Development of supramolecular hydrogels from cyclodipeptide consisting of unnatural amino acids and tuning their property through co-assembly approach

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Cyclodipeptides (CDPs) exhibit a variety of biological activities and resistance to enzymatic hydrolysis[1] unlike their linear-dipeptide counterparts as well as self-assembling ability to form hydrogels[2]. The notable ability of CDPs to self-assemble would emerge from their structural rigidity and well-defined intermolecular hydrogen bonding patterns. Furthermore, the self-assembly of peptides containing unnatural α,α-disubstituted α-amino acids (α,αAAs) remains unexplored despite their potentials to provide chemical diversity and allow for the modulation of supramolecular structures[3].

In this study, we investigated the self-assembling propensity of three new CDPs (**cyclo-mFG**, **cyclo-mFL**, **cyclo-mFF**) consisting of α-methyl-L-phenylalanine (**mF**) as an α,αAA as shown in **Fig. 1**. We found that **cyclo-mFL** exhibit hydrogel formation ability. Moreover, we disclosed that co-assembly of **cyclo-mFL** with its non-methyl counterpart (**cyclo-FL**), which is also a hydrogelator[4], allows for the modulation of the rheological property of the resultant supramolecular hydrogels by varying the molar ratios (**cyclo-mFL**/**cyclo-FL**).

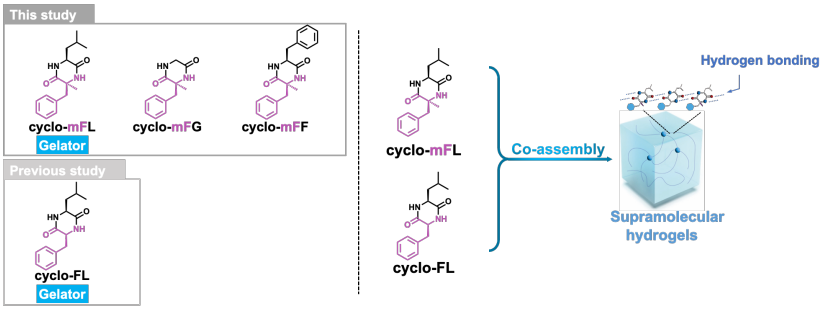

Fig. 1 Chemical structures of CDPs and schematic for the co-assembly behavior of **cyclo-mFL** and **cyclo-FL** to form hydrogels.

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