The power of chemoselectivity: Functional protein-conjugates for extra- and intracellular targeting

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Our lab aims to identify new bioorthogonal reactions for the synthesis and modification of functional peptides and proteins. We apply these highly selective organic reactions[1] to study functional consequences of naturally occurring posttranslational protein modifications (PTMs), in particular phosphorylated Lys- and Cystein-peptides,[2] as well as to generate novel peptide- and protein-conjugates for pharmaceutical and medicinal applications.

In this presentation I will focus on the **chemical modification of functional proteins** as well as their **cellular delivery**. Thereby, we employ cyclic cell penetrating peptides (cCPPs) to transport a functional full length protein to the cytosol of living cells as recently demonstrated by the direct delivery of GFP-conjugates.[3] For protein modification we use a combined approach of intein expression as well as recently developed bioorthogonal reactions and enzymatic ligations, for instance the so-called Tub-tag labeling.[4] This concept is finally applied to generate new **antibody-drug conjugates, multivalent protein-scaffolds** as well as **cell-permeable nanobodies**, i.e. small antigen binding proteins that remain active within the reductive milieu inside living cells, to interfere with intracellular targets.[5]

References

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