The prion protein requires cholesterol for cell surface localization.

Abstract:
The cellular prion protein PrP(c) is attached to the plasma membrane by a glycosyl-phosphatidylinositol (GPI-) anchor and is localized in lipid rafts, membrane microdomains characterized by a high content of sphingolipids and cholesterol. Previous studies revealed that perturbation of cholesterol synthesis prevents prion conversion, explained by redistribution of PrP(c) at the plasma membrane. We investigated the influence of inhibition of cholesterol synthesis by the HMG-CoA-reductase inhibitor mevinolin on the trafficking of PrP(c) in neuronal cells. Treatment with mevinolin significantly reduces the amount of surface PrP(c) and leads to its accumulation in the Golgi compartment. Analysis of mutant PrPs highlights the importance of the GPI-anchor for raft localization and provides information about domains implicated in lipid raft association of PrP in the secretory pathway. Our data show that cholesterol is essential for the cell surface localization of PrP(c), known to be necessary for prion conversion.