SWEET SPARKS: REMODELLING OF CELL SURFACES WITH CARBOHYDRATES VIA CLICK ELECTROCHEMISTRY

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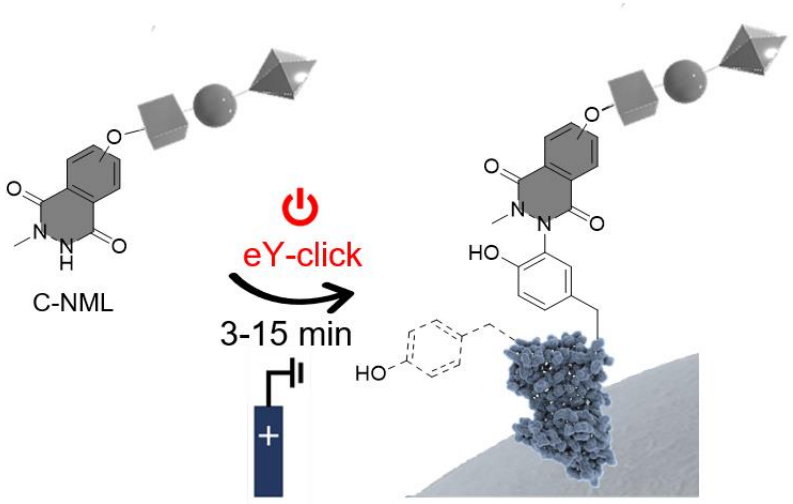
The chemo-selective modification of native proteins is crucial in chemical biology and for the development of therapeutic conjugates. Recently, we introduced eY-click, the first electrochemical method designed to functionalize tyrosine (Y) residues in proteins within biocompatible media [1]. Using a three-electrode system, this approach enables the selective oxidation (activation) of a functionalized diazodicarboxamide anchor in situ, allowing the labeling of peptides, enzymes, and antibodies in aqueous buffers.
In this study, we employed N-methylluminol (NML) [2], a highly selective Y-anchoring group upon one-electron oxidation [3], for the electro-bioconjugation of cell surfaces from viruses, living bacteria, and eukaryotic cells [4]. The click-electrochemistry method was successfully applied to therapeutic adeno-associated viruses (AAV2), *E. coli* (Gram-negative), S. epidermidis (Gram-positive), and eukaryotic cell lines. Within minutes, biologically relevant carbohydrates were grafted onto cell surfaces, providing a versatile alternative to metabolic engineering for vectorized biotherapies and the study of cell surface glycans.



References:
1. Alvarez-Dorta, D.; Thobie-Gautier, C.; Croyal, M.; Bouzelha, M.; Mével, M.; Deniaud, D.; Boujtita, M.; Gouin, S. G. *J. Am. Chem. Soc.* **2018**, *140* (49), 17120–17126.
2. Sato, S.; Nakane, K.; Nakamura, H. *Org. Biomol. Chem.* **2020**, 18, 3664-3668.
3. Depienne, S.; Alvarez-Dorta, D.; Croyal, M.; Temgoua, R. C. T.; Charlier, C.; Deniaud, D.; Mével, M.; Boujtita, M.; Gouin, S. G. *Chem. Sci.* **2021**, *12* (46), 15374–15381.
4. Depienne, S.; Bouzelha, M.; Courtois, E.; Pavageau, K.; Lalys, P.-A.; Marchand, M.; Alvarez-Dorta, D.; Nedellec, S.; Marín-Fernández, L.; Grandjean, C.; Boujtita, M.; Deniaud, D.; Mével, M.; Gouin, S. G. *Nat. Commun.* **2023**, *14* (1), 5122.