Effect of pre-existing memory B cells and antibodies on memory responses and reshaping immunodominance patterns to influenza A virus.

L. Reusch[1], N. R. Mathew[1], H. Axelsson[1], A. Emmanouilidi[1], D. F. Besavilla[1], K. Schön[1], D. Angeletti[1]

[1]Gothenburg University, Department of Microbiology and Immunology, laura.reusch@gu.se

Abstract

Influenza A virus is still a constant threat to public health with an estimated 290 000 to 650 000 deaths yearly (World Health Organization, 2018). Currently, seasonal vaccines target the immunodominant head of hemagglutinin (HA) but fail to induce long-term cross-reactive responses. How the epitope specificity of pre-existing memory B cells, polyclonal antibodies (Abs) and CD4 memory T cells can affect B cell differentiation, secondary GC formation as well as epitope targeting is not fully decoded yet.

In this work, we have taken advantage of B cells and Abs specific for the five canonical antigenic sites on the influenza A HA head domain to dissect B cell immunodominance of secondary responses. Using a virus panel with each mutant expressing only one antigenic site of HA, we explored secondary immune responses to drifted viruses in the presence of a defined amount of B cells and Abs. Adoptive transfers of antigenic site-specific polyclonal antibodies were accompanied by cell proliferation labelling to differentiate primary and secondary immune responses.

Our preliminary results validate previous observations regarding B cell immunodominance to antigenic sites on the HA head domain and show how recall of memory B cells during secondary challenges is influenced by a drifted antigen. Further, epitope-specific polyclonal Abs can redirect B cell fate decision, affect the recruitment of naive B cells, impact epitope targeting and skew immunodominance. Our data lay the foundation to further dissect the phenomenon of B cell immunodominance and inform how to focus immunity on the most protective targets. Which in turn could lie the basic knowledge to develop a universal vaccine against influenza A virus lasting several seasons.