Glycine Zipper Motif in the Association of Helices in a Designed Peptide

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The crystal structure of an apolar peptide Ace-Gly[1]-Ala[2]-ΔPhe[3]-Leu[4]-Gly[5]-ΔPhe[6]-Leu[7]-Gly[8]-ΔPhe[9]-Ala[10]-Gly[11]-NH2 is determined at 0.9Å resolution. The peptide was designed to mimic the interhelical interactions involving GxxxG like motifs seen in transmembrane helices. The peptide crystallizes as two conformers, one a right-handed and the other a left-handed 3_{10}-helix, displaying ambidextrous screw sense. It is interesting to note that despite the presence of L amino acids (Ala, Leu) in the sequence and more importantly bulky residues Leucine (Leu[4], Leu[7]) in the middle of the helix, one of the conformers is a left-handed helix. This is presumably to optimize helix - helix interactions, suggesting that global interactions can decide local conformation.

A remarkable feature is the occurrence of zipper like arrangement of main-chain to main-chain C^{α}-H···O hydrogen bonds consistently at three residue interval at Gly-Gly helix interface. The crystal structures of two other closely related peptides, where Gly at positions 5 and 8 have been replaced by Ala in one case and Val in the other have also been determined. Zipper like interaction motif involving Leucines is common to all the three peptide structures. A novel, aromatic side chain to main-chain C-H···O hydrogen bonded motif is observed in the last two peptides. The repertoire of weak interaction based motifs seen here, could be exploited for the de novo design of helical assemblies mimicking transmembrane helices.

Keywords: designed peptide, glycine zipper, transmembrane helix