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Cholesterol and cholesterol-rich membranes in prostate cancer: an update

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ABSTRACT

Cells maintain normal structure and function by responding appropriately to cues from the surrounding milieu. Extracellular stimuli are transduced from the surface through the plasma membrane by a complex series of interactions between ligands, their receptors and intracellular signaling partners (e.g., kinases, G proteins). Cholesterol-enriched membrane microdomains, generally referred to as "lipid rafts", exist within the lipid bilayer of all mammalian cells and play an important role in signaling from the cell surface to various subcellular compartments. Lipid rafts have also been implicated in tumor growth and aggressiveness. Epidemiological evidence suggests that the modern Western diet, which contains substantial levels of cholesterol and other fatty substances, promotes prostate cancer progression. Consistent with this idea, prolonged inhibition of the cholesterol synthesis pathway by pharmacologic intervention in men has recently been associated with reduction in risk of advanced prostate cancer. In this review, we discuss the possibility that membrane cholesterol promotes prostate cancer progression by a mechanism that involves dysregulation of lipid raft-resident signaling complexes. This hypothesis provides new avenues for mechanistic studies as well as therapeutic intervention.

Key words: prostate cancer, cholesterol, detergent resistant microdomains (DRM), caveolae.

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