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Protein mimicry with peptidic foldamers, structure and function

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Solvent exposed flat regions are responsible for many of the known protein–protein and protein-membrane interaction interfaces.[1] It is challenging, however, to construct artificial protein mimetic sequences, which fold (foldamers) and are able to cover these relatively large flat surfaces with programmable anchor points.[2] Peptidic sequences with unnatural building blocks (e.g., β-amino acids) are known to form compact secondary structures, which can be controlled through the stereochemical pattern along the peptidic backbone.[3] It will be shown how this principle affords the *de novo* desing of foldameric secondary structures.
In the second part of the presentation, examples will be given for the application of these protein mimetic sequences. We have successfully synthesized multivalent helical foldamer-dendrimer conjugates that recognize and inhibit the neurotoxic properties of the oligomeric β-amyloid (Aβ).[4] These foldamer conjugates can functionally mimic the molecular recognition properties of the anti-Aβ monoclonal antibodies in an ELISA setup.
Water soluble β-sandwich mimetic foldamers can have sufficiently large and flat surface, but their stabilization in water is a great current challenge. Here we present the design, main structural features and biological effects of the foldameric analogs of anginex, a 33-mer antiangiogenic peptide with a tendency to form β-sandwich. The effects of the β-amino acid substitutions in this β-sheet structure will be discussed.[5]

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