

Glycan engineering of the SARS-CoV-2 receptor-binding domain elicits cross-neutralizing antibodies for SARS-related viruses

Broadly protective vaccines against SARS-related coronaviruses that may cause future outbreaks are urgently needed. The SARS-CoV-2 spike receptor-binding domain (RBD) is comprised of two regions, the core-RBD and the receptor binding motif (RBM); the former is structurally conserved between SARS-CoV-2 and SARS-CoV. In order to elicit humoral responses to the more conserved core-RBD, the research group of Ryo Shinnakasu, Tomohiro Kurosaki (Lymphocyte Differentiation, IFRc), and Shuhei Sakakibara (Immune Regulation, IFRc) introduced N-linked glycans onto RBM surfaces of the SARS-CoV-2 RBD and used them as immunogens in a mouse model. The group found that glycan addition elicited higher proportions of the core-RBD-specific germinal center (GC) B cells and antibody responses, thereby manifesting significant neutralizing activity for SARS-CoV, SARS-CoV-2, and the bat WIV1-CoV. These results have implications for the design of SARS-like virus vaccines.

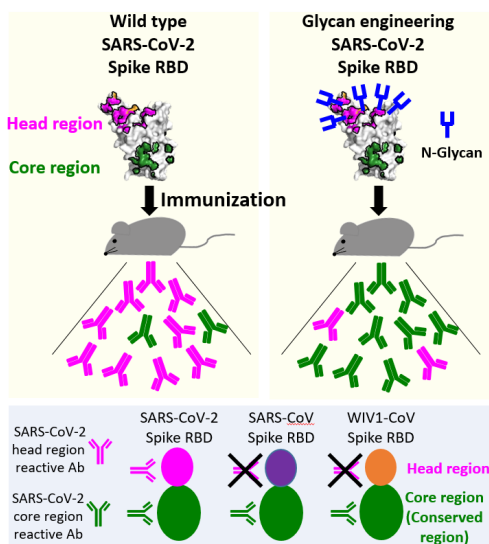


Figure: In order to induce the antibodies predominantly against the regions that are structurally conserved in RBD among SARS-related viruses, glycan engineering was performed to mask the dominant epitope on the RBD head region which is a structurally non-conserved region. When mice are immunized with this modified RBD vaccine, as expected, antibodies that recognize the core-RBD region of not only SARS-CoV-2 but also other SARS-related viruses such as SARS-CoV or WIV1-CoV are predominantly induced. Furthermore, these induced antibodies showed a high protective effect against various SARS-related viruses.

Journal: *Journal of Experimental Medicine (JEM)* October 8, 2021 online

Title: "Glycan engineering of the SARS-CoV-2 receptor-binding domain elicits cross-neutralizing antibodies for SARS-related viruses"

Authors: Ryo Shinnakasu#, Shuhei Sakakibara#, Hiromi Yamamoto, Po-hung Wang, Saya Moriyama, Nicolas Sax, ... Tomohiro Kurosaki* (#; contributed equally, *; corresponding)

<Message from Prof. Tomohiro Kurosaki>

We designed an immune antigen targeting the core region of the spike protein RBD (Receptor Binding Domain), which is structurally conserved among SARS-related viruses. We immunized mice with this antigen, and succeeded in efficiently inducing neutralizing antibodies with broad efficacy. We hope these results will lead to the development of the next-generation vaccines.