An α-helix is the most common type of secondary structure in proteins1,2. This structure is also quite compact, in contrast to other secondary structural elements such as the β-sheet or β-strand. Provided that the main interactions between two proteins are formed by residues fairly close to one another in threedimensional space – although not necessarily that close together in the primary sequence – drug-like molecules can be designed to mimic or interrupt these interactions.

It is well known that α-helix mimetics are biologically active in a number of therapeutically significant protein-protein interactions (PPIs). Notable examples include HDM2(HDM4)/p53 and the BCL-2 family of proteins. However, the range of potential applications of α-helix mimetics compounds in drug discovery extends beyond protein-protein interaction problems and includes G-Protein Coupled Receptors (GPCRs), ion channels and the rapidly emerging target class of solute carrier (SLC) proteins 3,4.

Using extensive computer modeling supported by in vitro experiments, ASINEX has designed and synthesized a number of novel structurally sophisticated scaffolds that are able to adopt α-helical conformations. The designed scaffolds can be divided in 2 classes: 1) backbone mimetics and 2) epitope mimetics:

One of the main problems in the design of α-helix mimics is maintaining a balance between lipophilicity and solubility; therefore we have experimentally measured the solubility of the resulting compounds in DMSO and PBS.

References: