
Group	:	Laboratory of Organic Chemistry / NanoChemical Biology group
Project	:	Development of bispecific antibodies
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Key-words: Bioconjugate chemistry, antibody modification, click chemistry, strain-promoted oxidation-controlled quinone-alkyne/alkene cycloaddition

Introduction: Bispecific antibodies (bsAbs) have received acceptance as a therapeutic because of their ability to target two different antigens. Due to its dual specificity, it can aid in redirecting T-cells to tumor cells, blocking two different signaling pathways simultaneously and delivering payloads to target sites. Most of the bsAbs are developed for cancer therapy, although they are also being developed as delivery vehicles and to block two signaling pathways simultaneously. Catumaxomab and blinatumomab are two US FDA approved bispecific antibodies while currently more than 85 bsAbs are in clinical development. We are developing bispecific antibodies from native antibody via chemoenzymatic approaches. We use mushroom tyrosinase to oxidize exposed tyrosine residues on the antibody and subsequently perform a strain-promoted oxidation-controlled quinone-alkyne cycloaddition (SPOCQ) with a pyridazinedione bearing a Fab and bicyclo[6.1.0]nonyne (BCN).

Goal: To prepare protein-antibody conjugates in order to generate develop bispecific antibodies without recombinant technology in a chemoenzymatic manner. The project involves the synthesis of functionalized handles like TCO-BCN bifunctional probes and MeTz-functionalized Fabs apart from deglycosylation of antibody and subsequent SPOCQ with strained alkynes.

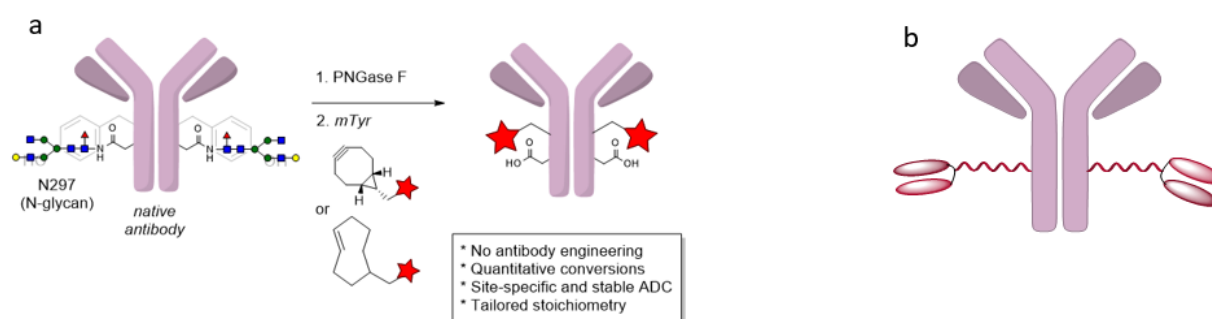


Figure 1: a) Deglycosylation of antibody followed by SPOCQ b) Bispecific antibody

Topics to be studied

Focus in the research project is on the:

- Synthesis of suitable bivalent probes that enable the crosslinking of the antibody with suitably functionalized proteins (*e.g.* with a MeTz handle).
- Development of a bispecific antibody from native antibodies using chemoenzymatic approaches.

Techniques to be used

Organic synthesis, analytical and preparative HPLC, LC-HRMS, NMR (^1H , ^{13}C , 2D NMR techniques), SDS-PAGE.

Information

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