Master Thesis Projects

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Project I: Deimmunising a protein

Therapeutic proteins have the advantage of high selectivity but are challenged with the risk of inducing an immune reaction in patients. Immunogenic proteins can induce the production of anti-drug-antibodies, resulting in altered pharmacokinetics, reduced efficacy and potentially severe anaphylactic or hypersensitivity reactions in patients. Deimmunisation of a protein may be achieved by deletion of T cell epitopes through site-directed mutagenesis. In this project, the student gets the possibility to deimmunize a small protein inhibitor and assess its inhibition capacity.

Methods

The student can learn the following methods which involve molecular biology as well as bioinformatical tools (optional):

- Protein expression in E.coli
- Protein purification: His-tag affinity purification
- Site-directed mutagenesis / PCR
- Biophysical assays
- Enzymatic assays
- SDS-PAGE / Western blot
- R / Python: In silico immunogenicity prediction (optional)
- Neural-network based T cell epitope prediction tool (optional)
- Structural Biology, PyMol: Protein Stability, Protein-Protein interactions (optional)

Project II: Post-translational protein modifications: Tyrosine sulfation

Posttranslational modifications (PMTs) of proteins can have multiple biological effects one of which could be improved protein-protein interaction. It could be shown that sulfated tyrosines improve the binding of our protein of interest with a serine protease of the complement system. Since PMTs only occur in eukaryotic cells, proteins expressed in a prokaryotic system lack those properties. We would like to express a soluble globular protein in E.coli and co-express mammalian Sulfosyltransferasen to modify tyrosines in a prokaryotic system. The student has to chance to investigate this PTM on biophysical as well molecular biological tools.

Methods

The student has the possibility to learn the following methods:

- Bacteria transformation
- Protein expression in E.coli
- Protein purification: His-tag affinity purification
- Biophysical assays
- Enzymatic assays
- SDS-PAGE / Western blot (anti-PTM antibody)
- Structural Biology, PyMol: Protein Stability, Protein-Protein interactions (optional)

Project III: Protein expression of a leech-derived protein (high risk project)

Bioinformatical sequence analysis revealed that gene products from a recently sequenced leech might inhibit multiple serine proteases. The student gets the possibility to recombinantly express for the first time a protein in E.coli, purify and assess the function and biophysical properties.

Methods

The student has the possibility to learn the following methods:

- Protein expression in E.coli
- Protein purification: His-tag affinity purification
- Biophysical assays
- Enzymatic assays
- SDS-PAGE / Western blot
- Structural Biology, PyMol: Protein Stability, Protein-Protein interactions (optional)