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Probing Lipid/protein Coupled Dynamics in Membranes by High-pressure Nmr Spectroscopy

Alexandre Pozza [1], François Giraud [2], Clarisse Fourel [2], Quentin Cece [1], Marina Casiraghi [1], Elodie Point [1], Christel Le Bon [1], Karine Moncoq [1], Jean-louis Banères [3], Laurent Catoire [1], Ewen Lescop [2]

[1] Laboratoire de Biologie Physico-Chimique des Protéines Membranaires, UMR 7099, IBPC, CNRS/Université de Paris, Paris, France

[2] Institut de Chimie des Substances Naturelles (ICSN), CNRS UPR 2301, Université Paris-Saclay, Gif-sur-Yvette, France

[3] Institut des Biomolécules Max Mousseron (IBMM), Université de Montpellier, CNRS, ENSCM, Pôle Chimie Balard Recherche, Montpellier, France

Cell membranes represent a complex and variable environment in time/space. Their physico-chemical and functional properties are determined by lipid and protein components and their respective interactions. In this work (Pozza et al. Nature Com. 2022), we used NMR spectroscopy under hydrostatic pressure to study the close dynamic relationships between lipids and membrane proteins in ~10 nm nanodiscs. Using 1H, 31P and 13C NMR, we demonstrate that the pressure-induced fluid-to-gel lipid phase transition leads to pronounced dynamic change at the center of the bilayer and that this transition is shifted to higher pressure in presence of the beta-barrel OmpX or of the BLT2 GPCR (G Protein-Coupled Receptor Protein), suggesting that proteins tend to preserve the fluidic nature of their surrounding lipids. In OmpX, the lipid phase transition is accompanied by changes in dynamics for the lipid-exposed methyl groups but also, surprisingly, by a conformational change at the core of the protein, suggesting an allosteric pathway between lipid bilayer and protein core. High pressure experiments also revealed major conformational/dynamic changes within BLT2, in line with distinct void distributions in the various states of this GPCR. The strategy proposed herein opens new perspectives to scrutinize the dynamic interplay between membrane proteins and their surrounding lipids in nanodiscs.