



Edzard Spillner
e.spillner@eng.au.dk
Gustav Wieds Vej 10, 3141-2.36



Group:
Anne-Sofie Ravn Ballegaard
Josephine Bauvrig Aagaard
Bjarke Krogstrup Jensen
Michaela Mieke
Jonas Karlsen
Pernille Ommen Andersen
Nanna Breum Nielsen

Visit us at www.bce.au.dk/en/research/biological-and-chemical-engineering/medical-biotechnology/immunological-biotechnology/

General research topics

The research of the 'Immunological Biotechnology' group aims at understanding disease processes and the development and optimisation of therapeutic and diagnostic concepts. Within this field, we address questions from basic immunology to patient tailored precision medical treatment.

A central application area of our research is within immune-mediated diseases including allergic and chronic diseases. With increasing prevalence allergies affect one third of the global population, asthma 300 mio people worldwide, the complexity of the allergenic matrix and the individual patient reactivity profile complicate reliable diagnosis and treatment.

For severe conditions such as anaphylaxis to food and venom, many questions and complex immunological mechanisms underlying the disease remain open.

Techniques used

We apply a broad spectrum of protein technologies. Thereby we develop, recombinantly produce and analyse proteins and their interactions with targets, receptors and other ligands. An important pillar is the use of tailored expression systems for establishment of precisely defined molecules. Obtained molecules are characterised for their immunological, functional and structural features using biophysical methods as well as in vitro and cellular assays.

Projects

Our research group offers challenging and interdisciplinary research projects for students within **medical biotechnology**, describing, designing and exploring the potential of highly evolved proteins and other biomolecules for a future patient-tailored **precision medical treatment**. Several projects are done in close collaboration with pharma and diagnostic biotech industry.

Current project topics may include:

- Identification, production, characterisation, and technical implementation of biologically or clinically relevant proteins
- De novo generation of novel antibodies and other ligands by combinatorial approaches for diagnostics and treatment
- Immunotherapy and vaccination concepts
- Functional and structural analyses of relevant biomolecules and their interactions
- Targeting immunologically relevant key molecules and biomarkers of disease

For further and more detailed information please contact us.

Recent references

- Jensen et al. (2020) Structure of intact IgE and the mechanism of ligelizumab revealed by electron microscopy. *Allergy* 75, 1956
- Jabs et al. (2018) Trapping IgE in a closed conformation by mimicking CD23 binding prevents and disrupts FcεRI interaction. *Nat Commun* 9, 7
- Plum et al. (2023) Structural and functional analyses of antibodies specific for modified core N-glycans suggest a role in TH 2 responses. *Allergy* 78 121
- Aagaard et al. (2022) Nanobody-based human antibody formats act as IgE surrogate in hymenoptera venom allergy. *Allergy* 77 2859

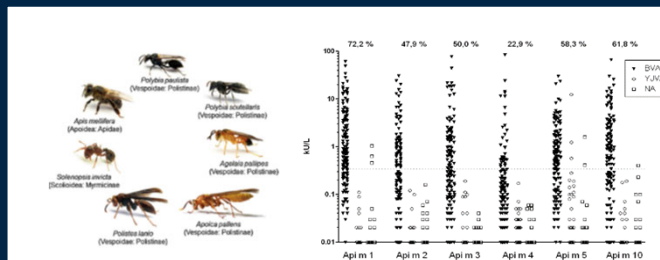


Figure 1: Component resolution in allergic diseases

Diagnosis and therapy of allergies to food, venom and pollen is highly complex and complicated by phylogenetic proximity. We aim for the identification of important allergens, subsequent recombinant production, assessment of clinical relevance and establishment of diagnostic and therapeutic solutions.

Left: Elicitors of allergic and anaphylactic reactions to insect stings. Right: Use of individual venom components for serological patient profiling. The data show the sensitization of a majority of patients against several of the venom components.

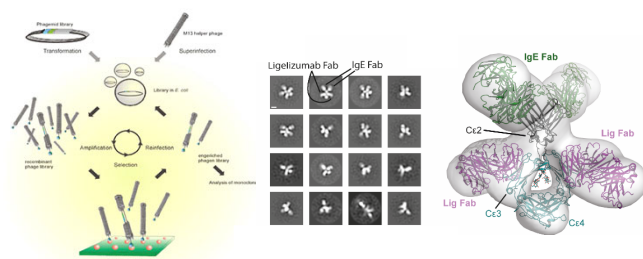


Figure 2: Antibody technologies and molecular interaction analysis

Left: Schematic overview of the selection process of an immune repertoire. Immune repertoire libraries can be established by cloning the entire repertoire into vectors that replicated in host cells. The specificity of the immune response and individual binders can be assessed by selection using approaches such as phage or yeast display.

Right: EM analysis and 3D reconstruction of a full size human antibody complexed by a therapeutic antibody fragment showing an extraordinarily rigid assembly.

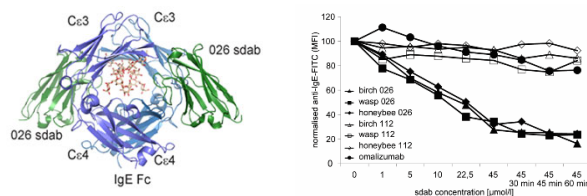


Figure 3: Therapeutic targeting by novel antibodies

Understanding principles of interaction and recognition offers a large potential for novel and optimised biologicals and targeting approaches.

Left: Structure of a complex of a single domain antibody with Fc domains of human IgE. The structure shows how 2 sdabs bind in the interface of the C3 and C4 domains of IgE resulting in conformational rearrangements and inactivation of allergic effector cells.

Right: Targeting of IgE on effector cells by the sdab results in efficient removal of IgE from the cellular surface compared to the controls and thereby inactivation of the allergic priming.