

USING PEPTIDES TO STUDY PROTEIN-PROTEIN INTERACTIONS: A BASIS FOR DRUG DESIGN

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Our group is interested in the use of peptides for the quantitative biophysical analysis of protein-protein interactions in health and disease, and the use of the data as a basis for rational drug design. We are looking at biological systems that are affected in disease, such as cancer-related pathways in the cell, or viral infection. The research involves three major steps: (1) Analyzing protein-protein interactions in health, to understand how the particular biological system works at the molecular level; (2) Understanding what goes wrong at the molecular level in disease, e.g. upon mutation; (3) Development of drugs that will restore the biological system to its healthy conditions (in cancer), or will inhibit undesired interactions (in viral infection). To achieve our goals, we are using an interdisciplinary approach combining peptide and combinatorial chemistry, with particular focus on peptide arrays, protein biochemistry and biophysical studies such as fluorescence, CD and NMR spectroscopy. We apply the above approach to several different biological systems, including for example:

1. Studying the interaction network of the ASPP family of apoptosis regulating proteins, as a basis for anti-cancer drug design (1-4).
2. Shiftides: peptides that affect the oligomerization equilibrium of proteins, and their application for inhibition of the HIV-1 integrase protein (5-7) or Rev protein as well as for activation of cancer-related proteins such as the tumor suppressor p53.

Selected references:

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