

Thesis Changes Log

Name of Candidate: Artem Mikelov

PhD Program: Life Sciences

Title of Thesis: DYNAMICS OF IMMUNOGLOBULIN REPERTOIRES IN MEMORY AND ANTIBODY-SECRETING B CELL SUBSETS IN HEALTH AND DISEASE

Supervisor: Associate Professor Dmitriy Chudakov

The thesis document includes the following changes in answer to the external review process.

- Fixed paragraph numbering p.29, p.31
- Added section 3.5 describing tools used for plots and statistical analysis
- Added points to plots Fig. 7,8 to better illustrate actual distributions
- Updated section 2.2 to provide contemporary view on somatic hypermutations in GC-independent memory B-cells
- Updated section 2.2 to point out that apoptosis is the fate of the majority of B-cells in GC-reactions.
- Updated Figure 1 and caption, to include statistical analysis of isotype distribution differences between cell subsets, and exclude excessive information
- p.57 corrected reference to Figures 10 and 11 (correct – Fig. 11,12)/
- Correction made to Table 1 (Donor AT, time point T3, PL cell subset – correct cell sample sizes – 400 and 400 cells)
- Included number of repertoires used from Gidoni et al. in second paragraph of 3.4
- Section 3.4 was augmented with the description of the samples not utilized in comparisons of repertoires in section 4.3 of results: “Cell samples with smaller numbers of clonotypes were excluded from comparisons: IM T1 repl. 1, MRK T1 repl. 1, MRK T3 replicate 2, IZ T3 replicates 1,2; all from PL subset.”
- Corrected the number of plasma cell clonotypes used for comparisons (200) in section 3.4 and Figure 11, 12 and 13 captions.
- Occasional text duplication was removed from the beginning of section 4.4
- Section 4.4 was extended with explanation of particular value for filtering the allelic variants by score: “The threshold of 0.35 for the final alleles filtering was initially chosen from a theoretical consideration of possible distributions of expressed alleles for a V-gene allowing the presence of three allelic variants due to possible V-gene duplications. This was then corroborated by examining empirical score distributions for alleles in repertoire sequencing of IGH repertoire of a healthy donor with known genotype; in this case the donor was different from the one in the benchmarking of the algorithm.”
- In results section 4.2 added sentence to emphasize that for IgE we might not observe statistically significant differences just due to low number of clonotypes: “Differences for IgE isotype, however, could not be reliably assessed due to low number of clonotypes”.
- Added Elsner RA, Shlomchik MJ 2020; Wickham H, 2016; Mayer et al 2017; Anderson et al. 2009 to bibliography
- Updated Table of Contents and section headings to match each other.
- Updated figures 13,15,16 and 17 with higher resolution versions
- Corrected minor typos and grammatical errors
- Added section “Author contribution” to List of publications section

