

Master thesis proposal

Selection of a calcium-dependent IgG1 binder

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Background

Many new therapies for difficult diseases are based on monoclonal antibodies where the majority are of the IgG1 subclass. The standard purification method in large scale production of antibodies is Protein A chromatography. Protein A binds specifically to IgG from many species and provides a convenient way to purify and concentrate IgG from a complex cell culture supernatant. The antibody binds strongly to Protein A and after washing the antibody is eluted by lowering the pH. This acidic treatment can be detrimental to some antibodies, why purification methods that allows for milder elution are of great interest. We have previously engineered a variant of Protein A (Z_{Ca}) to bind IgG in a calcium-dependent manner. The antibody binds to Z_{Ca} when calcium is present, and releases when calcium is removed. However, for IgG1 the reaction also needs a slight lowering of the pH, why there is room for improvement of the molecule.

Project

We would like to select for an IgG1 binding version of Z_{Ca} that can release the antibody upon calcium depletion at neutral pH. The project would consist of selections against IgG1 using a previously prepared phage display library to find binders that can elute IgG1 in a calcium-dependent manner at pH 7. After the selection, potential binders will be characterized using different laboratory methods such as ELISA, CD, SPR, and sequencing. If successful, the new molecule could be a radical improvement for Protein A-based IgG1 purification.

