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The heterogeneity of NaPi protein dynamics and NaPi cotransport activity in renal brush border membranes

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Abstract

Alterations in renal proximal tubule brush border membrane (BBM) cholesterol, sphingomyelin, and glycosphingolipid content play an important role in regulating the activity of the sodium-phosphate cotransporter (NaPi). The molecular mechanisms of how alterations in lipid composition may modulate NaPi activity are not known. We have fractionated BBM prepared from rat kidney using detergent-free density gradient ultracentrifugation (OptiPrep). We have found that the NaPi protein preferentially partitions into lipid rafts. To determine the potential consequences of the partitioning of the NaPi transporter in these lipid domains we have i) measured NaPi transport activity and ii) used fluctuation correlation spectroscopy (FCS) methods to determine NaPi diffusion. Partitioning of NaPi protein into lipid rafts results in i) decreased NaPi cotransport activity and ii) decreased diffusion of NaPi protein. Similar results were obtained in BBM isolated from the superficial cortex (SC) versus the juxtamedullary cortex (JMC). The three-fold decrease in NaPi cotransport activity in JMC-BBM is associated with a 3-fold decrease in NaPi protein diffusion. Our results therefore indicate that partitioning of NaPi protein into lipid rafts results in impairment of its activity and diffusion.