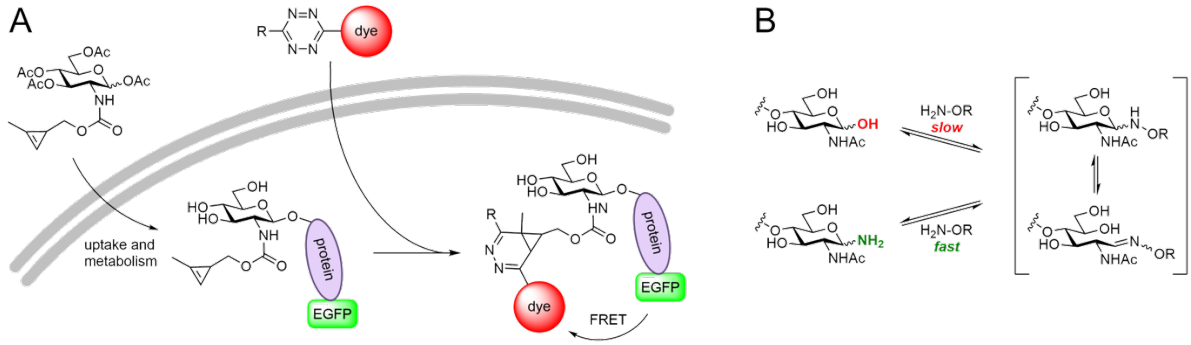
Chemoselective ligation reactions in the glycosciences

Valentin WITTMANN [1]

[1] Department of Chemistry, University of Konstanz, 78457 Konstanz, Germany

valentin.wittmann@uni-konstanz.de

Carbohydrates are involved in a myriad of cellular functions. In the form of glycoconjugates, they modulate activity and properties of proteins and lipids, and they are themselves involved in molecular recognitions processes. To study the biological roles of carbohydrates, chemoselective ligation reactions are of increasing interest for the tracing of carbohydrates in living cells and organisms, the synthesis of glycoconjugates, and the labeling and immobilization of unprotected (reducing) carbohydrates. This lecture gives an overview of our group's activities in these fields. The inverse-electron-demand Diels-Alder (IEDDA) reaction was employed in metabolic glycoengineering [1] to visualize dienophile-labeled glycoconjugates in living cells [2] and the extracellular matrix [3] and in combination with copper-free click chemistry and the photoclick reaction to achieve a triple-orthogonal labeling of glycans. For the convergent synthesis of complex N-glycopeptides, we developed a method for the introduction of thiocarboxylic acids into peptides that subsequently can be ligated with glycosyl amines [4]. During these investigations, we discovered a novel side reaction that can lead to an efficient and site-selective peptide cleavage using thioacids (CUT). The oxime formation of reducing carbohydrates is an important ligation method for the attachment of fluorescent probes and the preparation of glycoconjugates. We found that this ligation is significantly accelerated (up to 500-fold) without the need for a catalyst, such as aniline, when starting with glycosyl amines [5].



A) Metabolic glycoengineering in living cells with the IEDDA reaction. B) Rapid glycoconjugation with glycosyl amines.

Bibliographic references:

[1] M. Kufleitner, L. M. Haiber, V. Wittmann (2023), Chem. Soc. Rev. (52) 510-535.
[2] J. E. G. A. Dold, V. Wittmann (2021), ChemBioChem (22) 1243-1251.
[3] S. Nellinger, M. A. Rapp, A. Southan, V. Wittmann, P. J. Kluger (2022), ChemBioChem (23) e202100266.
[4] M. J. Schöwe, O. Keiper, C. Unverzagt, V. Wittmann (2019), Chem. Eur. J. (25) 15759-15764.
[5] M. A. Rapp, O. R. Baudendistel, U. E. Steiner, V. Wittmann (2021), Chem. Sci. (12) 14901-14906.