

## Ageing of the immune system, a BRepertoire® perspective.

Immune repertoire developmental processes are a balance between increasing diversity for maximising shape space and avoiding those shapes that result in autoreactivity. The human immunoglobulin repertoire is a hugely diverse set of sequences that are formed by processes of gene rearrangement, heavy and light chain gene assortment, class switching and somatic hypermutation. Early B cell development produces diverse IgM and IgD B cell receptors on the B cell surface, resulting in a repertoire that can bind many foreign antigens, but which has had self-reactive B cells removed. Later antigen-dependent development processes adjust the antigen affinity of the receptor by somatic hypermutation. The effector mechanism of the antibody is also adjusted, by switching the class of the antibody from IgM to one of seven other classes depending on the required function. There are many places in B cell/immunoglobulin development where positive and negative selection forces can act to shape the immunoglobulin repertoire. In studying normal repertoires in people of different ages we have indications that immune senescence is characterised by a loss of selection, thereby altering the balance between exogenous antigen-specific versus potentially autoantigen-specific sequences. Our studies have also highlighted several questions about the immune system.

### Questions

1. How can we use studies of repertoire identify an immunoglobulin that is of importance in vaccine/infection/anti-tumour/autoreactive response.
2. How promiscuous are antibodies and how does this affect the balance between positive/negative selection events?
3. What are the functions of the different classes of antibody in a response and how do they interact with each other in the system?

### Reading

Dunn-Walters DK. [The ageing human B cell repertoire: A failure of selection?](https://doi.org/10.1111/cei.12700) Clin Exp Immunol. 2016 Jan;183(1):50-6. doi: 10.1111/cei.12700. <http://onlinelibrary.wiley.com/doi/10.1111/cei.12700/abstract;jsessionid=AB36F0C240017168E6B3698859788D84.f01t03>

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Christian Margreitter, Hui-Chun Lu, Catherine Townsend, Alexander Stewart, Deborah Dunn-Walters and Franca Fraternali, BRepertoire®: A user-friendly webserver for analysing antibody repertoire data <http://mabra.biomed.kcl.ac.uk/BRepertoire/> Nucleic Acids Res. 2018 Jul 2;46(W1):W264-W270. doi: 10.1093/nar/gky276.