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Selection of FGF1 binding peptides from cyclic C7C Phage Display Library, which shows potential inhibition of FGF1-FGFR1 interaction

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Fibroblast growth factor 1 (FGF1) is a protein with a very high mitogenic activity. This polypeptide possesses ability to bind with high affinity to all isoforms of fibroblast growth factor receptor (FGFR), which are often overexpressed in different types of human cancers. Dissociation of FGF1-FGFR complex with specific low molecular weight inhibitors can be considered a new approach to anticancer therapy. Therefore by targeting at FGF1 we can prevent unwanted FGF1-FGFR interaction, which will decrease overall FGFR activation. To find FGF1 inhibitors we have used cyclic C7C Phage Display Peptide Library. We performed 3 rounds of *in vitro* biopanning using 96-well plates coated with FGF1. The enriched phages were analysed with ELISA assay. Fourteen clones that showed highest binding to FGF1 were sequenced and five selected peptides were synthesized, oxidized to form and purified on RP-HPLC. The proper molar mass of peptides was confirmed by MALDI-TOF mass spectrometry. We verified the ability to block FGF1-FGFR1 interaction by four selected peptides. The inhibitory effect of peptides was confirmed by blocking of *in vitro* FGF1-mediated activation of ERK1/2 pathway. Based on obtained data, we chose two peptides which possess the highest ability to inhibit FGF1-FGFR1 interaction. Currently we are working on reformatting selected peptides into peptibody format, to obtain more stable molecules with higher binding avidity to FGF1.

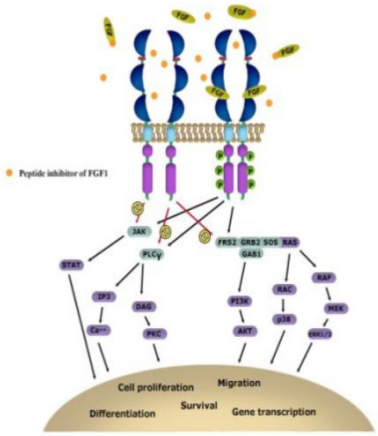

Figure 1: Activation and inhibition of FGF/FGFR signaling pathway.

Recent Publications

1. Kafarski P, Lipok M (2015) Structural analogy - direct similarity versus topographical Complementarity. Drug Discovery and Development DOI: 10.5772/59401.

Biography

Magdalena Lipok graduated from Opole University, Poland with an MSc degree in Chemistry. Currently, she is the student of PhD Studies in Molecular Biology at University of Wroclaw. The main topic of her PhD thesis focuses on finding FGF1-FGFR signalling pathway inhibitor, which potentially can be used in anticancer therapy. Her scientific interests are small molecule inhibitors, anticancer application of peptides and protein drug discovery and development in anticancer therapy.

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