

PhD project of Nathascia Ruggeri (Bio2Brain project)

Long version

Title: *Exploring Fc Receptor-Mediated Transport of Immunoglobulin G (IgG) Across the Olfactory Epithelium*

Antibodies, particularly Immunoglobulin G (IgG), play a crucial role in the immune response and have been employed in the treatment of complex conditions like cancer and central nervous system disorders. Despite their therapeutic potential, challenges remain in delivering these antibodies effectively to target tissues, such as the brain.

Nose-to-brain drug delivery has emerged as a promising strategy, utilizing the olfactory epithelium as a direct pathway to the central nervous system. However, accessing the human olfactory epithelium presents significant challenges. In this study, pigs were chosen as models due to their anatomical and physiological similarities to humans. Their use also aligns with ethical considerations, as it reduces the need for additional animal experiments by utilizing pigs from slaughterhouses.

My research employed both *in vitro* and *ex vivo* models to investigate how IgG is transported across the olfactory epithelium via neonatal Fc receptors (FcRn) and Fc gamma receptors (FcγRs). I explored the differential roles of FcγRI, a high-affinity IgG receptor, and analyzed the impact of genetic variations in FcγRs that affect IgG binding, focusing on the hinge and CH2 regions of the Fc domain.

To further understand the uptake, distribution, and elimination of IgG in airway mucosa, Fc-engineered IgG variants with reduced or enhanced Fc receptors binding were employed. These variants exhibited distinct binding properties to Fc receptors, providing insight into the mechanisms underlying FcRn- and FcγR-mediated transport.

This project contributes to the growing field of Nose-to-brain delivery, enhancing our understanding of antibody transport mechanisms and paving the way for more effective therapeutic strategies targeting neurological diseases.

Short version

Title: *Investigating IgG Transport Across the Olfactory Epithelium*

Immunoglobulin G (IgG) is crucial in treating diseases like cancer and neurological disorders. Nose-to-brain (N2B) drug delivery via the olfactory epithelium offers a direct pathway to the brain but is challenging to study in humans.

This project used pigs as models due to their similarity to humans and ethical benefits. Both in vitro and ex vivo models were employed to explore how Fc receptors (FcRn and FcγRs) mediate IgG transport. Five engineered IgG variants were tested to uncover the roles of receptor binding in uptake, distribution, and elimination, advancing our understanding of N2B delivery mechanisms.

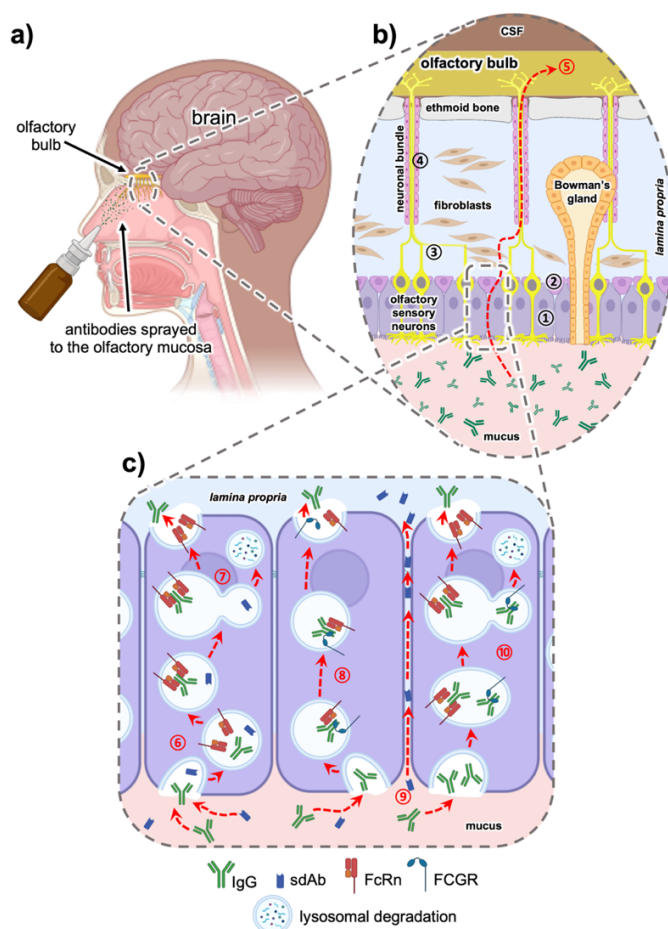


Figure from <https://doi.org/10.3390/antib10040047>

