PROGRESS IN THE SYNTHESIS AND BIOLOGICAL INVESTIGATION OF NEO-PUFAS USING CLICK CHEMISTRY

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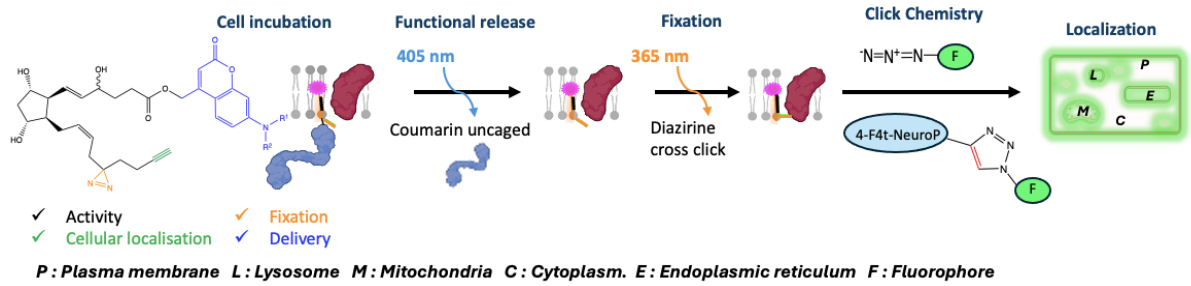

P : Plasma membrane L : Lysosome M : Mitochondria C : Cytoplasm. E : Endoplasmic reticulum F : Fluorophore

Oxidative stress plays a crucial role in various pathological conditions, making lipid oxidation products important mediators of cellular responses. 4(RS)-4-F_{4t}-NeuroProstane (4-F_{4t}-NeuroP), one of the major non-enzymatic oxidation products of DHA, has been recognised for its diverse beneficial biological properties. Our transdisciplinary research has identified its anti-arrhythmic properties[1] and potential anti-apoptotic activity[2]. Furthermore, 4-F_{4t}-NeuroP has been shown to possess anti-inflammatory effects in macrophages[3]. Despite these promising findings, the molecular mechanisms underlying these effects remain poorly understood. In this context, our research aims to explore the therapeutic potential of 4-F_{4t}-NeuroP by identifying its cellular targets through the use of bioorthogonal probes and click chemistry strategies, thereby shedding light on its mode of action.
Bioorthogonal clickable probes are now widely used in mechanistic studies of active molecules including lipids. In our case, this approach will allow the visualisation of intracellular localisation and profiling of the lipid-protein interactome of 4-F_{4t}-NeuroP. On one hand, advanced probes equipped with photo-crosslinking diazirines will enable proteomic analysis[4], and on the other hand, functionalized coumarins will allow organelle-specific delivery, providing insights into lipid-related signalling pathways at both cellular and subcellular levels[5].
In my presentation I will discuss the progress made in the synthesis of different fragments of multifunctionalized probes, including the diazirine containing clickable moieties and the coumarin organelle-specific tags. I will also highlight our innovative approach combining chemical synthesis and biological assays to decipher the therapeutic potential of 4-F_{4t}-NeuroP.

References:

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