A Pickering Emulsion–Stabilized Nanostructure to Degrade Lipid Droplets in Fatty Liver Disease

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Abnormal buildup of lipid droplets in hepatocytes is a central factor in the progression of fatty liver diseases associated with metabolic dysfunction. With the global rise in obesity and metabolic syndrome, these liver conditions have emerged as critical health concerns, spurring the need for advanced treatment strategies. Here, we introduce an innovative Lipid Droplet Modulator (LDM) composed of ultra-large mesoporous silica nanostructures, a diacylglycerol-binding peptide (DAG-binding peptide, derived from PKC), and triacylglycerol acylhydrolase, designed to actively identify and degrade lipid droplets within cells. This nanoplatform operates through a dual mechanism: the DAG-binding peptide selectively binds diacylglycerol, a key precursor in lipid droplet development, while triacylglycerol acylhydrolase catalyzes the hydrolysis of triacylglycerol into smaller lipid molecules. Amphiphilic biomolecular components within the LDM promote the formation of a Pickering emulsion, positioning the nanostructure stably at the lipid–water interface to optimize contact and activity with lipid droplets. In vitro studies using HepG2 cells showed that the LDM significantly suppressed the formation and enlargement of lipid droplets. In a high-fat diet-induced mouse model of fatty liver disease, the treatment notably alleviated hepatic injury, reducing damage scores. Lipidomic analysis confirmed substantial remodeling of the liver lipid profile post-treatment, underscoring the LDM's promise as a cutting-edge nanotherapeutic approach for managing lipid droplet accumulation in fatty liver disease.

References

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Figures

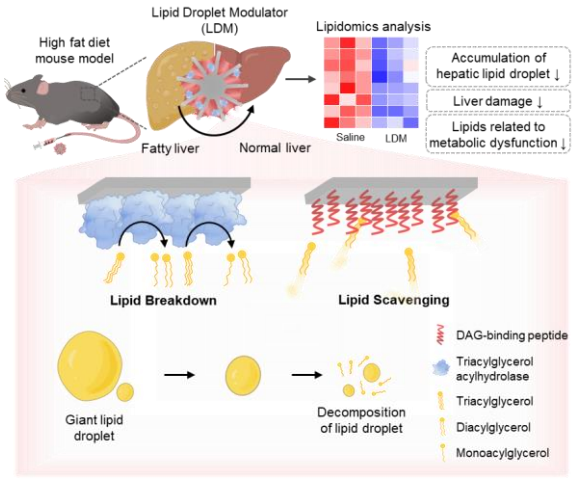

Figure 1: Administration of LDM in a high fat diet mouse model alleviated hepatic lipid accumulation and liver damage. Lipidomic analysis further confirmed that LDI modulated lipid species associated with hepatic metabolic dysfunction.