfDNA of healthy controls. Our hypothesis is that intestine toxicity from immunotherapy will lead to increased amount cfDNA being released from the intestine.

Project Goals

In this collaboration with Erasmus Medical Center, you will:

- Use public DNA methylation data to estimate the **methylation profiles of** different **organs and tissues**.
- **Build** statistical models and **deconvolution approaches** [8] to estimate the fraction of tissue-specific signals in cfDNA (blood, skin, intestine, others) from DNA methylation data.
- **Evaluate** their **sensitivity/specificity** in detecting intestine-specific signal.
- **Apply your methods to patient data** to test whether we can **detect intestine toxicity in skin cancer patients receiving immunotherapy**.

Prerequisites

- Multivariate Data Analysis (CS4070) or equivalent affinity with ***linear algebra*** and ***multivariate statistics***
- Experience with one scripting language (***R/Python/MATLAB***)

Contact

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References

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