Self-Immolative Molecular Capsules

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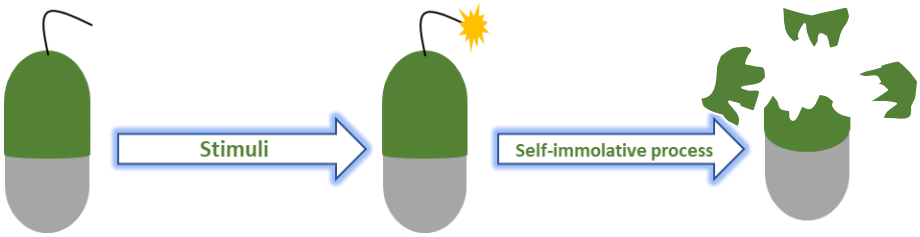
Traditional cancer chemotherapy lacks any intrinsic selectivity and it is very often accompanied by systemic toxicity to the patient. Therefore, drug targeting and controlled delivery in oncology is of particular interest in order to avoid unfavorable side effects and also to increase the dose achievable within the tumor. In this regard, drug delivery by carriers presents several advantages: a) drugs have not to be modified; b) drug is protected from the environment; c) carriers can be smartly designed to respond to stimulus.[1]

Several kinds of carriers have been used for this purpose, and yet molecular capsules have never been employed even when at first sight they might be considered optimal drug carriers. Indeed, they are systems composed by two or more molecules that are able to assemble into a hollow structure which can host other molecules inside the cavity.[2]One of the major problems is to find a way to disassemble the capsule in the right environment. Self-immolative moieties seem optimal for such a task, because they have been already used to break covalent compounds into pieces under the right stimulus.[3]

In this communication we report the design and development of novel self-immolative covalent molecular capsules that are dismantled in the presence of a specific chemical compound or enzyme.[4]These capsules are assembled using a methodology developed in our group based in the thiol-ene reaction,[5] which allows to obtain covalent capsules in high yields and short times of reaction. After such a proof of concept, modifications are underway towards a real drug carrier.



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