Bacterial life based on fluorinated amino acids

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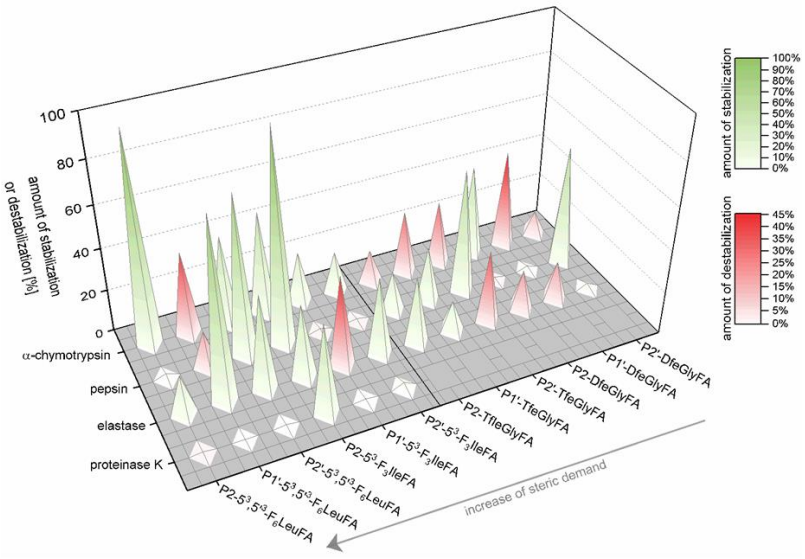
In a league of its own, fluorine has the potential to enable us to engineer biopolymers with highly desirable properties. However, the particular challenge in using it as a tool lies in our ability to juggle the interplay between the specific properties of the fluorinated building block and its responsiveness to the environment it is exposed to. Fluorine has been shown to impart often favorable but seldom predictable properties to peptides and proteins, a phenomenon that is caused by the nature of the fluorine atom and properties of the C-F bond.[1] These properties are crucial factors in peptide and protein engineering as they direct properties as important as proteolytic stability[2] (Figure) and folding,[3] and thus affect protein function.[4] This talk will present some of our recent advances in studying the impact of fluorinated amino acids on the interaction of peptides with proteins.



One of our current projects studies the way in which not just biomolecules in the laboratory, but whole living organisms accommodate fluorine. Fluorine incorporation into single proteins via related amino acid analogues has become common practice. Recently, we started studying whether fluorinated amino acids can generally be used to build up biomass and what would be the effect of long-term exposure of living cells to fluorinated metabolites. We constructed an experimental model based on bacterial adaptation in artificial fluorinated habitats. In particular, we propagated Escherichia coli (E. coli) in the presence of either 4- or 5-fluoroindole as essential precursors for the in situ synthesis of tryptophan analogues. We illustrate the in vivo synthesis of 4- and 5-fluorotryptophan from 4- and 5-fluoroindole via intracellular metabolic conversion and subsequent proteome-wide translation in response to more than 20000 UGG codons in E. coli. Genomic, proteomic and metabolomics analyses reveal that full adaptation requires astonishingly few genetic mutations but is accompanied by large rearrangements in regulatory networks, membrane integrity and quality control of protein folding and this talk will introduce our recent results.[5]

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