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Lipoprotein receptors in neuronal cholesterol homeostasis and function

Abstract:

Although the regulation of cholesterol homeostasis in the body has been extensively studied, there is little information on how this regulation takes place in the brain. Cholesterol does not cross the blood-brain barrier; therefore cholesterol metabolism in the brain is independent from that in peripheral tissues. Lipoprotein receptors from the LDL receptor family (LRPs) have key roles in lipid particle accumulation in the bloodstream. For example, activation of a specific LRP induces lipid uptake in several cells, tissues and organisms both in vitro and in vivo. However whether LRPs are involved in the regulation of cholesterol levels in the brain is still not known. To determine the role of lipoprotein receptors in the brain we analyzed the expression of different LRPs and components and targets of their downstream signaling pathways in brains of Wt and Lrp-/- mice and in a neuroblastoma cell line. Although sever- al LRPs expression are increased in a time dependent and dose dependent manner in lipid loaded neurons, specific LRPs do not participate in lipid uptake as neurons without lipoprotein receptors accumulate intracellular lipids in a similar way as control cells. Because the activa- tion of the canonical WNT signaling pathway induces survival processes we tested whether lipoprotein receptors were involved in apoptotic and/or autophagic processes and found that LRP has both, anti- apoptotic and anti-autophagic functions indicating a role for this receptor in neuronal survival. Furthermore, we show that LRP is indispensable for life as brains of Lrp-/- mice show low but quantifiable LRP gene expression. Taken together, our results support a prosurvival role for LRP in brain.

Biography

Borrell, is a senior investigator in the Cardiovascular Program at the Hospital de la Santa Creu i Sant Pau, Barcelona. Prior appointments include a postdoctoral position in the Neurology Department of the Curie Institut, Paris, France studying Huntington's disease. She leads a project based in the role of different lipoprotein receptors in cholesterol metabolism in the vascular system. The results have been published in different journals including EHJ, BRIC or CVR and lead to the concession of projects financed by both, the government and the industry.