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Identification of new peptide ligands for epidermal growth factor receptor using phage display technology

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Background and Aims: The epidermal growth factor receptor (EGFR) is one of the most important growth factors that play critical roles in the regulation of cell proliferation, differentiation, and survival. The EGFR is overexpressed in a variety of human malignancies of epithelial origin. It has been a major target of molecular anticancer therapy. Although two important treatment strategies, monoclonal antibodies (mAb) and tyrosine kinase inhibitors (TKIs), have been developed to block EGFR activation, several reports of drug resistance necessitate identification of additional therapeutic agents for the treatment of human epithelial cancers. Phage display, a versatile technology has proved to be a powerful tool for isolating novel ligands for drug discovery. The aim of current investigation was to identify new, short oligo-peptide ligands capable of binding to EGFR using phage display method.
Methods: In this study, A-431 cells expressing EGFR were used as the matrix in a cell based subtractive biopanning approach using a 7-mer peptide displaying phage library. The ligands were tested for their affinities and functional effects on EGFR.
Results: The results showed that the identified peptides (P1 and P2) were able to inhibit the epidermal growth factor-induced phosphorylation of EGFR in a concentration-dependent manner. The results of affinity binding experiments showed that the natural ligand, that is epidermal growth factor, was able to inhibit competitively the binding of peptide-bearing phage to epidermal growth factor receptor expressing A-431 cells.
Conclusions: In conclusion, two novel peptides specific for EGFR were identified using phage display technology. From drug discovery and design point of view introducing short oligo-peptides inhibiting the binding of EGF to the receptor is of great importance and hence can be used as lead compounds for designing new pharmaceuticals effective in cancer therapy.

Keywords: Phage display; EGFR; Peptide; Cancer