

Controlling Fat Secretion from the Liver

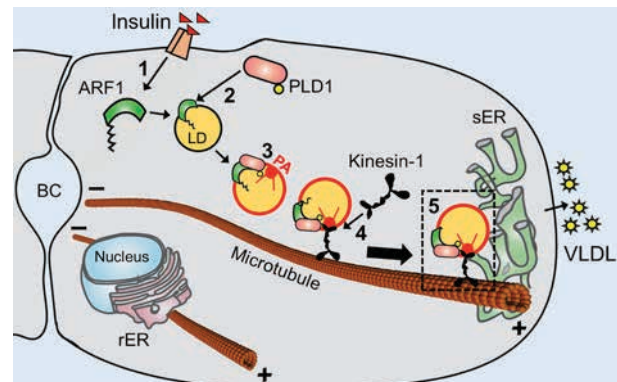
Problem Statement: The Liver packages fat and cholesterol into Very Low-Density Lipoprotein (VLDL) particles and then releases VLDL into the blood for delivery to different organs where fat and cholesterol is utilised. When this equilibrium is disturbed, it manifests into diseases such as obesity, diabetes, dyslipidemia, cardiac problems, or fatty liver. This team discovered a mechanism that controls how much fat is secreted from the liver into the blood. They show that the nanoscale motor protein Kinesin-1 delivers fat molecules to a specific location in the liver from where it is repackaged into VLDL particles and circulated in the blood. With an understanding of this fundamental mechanism now available, they propose to intervene in a targeted manner that may benefit patients with chronic dyslipidemia and/or fatty liver.

Uniqueness of the Solution: This discovery is a first-of-its-kind intervention via this pathway as the mechanism that

controls VLDL secretion through Kinesin motors. Furthermore, it has been proven to work in a cell culture model and in rats; it also provides very selective and targeted intervention. As their next steps, the team envisages finding better and more specific inhibitors of Kinesin on fatty particles and collaborating with industry experts in drug formulation and delivery.

Current Status of Technology: A peptide that specifically blocks fat secretion from the liver by preventing the Kinesin motor from docking on fat bodies has been identified. The team has also shown that it is possible to control this mechanism through external intervention in cultured cells and rats. They now look for higher affinity peptides and peptidomimetic drugs that can be delivered to the liver for further progress. Another possible direction is targeted gene delivery that could be attempted using an adeno-associated virus.

Societal Impact: Targeting a novel



pathway that controls fat circulation in blood could help control the epidemic of obesity, diabetes and accompanying maladies.

Patent(s): Nil

Relevant Industries: Pharmaceutical with experience in drug formulation or delivery.

Faculty: Prof. Roop Mallik, Biosciences and Bioengineering.