

Click-redox anchoring of drugs onto nanocarriers and studies of their therapeutic and pharmacological properties under biological conditions

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Scientific context

Macromolecular vectors are revolutionizing therapeutic targeting by improving the efficacy, specificity, and safety of treatments, with major successes in oncology and infectious diseases.¹ The wide variety of nanovector architectures allows for tailoring the physicochemical properties, biodistribution, and drug release profile to the therapeutic application.

However, strategies for covalently anchoring drugs to these nanovectors remain far less diverse.² Coupling strategies rely on classical organic reactions where active ingredients are selected or modified to include functional groups (amines, alcohols, thiols, ketones, acids) necessary for the formation of amides, imines, esters, ethers, disulfide bridges, thioethers, or hydrazones. These largely unrevised conjugation strategies rely exclusively on N, O, and S heteroatoms as anchor points, risking a loss of pharmacological activity because these functions are often essential for the drug's interaction with its biological target. This dependence excludes many classes of active ingredients lacking usable heteroatoms or causes conjugation selectivity problems.

PhD objectives

Faced with these challenges, our interdisciplinary project aims to explore alternative click-redox strategies for conjugating therapeutic tools, to study their therapeutic properties as well as the stability of the biolabile bonds formed. These new anchoring methods will be more selective and exploit new functional groups present in numerous active compounds, thus broadening the range of compatible molecules. In parallel, the therapeutic and pharmacological properties of the drug-carrier conjugates will be studied and compared to conjugates obtained through conventional anchoring methods. These new biolabile bonds could pave the way for new, more specific biomechanisms of drug delivery.

Candidate profile

The candidate will have a master's degree related to innovative methodologies in drug design and active agents delivery, with skills in organic and medicinal chemistry and pharmacology.

¹ F. Kratz *et al.* *Angew. Chem. Int. Ed.* **2006**, *45*, [1198](#).

² G.K Such *et al.* *Chem. Rev.* **2024**, *124*, [5505](#)