Smart functionalized nanogels as selective carriers for intracellular drug release

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Over the past years, the application of nanotechnology to the administration of therapeutic molecules has been a crucial investment in the treatment of human diseases. The importance of controlled intracellular delivery of drugs is two-fold: i) to augment the delivery efficiency of the active principles, avoiding under- and over-dosing, and ii) to precisely reach the biological target, limiting undesirable offtarget activities. Among the nanovectors, nanogels are promising tools to performcontrolled and sustained drug release. However, loading nanocarriers with hydrophilic drugs presents the main drawback of undesired rapid diffusion and reduced curative activity at the target site. To overcome this limitation, chemical or physical functionalization methods can be pursued. We propose the synthesis of nanogels for controlled intracellular drug release following two routes: the formation of chemical bonds between the drug and the nanogel through a thiolsensitive linker, and the generation of ionic interactions between the drug and the polymeric network. In the first case, the selectivity of drug delivery is due to the disulphide bond that can be disrupted intracellularly by glutathione or cysteines present in the cytosol; in the second case, the drug release is tuned by the electrostatic interactions between the nanogel and the drug in the biological environment. However, the in vivo application of these biomaterials is strictly linked to their capability to selectively interact with specific inflamed, damaged or malignant cells, avoiding the immune response and the undesired macrophage uptake. For this reason, we are working on nanogel coating, using sensitive peptide sequences or chemical groups, to promote the selective interaction with target cells. Fields of interest are the damaged central nervous systems, with a focus on the activation of microglia pro-inflammatory phenotype, and the Epidermal Growth Factor Receptor signalling in liver disease and cancer.