Lipid efflux from liver

Secretion of lipids in the form of very low-density lipoproteins (VLDL) by the liver plays an important role in maintaining overall body lipid homeostasis. Any abnormality associated with this physiological process can lead to severe metabolic disorders such as hyperlipidemia, hepatic steatosis, etc. The rate-limiting step in the secretion of VLDLs from the liver is their transport from the endoplasmic reticulum (ER) to the Golgi and represents a potential therapeutic target in controlling VLDL secretion. We have identified a distinct ER-derived vesicle, VLDL transport vesicle (VTV), which facilitates the targeted delivery of VLDLs from the ER to the Golgi. To find out the factors that regulate the biogenesis of these vesicles, we performed detailed proteomic and biochemical analyses. Our data revealed that two small MR proteins, cideB and SVIP are present in VTV but not in other ER-derived vesicles. Our morphological and co-immunoprecipitation data revealed that both cideB and SVIP specifically interact with VLDL structural protein, apolipoproteinB100. To examine the roles of these proteins in VTV-biogenesis, we carried out an in vitro ER-budding assay. We showed that either blocking or knockdown of cideB and SVIP abrogates VTV-budding and VLDL secretion from hepatocytes. We conclude that cideB and SVIP control VLDL/lipid secretion from the liver by regulating VTV-formation and their identification is critical for the development of novel therapeutics for dyslipidemia.

Biography

Shadab A Siddiqi is an Associate Professor at the UCF College of Medicine and earned his PhD from the Central Drug Research Institute/Lucknow University in India. He did his Post-doctoral training at the National Institute of Immunology in India and at the Gastroenterology Division, University of Tennessee Health Science Center. His research is focused on: Deciphering the cellular and molecular mechanisms underlying the lipid metabolism. His major contribution to the field is the discovery of a new paradigm for the ER-to-Golgi transport of nascent lipoproteins. He serves on Editorial Boards of several journals and as a reviewer for numerous journals.

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