Title: The Power of Chemoselectivity: Functional Protein-Conjugates for Proteomic and Pharmaceutical Research

Abstract:
Our lab constantly aims to identify new bioorthogonal reactions for the synthesis and modification of functional peptides and proteins. We apply these highly selective organic reactions to study functional consequences of naturally occurring posttranslational protein modifications (PTMs), in particular phosphorylated Lys- and Cystein-peptides, 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. For protein modification we use a combined approach of intein expression as well as recently developed bioorthogonal reactions and enzymatic ligation, for instance the so-called Tub-tag labeling. This concept is finally applied to generate new antibody-drug conjugates 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.

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