Caveolae membrane domains connect G protein – mediated calcium signals with mechanical deformation

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Caveolae are membrane invaginations that are thought to provide a scaffold that sequesters related groups of signaling proteins into functional domains. Caveolae have also been shown to provide mechanical strength to cells by flatting to accommodate deformation when cells are subjected to mechanical stretching or hypo-osmotic pressure. We have previously found that caveolin, the main structural component of caveolae, specifically binds the Gαq family of heterotrimeric G proteins and stabilizes its activation state. This stabilization in turn enhances activation of its main effector, phospholipase Cβ and ultimately resulting in enhanced calcium responses to agents such as acetylcholine, dopamine and bradykinin. Additionally, using normal and super-resolution fluorescence spectroscopic methods, we find that moderate osmotic stress reversibly changes the morphology and configuration of caveolae but leaves the aggregated state of the domains fairly intact. However, when the structure of caveolae are perturbed, they no longer stabilize the activated state of Gαq resulting in a reversible reduction of Gαq/PLCβ mediated calcium signals, and a movement of PLCβ into the cytoplasm where it can bind to the RNA-induced silencing complex and interfere with its activity. These results suggests a feedback mechanism that connects mechancal deformation of cells with the strength of calcium signals, and possibility, RNA-induced silencing.