EXPLORING PROTEIN GLYCOSYLATION *VIA* CHEMICAL TAGGING OF METHIONINES

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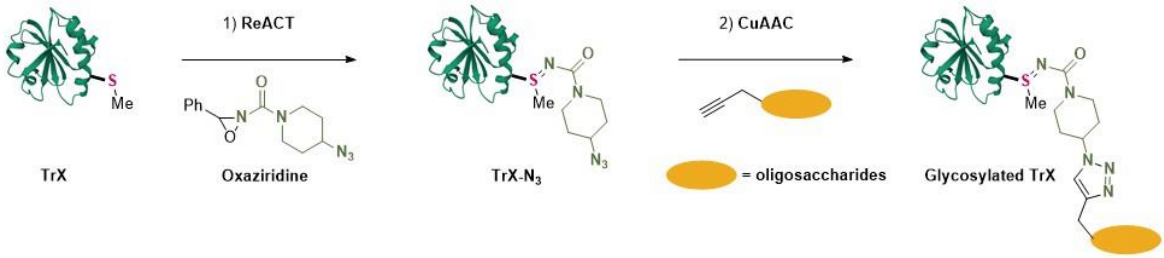
Glycosylation is a major post-translational modification of proteins that significantly influences their folding, distribution, stability and activity [1]. Despite significant advancements in protein expression systems, mixtures of glycoforms are often produced and glycosylation profiles are specific to each host organism. Controlling protein glycosylation is thus a major challenge, particularly when therapeutic proteins are targeted. Chemical conjugation is an interesting alternative method to this purpose. Redox Activated Chemical Tagging (ReACT) has recently emerged as an efficient bioconjugation method for protein modification. This click reaction consists of the addition of methionine sulfur atom to an electrophilic oxaziridine leading to a sulfimide adduct [2]. In the present work, we combine ReACT and CuAAC click reactions in a one pot sequence as a general strategy to access glycosylated proteins. As a proof of concept, the methodology was first applied to a pentapeptide derived from the sequence of thioredoxin, a model protein, before extending its application to the entire protein (Scheme 1). To go further, the impact of glycosylation on the activity and stability of a target enzyme was assessed.



Scheme 1. General strategy towards protein glycosylation based on one-pot sequential ReACT-CuAAC reactions

Acknowledgements: This work is supported by the French National Research Agency (ANR) through Labex ARCANE/CBH-EUR-GS (ANR-17-EURE-0003)

References:

1. Kightlinger *et al*. *ACS Synth. Biol.* **2020**, 9, 1534-1562.
2. Lin *et al*. *Science*, **2017**, *355*, 597–602.