

Converting Protein into a Bioactive Peptide: Discovery of IL-6 antagonist

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We have developed a novel peptide discovery technology which we called PepFusion. It is based on simultaneous identification and optimization of the sequences critical for protein-protein interactions or ligand binding. We tested it by selecting peptide antagonists of interleukin-6 (IL-6), a key mediator of several inflammatory diseases. The PepFusion library demonstrated superiority over a random library by yielding a peptide with low micromolar affinity for IL-6, whereas the random library failed. The affinity of the lead peptide was improved through additional round of mutagenesis leading to peptide variants with low nanomolar affinity toward IL-6 as well as low nanomolar IC50 in cell-based assay.