CONTROLLED RELEASE OF MICELLE PAYLOAD VIA SEQUENTIAL ENZYMATIC AND BIOORTHOGONAL REACTIONS IN LIVING SYSTEMS

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Our group has extensively explored the chemistry of mesoionic compounds. In 2017, we described for the first time the reactivity between iminosydnones (ImSyd) and cycloalkynes. [1] This transformation, defined as a "click and release reaction", has the particularity to allow simultaneous formation of a new compound and release of a second one. Despite its novelty, the biological application of this reaction is limited due to low reaction speed. The main goal of my work is to increase the reaction rate of this click and release process and to explore its potential as a powerful tool for drug delivery. With this in mind, we designed an amphiphilic compound, containing an ImSyd moiety, which is able to self-assemble in water and form micelles. After exposing theses ImSyd-containing micelles to cycloalkynes, we observed a dramatic increase of the reaction kinetics due to the high local concentration of the cycloalkyne inside the nanostructures. When the click and release occurs, we observed the rapid cleavage of the nanoparticles, which can be used for the controllable release of dyes or drugs. We developed an *in vivo* approach for an "on demand" release of dyes by using the ImSyd micelles and a cyclooctyne designed to target the tumor. The first *in vivo* proof of concept gave us encouraging results for a potential drug release applications. [2]

[1] S. Bernard *et al. Angew. Chem. Int. Ed.* **2017**, *56*, 15612–15616.

[2] K. Porte *et al. Angew. Chem. Int. Ed.* Just accepted. DOI: 10.1002/anie.201902137.