

This week's objective : why studying the Bcell repertoire's diversity is important? how to do it ?

Readings : the following document about the importance of repertoire diversity in immunological and clinical contexts and “A bioinformatic framework for immune repertoire diversity profiling enables detection of immunological status.”by Greiff et al. for more detailed explanation.

Next-generation sequencing (NGS) has enabled the scientific community to undertake insightful analyses of the immune behavior and immune responses. These studies are based on the B cell receptor (BCR) repertoire sequencing (B-cell Rep-Seq). In order to interpret the output of such data, it is necessary to quantify the repertoire diversity.

The quantification of the repertoire diversity helps to :

- characterize a repertoire and associate it with an immunological status (e.g., healthy, infected, vaccinated, etc.) [1]
- compare multiple repertoires:
 - from the same person at different time points, which could be particularly interesting for studying the effect of a treatment or the vaccination,
 - from different people for the study of stereotyped BcR immunoglobulins [2]

However, the peripheral blood compartment, which is currently the principal source of Rep-Seq data mainly for lymphoproliferative diseases, contains only 2.5% [3] (10^9 B cells) of the estimated total number of cells (10^{11}) [4–6]. Sampling from this compartment provides around 10^6 B cells. This implies that only a fraction of the total diversity repertoire can be identified by IG-Seq. Therefore, the total diversity analysis must include the estimation of the undetected clones.

To Do : Write a reflexion note answering the main questions of the week, providing examples. You can also use the comments on your previous reflexion note to enrich your report. It is good and even necessary to “google”the pieces of information that you don't find in the articles you have, however it is essential to mention their references in your reflexion note :)

[1] Greiff, V., Bhat, P., Cook, S. C., Menzel, U., Kang, W., & Reddy, S. T. (2015). A bioinformatic framework for immune repertoire diversity profiling enables detection of immunological status. *Genome Medicine*. <https://doi.org/10.1186/s13073-015-0169-8>

[2] Agathangelidis, A., Psomopoulos, F., Stamatopoulos, K. (2019). Stereotyped B Cell Receptor Immunoglobulins in B Cell Lymphomas. *Methods Mol Biol*. 1956:139-155. <https://doi.org/10.1007/978-1-4939-9151-8>.

- [3] Greiff, V., Miho, E., Menzel, U., & Reddy, S. T. (2015). Bioinformatics and Statistical Analysis of Adaptive Immune Repertoires. *Trends in Immunology*. 36:738–749. <https://doi.org/10.1016/j.it.2015.09.006>
- [4] Morbach, H., Eichhorn, E. M., Liese, J. G., & Girschick, H. J. (2010). Reference values for B cell subpopulations from infancy to adulthood. *Clinical and Experimental Immunology*. <https://doi.org/10.1111/j.1365-2249.2010.04206.x>
- [5] Ganusov, V. V., & De Boer, R. J. (2007). Do most lymphocytes in humans really reside in the gut? *Trends in Immunology*. <https://doi.org/10.1016/j.it.2007.08.009>
- [6] Trepel, F. (1974). Number and distribution of lymphocytes in man. A critical analysis. *Klinische Wochenschrift*. <https://doi.org/10.1007/BF01468720>