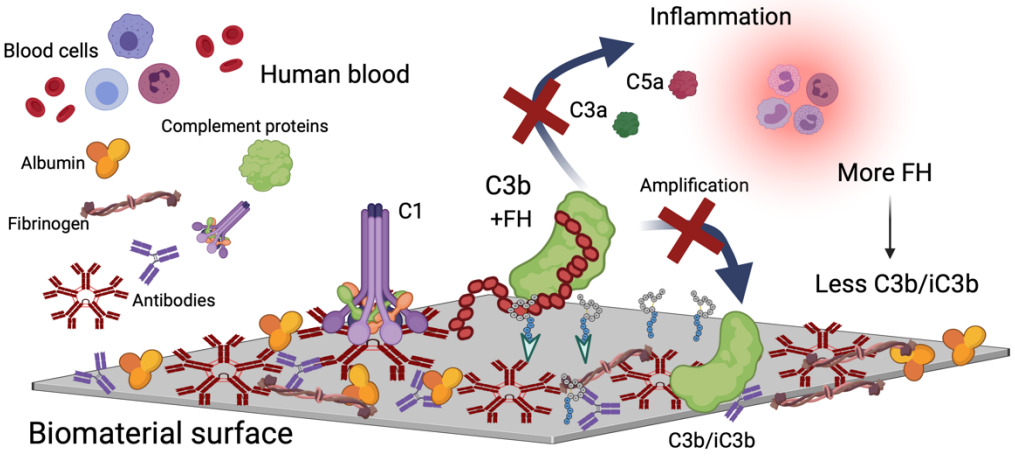
Protection of transplants and biomaterials from immune attack. Development of model systems and therapeutic strategies

Supervisor: Dr. Ekaterina Umnyakova

Project description.
Under normal circumstances, the host defence functions of the human complement system help protecting our bodies from microbial threats and accumulating debris. However, the unique ability of complement to swiftly recognise foreign surfaces may suddenly turn into a burden when we are exposed to biomaterials, drug delivery vehicles (e.g. lipid nanoparticles), and cell, tissue or solid organ transplants. Prevention of complement activation directly on such non-self surfaces via protective coating is therefore considered a promising strategy for avoiding inflammatory complications.



This project aims to design small complement-modulatory entities as a platform technology to be employed either as a surface coating or as a “molecular bridge” that guides physiological complement regulators to tissue, cell or material surfaces facing adverse activation of host defence pathways. The central element of our efforts is the cyclic peptide 5C6, which binds to the major complement regulator in circulation (i.e., Factor H; FH) and recruits it to 5C6-coated surfaces. Using a number of cell-based and biomaterial-based assays we showed that this peptide was not able not only to recruit FH to coated surfaces but also decrease the level of complement activation.

The aims of the project at this stage are identifying promising coupling/targeting entities by focusing on three model systems: 1) liposomal formulations used as drug delivery vehicle; 2) different cells that are relevant to transplantation/xenotransplantation and immunotherapies; and 3) biomaterials used for filters, implants, that are a frequent target of intensive complement attack.
Coupling/targeting moieties will be evaluated for their selectivity and suitability to be linked to 5C6.
These targeted, FH-binding peptides are expected to provide attractive options for therapeutic modulation of complement activity on cells and surfaces with broad applicability of this versatile platform technology in transplantation medicine, inflammatory conditions and beyond.

Further information can be provided upon request.

Literature:

1. Wu, Y. Q. et al. Protection of nonself surfaces from complement attack by factor H-binding peptides: implications for therapeutic medicine. _J. Immunol._ **186**, 4269–4277 (2011).
2. Nilsson, P.H. et al. Autoregulation of thromboinflammation on biomaterial surfaces by a multicomponent therapeutic coating. Biomater. 34, 985-994 (2013)
3. Bechtler, C. et al. Complement-regulatory biomaterial coatings: activity and selectivity profile of the factor H-binding peptide 5C6. _Acta Biomater._ **155**, 123–138 (2023)