Different Protein Receptor Responses Resulting from Different Membrane Environments

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G protein-coupled receptors (GPCRs) play a crucial role in many physiological processes, first by detecting signals from external stimuli, such as hormones, neurotransmitters, and drugs, and then by transmitting those signals to the inside of the cell. Despite their significance as drug targets, the impact of the cellular membrane environment on the function of GPCRs is still largely unknown.

In this interdisciplinary collaborative study, MagLab users investigated how phospholipids within the cellular environment strongly influence the response of GPCRs to stimulating drugs. *NMR spectroscopy played a central role in this study, allowing researchers to carefully observe receptors and their responses to drugs in different membrane environments (see **Figure**). State-of-the art NMR instrumentation at the MagLab is uniquely suited for precise measurements of lipid compositions and simultaneous investigation of receptor proteins on the same instrument through visualization of multiple nuclei, in particular 1H, 19F, and 31P.* By combining NMR data with computational modeling and *in vitro* experiments, the research team obtained new insights into the molecular mechanisms underlying receptor-lipid interactions.

The specific focus of this work was an adenosine receptor, the target for caffeine and a validated drug target for Parkinson's disease and several cancers. *The success of this study has broad implications for many other receptors, including human receptors for opioids, hormones, and neurotransmitters*.

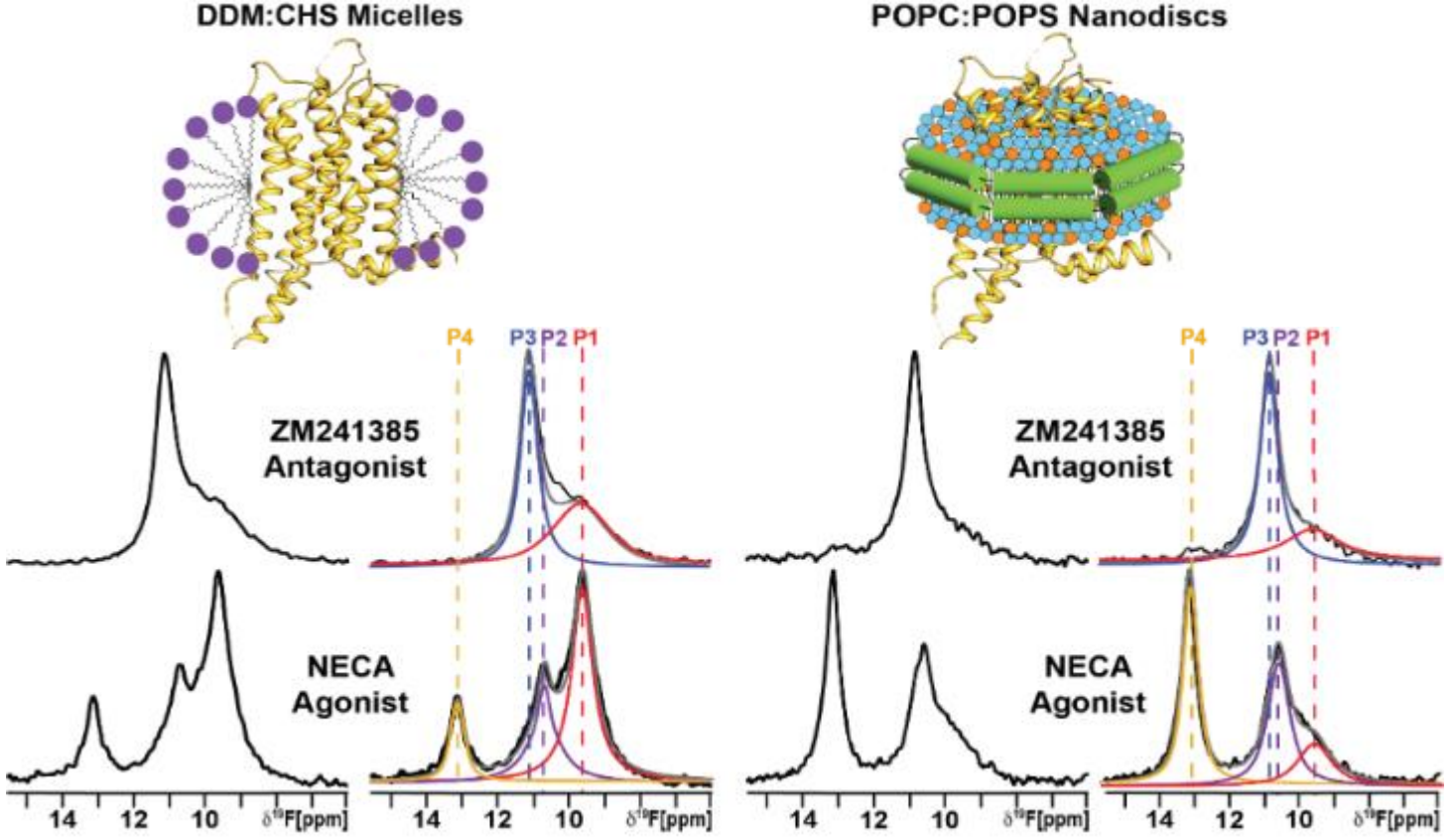

Figure: Receptor proteins respond differently to drugs depending on the environment in which they are studied. NMR spectroscopy at the MagLab's AMRIS facility enabled the investigation of the synergistic response between drug efficacy and the membrane environment, demonstrated above by different responses of the same receptor protein in **(left)** detergents and **(right)** lipid nanodiscs.

Facilities and instrumentation used: The MagLab's AMRIS Facility at the University of Florida, particularly the ^{19}F NMR probe on the 600MHz wide bore NMR instrument

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