Antibody Germline Evolution within the Context of Pre-Vaccination Antigen Exposure

Requirements Specification

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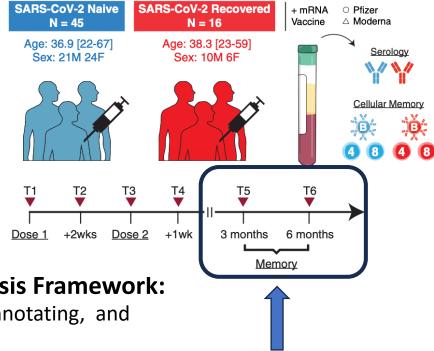
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DS 288: Capstone Project

High-Level Requirements and Data Sources

Goal: To compare the post-immunization germline evolution of two groups— those who were pre-exposed to the antigenic material through wild-type infection, and those who were naïve to it.

Question: How does prior infection modulate antibody germline evolution in the context of vaccination?



Adaptive Immune Receptor Repertoire (AIRR-seq) Analysis Framework:

• Immcantation – library for cleaning, aligning, structurally annotating, and assessing the clonal diversity of AIRR-seq data.

AIRR-seq Data Source:

- iReceptor Database
 - 45 Naïve Participants, and 16 Participants who recovered from the virus.
 - 9,104,391 associated germline sequences
 - Goel, et al. mRNA vaccines induce durable immune memory to SARS-CoV-2 and variants of concern. Science (2021)

Timepoints of interest Goel, et al. (2021)

Questions, Target Audience, Users

Specific Questions:

- Does pre-exposure to wildtype antigenic material act to diversify the antibody repertoire?
- 2. Is there a difference in the:
 - 1. Complementary Determining Regions (CDRs)?
 - Rates of Somatic Hypermutation (SHM)?
 - 3. Lineage (Breadth vs. Depth of evolution)?
- 3. (Wishlist) Is the germline data predictive of whether an individual had a prior infection?

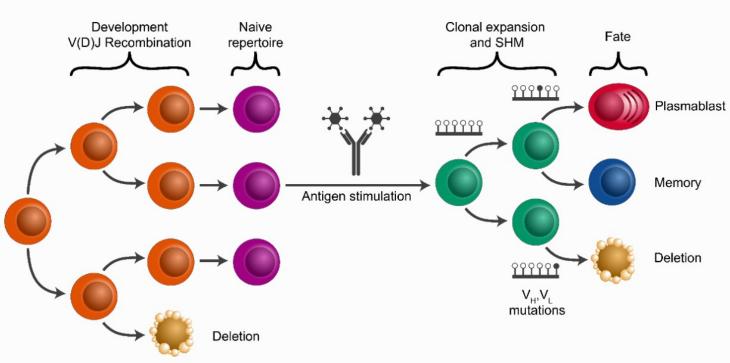
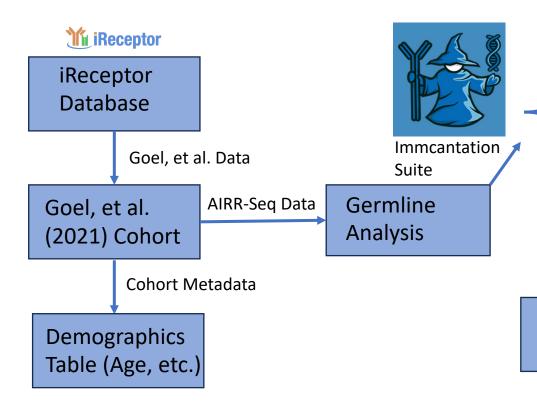


Image from Immcantation documentation, demonstrates antigen stimulation and diversity of clonal lineage.

Target Audience/Users:

 Biochemists, Computational Biologists, Physicians, Immunologists, Virologists and Vaccinologists

Inputs/Outputs



Set of Experiments

- Clonal Abundance/Diversity
- 2. Gene Usage
- Rates of Somatic Hypermutation
- I. Lineage Analysis
- 5. CDR3 Properties

Statistical Comparison Naïve (n = 45) vs. Pre-Exposed (15)

Results Tables and Graphs

(Wish-list)

Possible to model the probability of pre-vaccine exposure?

References:

- Goel, et al. mRNA vaccines induce durable immune memory to SARS-CoV-2 and variants of concern. Science (2021)
- Cizmeci, et al. Distinct clonal evolution of B-cells in HIV controllers with neutralizing antibody breadth. eLife (2021)
- Corrie et al. iReceptor: a platform for querying and analyzing antibody/B-cell and T-cell receptor repertoire data across federated repositories, Immunological Reviews (2018)
- Vander Heiden, Yaari, et al. pRESTO: a toolkit for processing high-throughput sequencing raw reads of lymphocyte receptor repertoires. Bioinformatics (2014)
- Gupta, Vander Heiden, et al. Change-O: a toolkit for analyzing large-scale B cell immunoglobulin repertoire sequencing data. Bioinformatics (2015)