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Protein surface recognition using aromatic oligoamide foldamers

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Since proteins are at the basis of many biological processes, they are widely studied as therapeutic targets. Aromatic oligoamide foldamers have a very well defined structure, predictable and stable both in solution and solid state. Because of their medium size, they appear as potent candidates for protein surface recognition thanks to their proteinogenic side chains. This manuscript presents the different steps of their design, from the scaffold's synthesis to obtaining a functionalized foldamer, thanks to solid phase synthesis. The strategy to investigate protein/foldamer interactions will be detailed. Its originality lies in the fact that the foldamer is anchored to the protein. Circular dichroism has been used as a screening method to detect foldamer/protein interactions. Structural analysis of the hits will allow the design of new foldamers with the objective of enhancing foldamer/protein interactions: it is an iterative strategy. This approach has been applied firstly to human carbonic anhydrase II (HCA). This protein is used as a model system and proof of concept before moving to more therapeutically relevant proteins; interleukin 4 and cyclophilin A. Finally, a study on introducing flexibility in quinoline foldamers is presented.

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