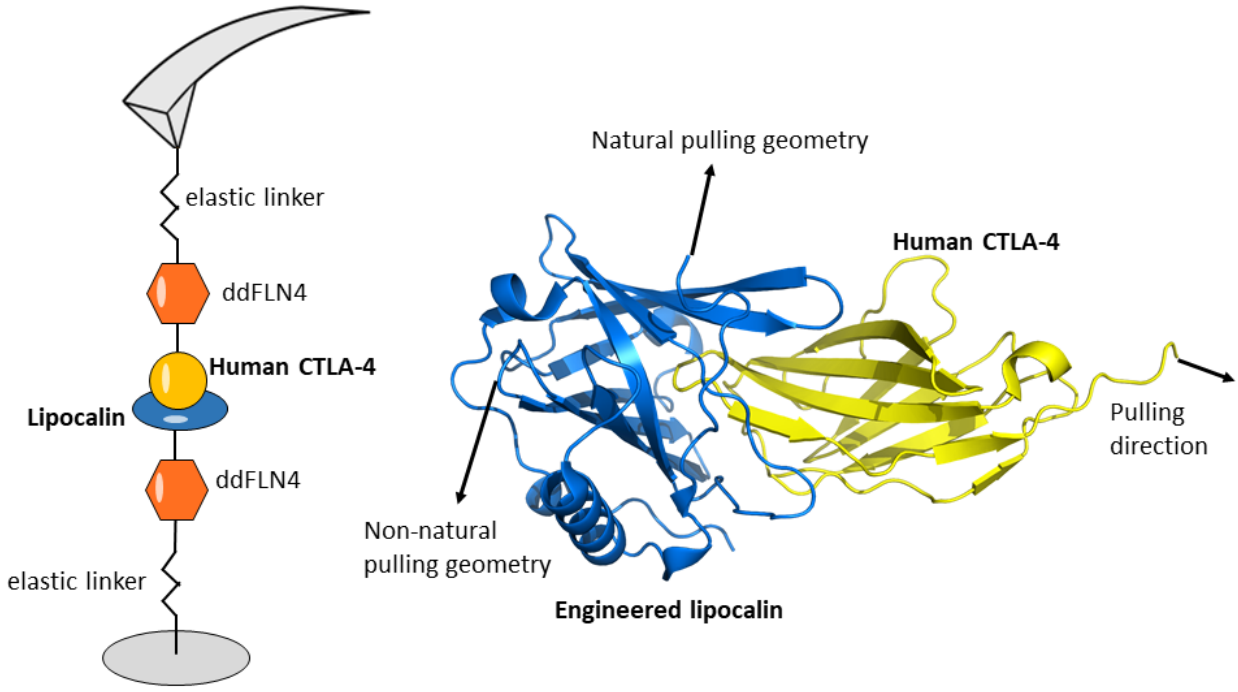
Master Thesis Project in Biomolecular Engineering:

AFM study of protein mechanics under non-natural pulling geometry

The mechanical stability of protein complexes is important in many biological and biomedical processes including cell-cell adhesion, bacterial pathogenesis and targeted drug delivery. Atomic force microscopy (AFM) enables us to apply force on a single protein complex and precisely measure the rupture force of the complex, which is a method known as single-molecule force spectroscopy (AFM-SMFS). In most of the AFM-SMFS measurements, the force is applied to the protein molecules through their N or C terminus (natural pulling geometry). Although previous research has demonstrated that the pulling geometry has a significant influence on the mechanical properties of proteins, a systematic study on the force response of protein complexes under non-natural pulling geometry (i.e. the force is applied to the complex through other positions except the N or C terminus) is still missing.

The aim of this project is to find out the most mechanostable pulling geometry of an engineered lipocalin which acts as an antibody against a tumor-associated receptor, cytotoxic T lymphocyte antigen-4 (CTLA-4). The results will deepen our knowledge of the mechanical properties of proteins and help us optimize the design of drug delivery nanoparticles. In this master thesis project, you will incorporate a non-natural amino acid into a preselected position on the lipocalin and use AFM to measure the rupture force between the lipocalin and CTLA-4 under non-natural pulling geometry, which is enabled by the incorporated non-canonical amino acid. Various biochemical and biophysical experimental methods as well as programming and data analysis skills will be taught and deepened.



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