Rational Design of a peptide aptamer targeting P53 tumor suppressor protein by Computational Methods

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Abstract: One of the greatest challenges in the medical science is cancer in fact cancer affect so many lives all around the world. Designing an effective drug to treat cancer is a big hope for researchers in this field .We decided to design a peptide aptamer with therapeutic effect by in silico methods. In the priority, we needed to select a target; Among all factors participating in tumor formation, P53 mutations are the most abundant. Although there are many chemical drugs that restore and stabilize native P53, peptide aptamers may be the most effective tool for this usage. Peptide aptamers are essentially a "loop on a frame" design, where the 5-20 residue peptide loop grafted onto a neutral scaffold is the source of variability for selecting high affinity binders to a target protein.[1] In the next step we should find best matching proteins to p53. Some of proteins which were reported in literatures that have had more interaction with p53, were chosen. Then we should determine their interaction zones, precisely due to find repetitive sequences or amino acids. Therefor every single protein was docked with p53 by means of protein-protein docking ClusPro server[2] . Interaction hot spots were detected and a library of them was organized. Among all data, the most frequent amino acids were chosen. During peptide design procedure, all nominated amino acids were arranged in the designed peptide sequences. In the following, achieved sequences were grafted into the Thioredoxin scaffold. Complexes of peptide aptamer-p53 were studied by Hex software [3] and top complexes were reported.

Keywords: Rational Design ; Peptide Aptamer ; P53 ; Computational

References

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