Investigator Choices Influence Biological Interpretation of Transcriptomic Signatures of Vaccination

Arthur Hughes[1], Rodolphe Thiébaut[12], Boris Hejblum[1]

1) INSERM Bordeaux Population Health, INRIA SISTM, University of Bordeaux

2) CHU de Bordeaux, Service d'Information Médicale, INSERM, Bordeaux

Motivation

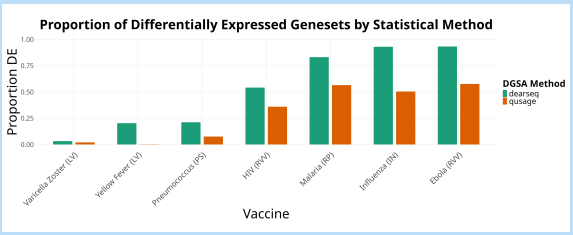
- Deriving transcriptomic signatures helps understanding of vaccine-induced immunity
- Previous studies identified common signatures of vaccines [1]
- **Analytical flexibility** can lead to **diverging results**
- Need for tools to evaluate robustness to investigator choices

Methods

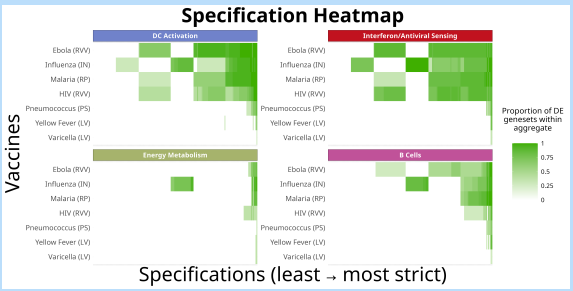
- **Differential Geneset Analysis** of vaccinees at 1 day post-vacination
- **Specification analysis :** view results as a function of combinations of investigator choices [2]
- Focus on reasonable choices of statistical parameters:
  - Significance level $\alpha = (1e^{-4}, 1e^{-3}, 0.01, 0.05, 0.1)$
  - Differential analysis method (dearseq, QuSAGE)
  - p-value adjustment procedure (BH, bonferroni, holm,...)
  - Fold-change threshold (0, 0.5, 1)

Results

- **Investigator parameters** have a **large impact** on results!



- **Visualising results** as a function of **all specifications** assesses **robustness** of biological conclusions



Discussion

- Complex analyses → more choices → results variability
- Specification analysis allows to identify **robust signals** which are **common to many vaccines**
- Future work: larger range of choices (normalisation, batch corrections, differential methods...)

References

[1] Hagan, T., et al. Transcriptional atlas of the human immune response to 13 vaccines reveals a common predictor of vaccine-induced antibody responses. Nat Immunol 23, 1788–1798 (2022).

[2] Simonsohn, U., Simmons, J.P. & Nelson, L.D. Specification curve analysis. Nat Hum Behav 4, 1208–1214 (2020).