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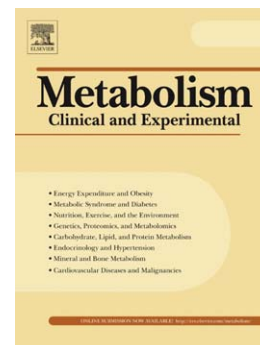
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siRNA-mediated inhibition of SCAP reduces dyslipidemia in spontaneously dysmetabolic rhesus monkeys

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Abstract**Background:**

SREBP cleavage-activating protein (SCAP) is a cholesterol binding endoplasmic reticulum (ER) membrane protein that is required to activate SREBP transcription factors. SREBPs regulate genes involved in lipid biosynthesis. They also influence lipid clearance by modulating the expression of LDL receptor (LDLR) and proprotein convertase subtilisin/kexin type 9 (PCSK9) genes. Inhibiting SCAP decreases circulating PCSK9, triglycerides (TG), and LDL-cholesterol (LDL-C), both *in vitro* and *in vivo*.

Type 2 diabetics with dyslipidemia are at high risk for cardiovascular diseases. These patients present a unique pathophysiological lipid profile characterized by moderately elevated LDL-C, elevated TG and reduced HDL-cholesterol (HDL-C). The spontaneous dysmetabolic rhesus monkey model (DysMet RhM) recapitulates this human dyslipidemia and therefore is an attractive preclinical model to evaluate SCAP inhibition as a therapy for this disease population. The objective to of this study was to assess the effect of SCAP inhibition on the lipid profile of DysMet RhM.

Method:

We assessed the effect of inhibiting hepatic SCAP on the lipid profile of DysMet RhM using a siRNA encapsulated lipid nanoparticle (siRNA-LNP).

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