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Effects of cholesterol and PIP2 on membrane domain formation
PAUL JANMEY, FITZROY BYFIELD, DAVID CHRISTIAN, University of Pennsylvania, ILYA LEVENTAL, MPI-Dresden — Lipid head group size, acyl chain saturation, the relative amounts of cholesterol, phospholipids and sphingolipids, and electrostatic effects due to highly charged anionic lipids such as phosphatidylinositol bisphosphate (PIP2) all contribute to the force balance that determines the conditions at which domains form as well as their size, shape and stability. Giant plasma membrane vesicles derived from intact cells reveal lipid phase separation in a system with appropriate biological complexity. Formation of liquid ordered domains large enough to visualize by light microscopy form under physiologically realistic conditions in cell-derived vesicles, and their dependence on cholesterol content and temperature are consistent with studies of purified lipids. Compared to the effects of cholesterol, PIP2 has a smaller but still significant effect on liquid ordered / liquid disordered domain formation, but compared to other lipids, PIP2 is much more strongly segregated in the liquid disordered domains, away from those enriched in cholesterol. These results suggest physical mechanisms by which the cell can rapidly alter local PIP2 concentration to trigger cellular signals.

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