Evaluation of ADAPTs against cancer targets for therapeutic applications

Project type
Master thesis project

Duration
Spring term 2024

Location
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Contact
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Project description
Antibodies have proven great success in modern oncology due to their specific targeting of cancer-associated proteins, as a mean of directing the treatment to cancer cells and spearing healthy tissues. However, the large size of antibodies presents challenges like limited tissue penetration and expensive production. As a response to this, small alternative scaffold proteins have arisen. Our research group has developed such a scaffold called ADAPT, a small triple helical bundle protein derived from an albumin binding domain of streptococcal protein G. By introducing a novel binding surface on the ADAPT scaffold, these small proteins have been engineered to bind novel target proteins involved in human diseases, like cancer and autoimmune disorders. The protein domain's inherent binding to albumin, the most abundant protein in blood, can either be harnessed or silenced, giving ADAPT dual purposes. As therapeutics, the albumin binding offers an extended half-life necessary for high delivery and efficacy at the disease site. On the contrary, abolishing of the albumin interaction leads to fast blood clearance after tumor accumulation, which can be utilized in diagnostics for high contrast tumor visualization.

This project involves characterization of ADAPTs that bind to human disease targets. This involves protein production and purification of ADAPTs, followed by investigation of the binding strength to the target protein, and evaluation of important biophysical properties like thermostability and aggregation propensity. The albumin binding will be evaluated and modified depending on the appropriate application. The function of the ADAPTs will be further evaluated in *in vitro* cell assays. Depending on the outcome, optimization and protein engineering of the ADAPTs may be employed to improve properties that are important for biopharmaceutical use.