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Phage Display Libraries of Stapled α -Helical Peptides for Cancer-related Proteins

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Protein interactions are the major biological components that play significant roles in biological events, for example, cell signaling, membrane transportation and cell metabolism. In addition, an α -helical peptide is often found at the interface of proteins. However, peptides do not always keep stable structure that conserve their originality under biological environments. Thus, it is important to develop the structure constrained peptide system and search for novel peptide ligands for cancer-related proteins.

In this study, a peptide phage library was designed with tailored randomization and chemically modified by cysteine-reactive hydrocarbon staple linkers to create the stapled α -helical peptide phage libraries. Several proteins were chosen as targets to demonstrate the ability of the stapled peptide phage libraries in the development of peptide binders against protein isomers (Galectin-3 and Galectin-1) and as protein-protein interaction (hDM2/p53 PPI) inhibitors. After affinity selections, the stapled peptide ligands binding to target proteins with high binding affinity and specificity were obtained.

Ultimately, the stapled α -helix peptide phage libraries could be an effective tool to discover the peptide ligands with high affinity and specificity binding properties.