Evaluating High-Dimensional Surrogate Markers of the Yellow Fever Vaccine Response

M2 Internship

Background

Measuring the primary outcome in a clinical trial is often time-consuming, expensive, impractical, or even unethical. For instance, when the outcome is rare, demonstrating a statistically significant difference between treatment groups can take many years. Consequently, there is considerable interest in identifying *surrogate markers*—variables that can be observed more quickly, at lower cost, or with greater ease, and that can serve as reliable substitutes for the primary outcome to accurately infer the treatment effect [1].

The identification of novel surrogate markers has profound implications for vaccine development. Validated surrogates can accelerate the process by providing strong evidence for selecting candidate vaccines before full-scale trials [2]. They also allow for the validation of new-generation vaccines in cases where an efficacy trial may be unethical, such as when a successful vaccine already exists or when a phase 3 trial is not feasible due to the absence of a disease outbreak [3]. Moreover, these surrogates offer crucial insights into the mechanisms behind vaccine-induced immunity, a central focus of modern vaccinology [4].

Emerging high-throughput technologies hold great promise for informing effective vaccine design [5]. A prime example is transcriptomic data, which describe gene expression—the process by which information encoded in DNA is transformed into proteins that shape phenotypes. Gene expression changes can be observed within days after vaccination, while traditional immunological measures, such as antigen-specific antibody titres or T-cell responses—commonly used as surrogate endpoints in vaccine studies—take weeks or months to fully establish [6]. Research has shown that early gene expression measurements can predict individual immune responses to vaccination, including responses to the yellow fever vaccine, among others [7, 8, 9]. This is particularly important as the ability to reliably predict individual responses to vaccination paves the way for personalized vaccine regimens. However, it remains unclear whether these gene expression markers, individually or in combination, can serve as surrogates for vaccine response in a future trial. This project aims to address this gap by systematically evaluating the potential of high-dimensional gene expression markers as surrogates for the yellow fever vaccine response.

Objectives

- Conduct a literature review of methods for the identification and/or evaluation of high-dimensional surrogate markers.
- Perform a simulation study, identifying the strengths and weaknesses of existing approaches.
- Apply the approaches to a public systems vaccinology dataset [10], evaluating early gene expression surrogates of the response to yellow fever vaccination.

Required Skills

- Master 2/Bachelor/Engineering school with a major in biostatistics or similar
- Programming proficiency with R
- Interest in biomedical research and scientific curiosity
- Written and spoken English proficiency

Hosting laboratory
SISTM Team
INSERM U1219 and INRIA Sud-Ouest

Location
Bordeaux Population Health Research Center
Université de Bordeaux – ISPED
146, Rue Léo Saignat
33076 Bordeaux

Duration:
Internship of 4 to 6 month available starting from January 2025.

Compensation:
Intern gratification according to government recommendations (15% of social security ceiling, i.e. around 685€/month).

Contact:
Send a detailed CV and a motivation letter to Boris Hejblum (boris.hejblum@u-bordeaux.fr) and Arthur Hughes (arthur.hughes@u-bordeaux.fr).

References

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