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Synthetic HDL nanodiscs show potent anti-inflammatory properties.

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Background: High density lipoproteins (HDLs) are complex particles whose function and composition are critically altered in disease. Therefore, it is reasonable to replace or even increase the loss of function of HDL in inflammatory diseases. Apolipoprotein A-1 (apoA-I) is the most abundant protein of HDL and is primarily responsible for the its well documented anti-inflammatory effects. Artificially synthesized 18-37 amino acid long peptides, that mimic the activity of full length apoA-I, are being actively researched as HDL-mimics. Due to the ease of production and highly specific nature, peptidomimetics are a naturally preferable choice. However, there is a need to test the anti-inflammatory potential and toxicity to eliminate the limitations associated with the free peptides, which reduce the bioavailability and hence affect the bioactivity.

Results: We prepared differentially lipidated apoA-I mimetic nanoparticles using the NanoAssemblrTM platform. We characterized the size and confirmed the discoidal morphology of the nanodiscs using Transmission Electron microscopy and Native gel electrophoresis. We first tested the functionality of the nanodiscs compared with native HDL using an in- vitro cholesterol efflux capacity assay. We found that the nanodiscs mobilize cholesterol from mouse macrophages more effectively than native HDL. Moreover, the nanodiscs potently suppressed lipopolysaccharide induced human neutrophil activation and downmodulated human eosinophil migration response to eotaxin-1 and prostaglandin D2. We observed that the lipidation status of the nanodiscs strongly influenced their anti-inflammatory properties.

Conclusion: The apo A-1 mimetic based nanodiscs may have therapeutic potential, targeting hyper-inflammatory and hyper-eosinophilic conditions such as sepsis and asthma, where migration and activation of immune cells is the decisive point for disease exacerbation