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Probing the coupled dynamics between lipids and membrane proteins in nanodiscs by high-pressure NMR spectroscopy

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Cell membranes represent a complex and variable environment in time and space of lipids and proteins. Their physico-chemical and functional properties are determined by lipid and protein components and their respective interactions. Here, we used NMR spectroscopy under hydrostatic pressure to study the close dynamic relationships between lipids and membrane proteins in ~10 nm nanodiscs. We demonstrate that nanodisc particles can reversibly accommodate high-pressure, in absence or in presence of embedded membrane proteins such as the beta-barrel OmpX porin and the alpha-helical BLT2 G Protein-Coupled Receptor [1]. Yet, the lipid fluid-to-gel phase transition triggered by pressure, as monitored by 1H NMR (Fig 1), is delayed to higher pressure in presence of OmpX or BLT2, suggesting that proteins tend to preserve the fluid nature of their surrounding lipids. Pressure can also modify the conformational landscape of the membrane protein per se. Indeed, we observed a population redistribution in the complex conformational landscape of BLT2 [2], and a dynamic change at the micro-millisecond timescale leading to a dramatic 4-5x NMR signal increase for BLT2. In OmpX, we observed at high pressure a distortion of the H-bond network in the beta-barrel and a specific dynamic change for methyls groups exposed to the lipid bilayer, suggesting concerted motion of methyls surrounded by lipids. The strategy proposed [1] herein opens new perspectives to scrutinize the dynamic interplay between membrane proteins and their surrounding lipids in nanodiscs.

[1] Pozza A, Giraud F, Cece Q, Casiraghi M, Point E, Damian M, Le Bon C, Moncoq K, Banères JL, Lescop E, Catoire LJ. (2022). Exploration of the dynamic interplay between lipids and membrane proteins by hydrostatic pressure. Nat Commun. 13(1):1780. doi: 10.1038/s41467-022-29410-5.
[2] Casiraghi M, Damian M, Lescop E, Point E, Moncoq K, Morellet N, Levy D, Marie J, Guittet E, Banères JL, Catoire LJ. (2016) Functional Modulation of a G Protein-Coupled Receptor Conformational Landscape in a Lipid Bilayer. J Am Chem Soc. 138(35):11170-5. doi: 10.1021/jacs.6b04432.

Session

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Primary authors: POZZA, Alexandre (IBPC); GIRAUD, François (CNRS-ICSN); CECE, Quentin (CNRS-IBPC); CASIRAGHI, Marina (CNRS-IBPC); POINT, Elodie (CNRS-IBPC); DAMIAN, Marjorie (IBMM); LE BON, christel (CNRS-IBPC); MONCOQ, Karine (CNRS-IBPC); BANÈRES, Jean-Louis (IBMM); LESCOP, Ewen (CNRS); CATOIRE, Laurent (CNRS-IBPC)

Presenter: LESCOP, Ewen (CNRS)

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