GRK 2046 – Current Openings

Project Title: Anti-Glycan Nanobodies for the Diagnosis and Treatment of Parasitic Infections

Research Group: Biomolecular Systems,
Glycan-Targeted Therapeutics Group
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Project Description:

In the1980`s it was discovered that the Camelidae family produce special IgG3 antibodies lacking the light chain. The antigen-binding sites in each of these unusual heavy chain antibodies (hcAbs) are formed only by a single domain (VHH or “Nanobody” (Nb)). Several structural characteristics make Nb`s different and superior compared to conventional antibodies.

Similar to any other recombinant proteins, Nb`s can be easily expressed in bacteria, yeasts, plants or human cells systems. Since Nb`s are small monomeric proteins, the molecular engineering tools to functionalize and modify multivalency, specificity and/or effector molecules, are already well-established. Nb`s are highly stable and soluble as they were shaped by evolution as a “stand alone” single chain binding unit, and in general can withstand harsh conditions.
Interestingly, Nb`s can be expressed as monomers, dimers or higher oligomers to form several binding entities simultaneously (“chain of beads”). Moreover, these “chains of Nbs” can have different specificities as part of a single multispecific chain. The multispecific chain is then able to simultaneously bind multiple antigens or different epitopes on a single antigen.

While hundreds of Nb`s target different proteins, none target glycans. The automated glycan assembly technology developed at the Max Planck Institute of Colloids and Interfaces, provides the basis to develop Nb`s that recognize glycans (“Glycobodies”).

The possibility to multimerize Nb`s is particularly suitable when targeting glycans, notoriously known molecules for their dense and heterogeneous cell membrane dispersion.

Targeting Glycosyl-inositol-phosphotidyl(GPI) Molecules on Parasitic Infections with Nanobodies

Malaria is a devastating parasitic disease that threatens 40% of the world’s population and claims more than 600.000 lives each year. The cell surface of *P. falciparum* expresses abundant amounts of GPIs, in both the protein-linked and protein-free forms. GPI constitutes more than 95% of the total carbohydrate modification of *P. falciparum* parasite and reflects the virtual absence of N- and O-linked glycosylation in these parasites.
Synthetic *P. falciparum* GPI of different length were used to determine the minimal epitope required to raise an immune response in mice that resulted in the protection from malaria.

Nb`s against the cell-surface GPI glycans have been produced as a means to study the role of glycans during infection and for passive vaccination to protect from malaria and other Apicomplexan parasites diseases.