Although many modifications of peptide sequences have been utilized to tune their self-assembly, halogenation has rarely been pursued. The advantage of a strategy based on the introduction of halogen atoms on peptide motifs lies in the fact that halogenation is a minimal structural modification, which, on the other hand, may induce a large difference in the peptide supramolecular behavior as a consequence of the rich variety of noncovalent interactions given by halogen atoms [1].

In this presentation, it will be shown how halogenation strongly influences both solution and solid-state self-assembly behavior of amyloidogenic peptides. We have applied this new supramolecular concept to the augmented fibrillation of amyloidogenic peptides and proteins, such DFNKF [2], KLVFF, and hCT. Furthermore, halogenation facilitated obtaining high-quality single crystals of fibril-forming peptides. In particular, iodination of the widely studied amyloidogenic peptide sequence DFNKF facilitated crystallization and allowed for its high-resolution single crystal structure determination for the first time. The structure unveils the importance of aromatic-aromatic interactions in stabilizing the amyloid self-assembly (Figure) [3].

Implications of oxidative stress-induced halogenation of proteins are discussed in terms of biomarkers of diseases such as Parkinson and Alzheimer's. The obtainment of a novel unnatural amino acid functioning as strong halogen-bond donor may pave the way to totally new design principles in peptide-based supramolecular self-assembly.

Acknowledgement: P.M. gratefully acknowledges the European Research Council (ERC) for funding the project “Folding with Halogen Bonding” to PM (FoldHalo, www.foldhalo.eu; Grant agreement no. 307108).


Keywords: halogenation, peptide, self-assembly