Chemical Biology and Fragment based screens using solution NMR

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Chemical biology comprises interdisciplinary efforts to understand and characterize interactions between biological targets and natural or synthetically produced molecules and to develop these findings in a biological context. NMR spectroscopy is well suited to studies of transient or strong interactions between specific protein targets and low molecular weight molecules such as natural products or lipids, or synthetically produced fragments, drug candidates or approved drugs. Fragment based drug discovery approaches are used for the design and development of novel lead compounds and NMR spectroscopy has emerged as a powerful method to study non-covalent protein-ligand complexes using ligand-observed techniques. Complementary, high resolution NMR spectroscopy studies of protein – ligand complexes can be made with protein target observed methodologies, for both low- and high-affinity complexes.

Fragment based screens (FBS) using NMR spectroscopy enables joint testing of a large number of fragments with low molecular weight (typically < 500 Da) against a target protein molecule or molecular complex. The Swedish NMR Centre is equipped with high field spectrometers (600-800 MHz) with cryogenically cooled probes optimized for either 1H or 19F-detection and SampleJet sample changers as well as liquid handling systems for sample preparations for FBS campaigns. With this setup, libraries of 1.000 fragments can be screened against a target protein molecule within days.