



Different Protein Receptor Responses Resulting from Different Membrane Environments

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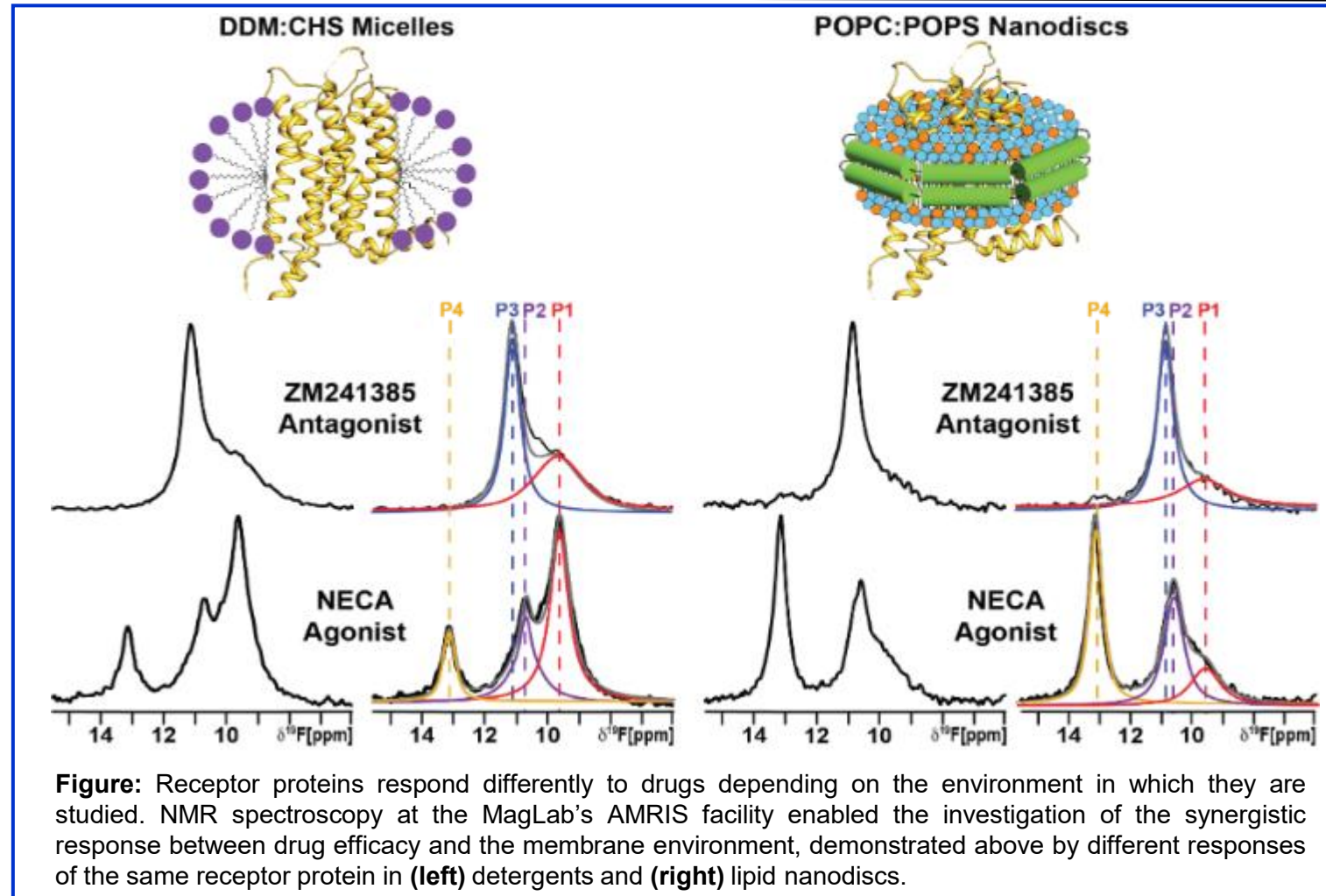
Funding Grants: Boebinger (NSF DMR-2128556); Eddy (NIH R35GM138291), Lyman (R01GM120351), Gao and Jin (ZIA DK031117)



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.



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

Citation: Thakur, N.; Ray, A.; Sharp, L.; Jin, B.; Duong, A.; Gopal Pour, N.; Obeng, S.; Wijesekara, A.; Gao, Z.; McCurdy, C.; Jacobson, K.; Lyman, E.; Eddy, M.T., *Anionic Phospholipids Control Mechanisms of GPCR-G Protein Recognition*, *Nature Communications*, **14**, 794 (2023) doi.org/10.1038/s41467-023-36425-z - [Data Set 1](#), [Data Set 2](#)