Multimodal Microscopy to Study Plasma Membrane Microdomains

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The plasma membrane forms a barrier to protect the cell from the outside world. However, the cell surface is not a static impermeable barrier but a dynamic mosaic of distinct domains with unique properties and functions. Our work is aimed at understanding the formation, function, and dynamics of these cell surface domains at the molecular level. I will describe the use of light and electron microscopic techniques, including electron tomography, serial blockface scanning electron microscopy, and genetically-encoded electron microscopic tags, to gain a quantitative understanding of the formation of these specific plasma membrane domains and their role in endocytosis, mechanoprotection, and specific signal transduction pathways. In particular, I will describe our studies on cell surface pits called caveolae, and how structural studies of caveolar proteins together with cellular and whole animal systems are providing insights into the multiple functions of caveolae and the diseases associated with caveolar dysfunction.