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Ultrashort Peptides-based Hydrogels Exposing Thiol Groups Forming Complexes with Peptide Nucleic Acid as Potential Tools for Smart Drug Release

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Ultrashort aromatic peptide-based multicomponent hydrogels (HGs) have been used as biocompatible matrix for tissue engineering, drug delivery, and biosensor production. One of the most explored hydrogelators is the low molecular-weight Fmoc-FF (N^{α}-fluorenylmethoxycarbonyl-diphenylalanine) homodimer because of its ability to gel under physiological conditions such as of pH and ionic strength.[1] Additional molecules, such as proteins, chemical compounds, or different peptide sequences, can be included into the Fmoc-FF hydrogel to create unique hydrogels with enhanced mechanical and functional characteristics. From this standpoint, a collection of unique multicomponent hydrogels based on Fmoc-FF that were doped with a range of concentrations of the tripeptide Fmoc-FFX, where X can be Cys, Ser, or Thr have been examined.[2] Among these tripeptides, Fmoc-FFC was chosen as it generates hydrogels functionalized with thiol groups, which can be post-derived chemically with desirable bioactive compounds, such as biosensing, therapeutic or diagnostic agents. One of the most valuable nucleic acid mimetics is Peptide Nucleic Acid (PNA).[3] Hybrid hydrogels are non-toxic and can serve as scaffolds for various applications in biotechnology, such as for controlled drug release in the presence of a reducing environment, such as the tumour microenvironment.[4] In this regard, the functionalization of mixed (Cys)HG at different molar ratios compared to Fmoc-FF (1/5, 1/10 and 1/20, respectively) with (Cys)PNA molecules *via* specific and non-specific interactions is shown here, followed by the supramolecular characterization through several techniques, such as HPLC, MS, CD, FT-IR, NMR and microscopy.

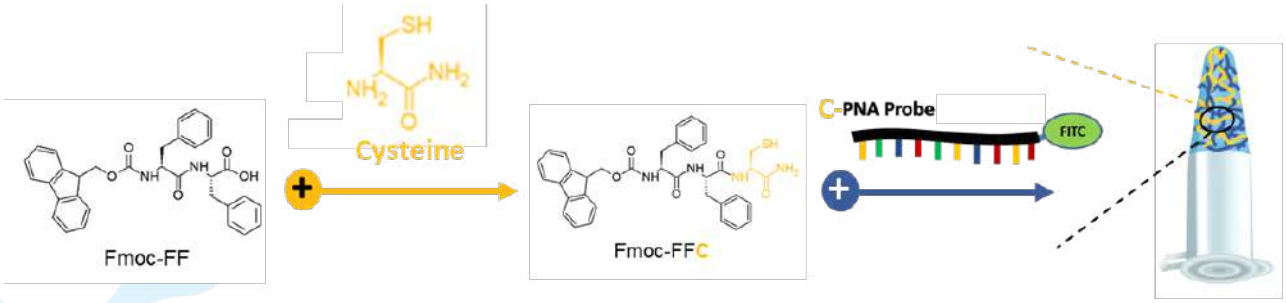

Figure 1: Schematic representation of Fmoc-FFC and C-PNA-FITC probe forming supramolecular hydrogels.