

P008 Role for dynamin in late endosomal transport of cholesterol: effect on sterol sensitive genes regulation and cholesterol homeostasis

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Cholesterol is one of the most essential membrane components in mammalian cells and plays a critical role in several cellular functions. It is now established that intracellular cholesterol transport contributes to the regulation of cellular cholesterol homeostasis by mechanisms that are poorly defined. In this study, we examined the role of clathrin- and dynamin-dependent trafficking in the cell response to exogenous low-density lipoprotein (LDL)-derived cholesterol. Expression levels of three major sterol sensitive genes i.e. sterol-regulatory element binding protein 2 (SREBP-2), hydroxymethylglutaryl-coenzyme A (HMGCoA) reductase, and LDL receptor were monitored to study the role of trafficking on the regulatory machinery involved in cholesterol homeostasis. While inhibition of clathrin-dependent endocytosis showed no major effects, we found that dynamin inactivation resulted in a strong alteration of both SREBP-2, HMGCoA reductase and LDL receptor genes expression and cholesterol esterification, indicating a defect of cholesterol delivery to the reticulum endoplasmic. Immunolocalization and filipin staining studies suggested that the alteration of genes expression observed after dynamin inactivation was due to the accumulation of free cholesterol retained in the late endosomal/lysosomal compartment. Thus, our results indicate a new role for dynamin in endosomal cholesterol transport and highlight its importance in cholesterol homeostasis.