InSyTe FLECT/CT Application Spotlight

Non-alcoholic fatty liver disease, gene therapy

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Title: Redox-Unlockable Nanoparticle-Based MST1 Delivery System to Attenuate Hepatic Steatosis via the AMPK/SREBP-1c Signaling Axis
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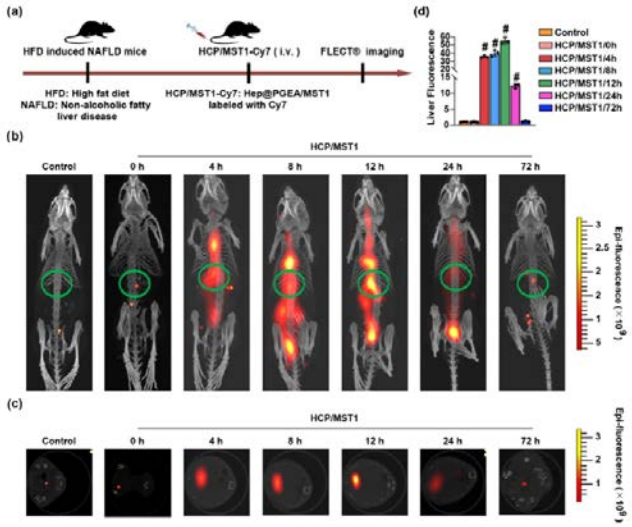
Keywords: Non-alcoholic fatty liver disease, nanoparticles, gene therapy

Summary: Non-alcoholic fatty liver disease (NAFLD) is characterized by an elevation of liver lipids not due to typical causes, such as alcoholism, drug abuse, or genetic predisposition. NAFLD may advance to non-alcoholic steatohepatitis and eventually to liver cirrhosis or liver cancer, where treatment requires a liver transplant. Treatments for NAFLD are limited and there is not a currently accepted drug therapy. MST1 is a mammalian kinase that has demonstrated ability to regulate lipid disorders of the liver. Previously, the research team had reported MST1 downregulation was linked to increased liver lipid accumulation. In this follow up study, the research team developed a heparin polysaccharide-based nanoparticle (Hep) modified with a ethanolamine-modified poly(glycidyl methacrylate) vector (Hep@PGEA) to transport either the MST1 plasmid or signal interfering MST1 RNA (siMST1) to the liver to assess the effect of upregulation and downregulation of MST1 on liver lipid levels.



(a) Experimental parameters and timeline for FLECT/CT imaging. (b) 3D full body FLECT/CT images from 0h to 72h post administration of HCP/MST1 showing the full biodistribution. (c) Transverse view images of the liver region over the 72h time period for fluorescence quantification. (d) Bar graph comparing the quantified fluorescence at each time point within the 72h study

InSyTe FLECT/CT Spotlight: Using the InSyTe FLECT/CT, the research team monitored the biodistribution of the HCP/MST1 complex (MST1 plasmid + Hep@PGEA vector) in vivo over 72h. The HCP/MST1 complex was conjugated to a Cy7 fluorescent dye and injected via tail vein injection for in vivo biodistribution studies. Fluorescence in the liver region was isolated and quantified, showing significant accumulation of the HCP/MST1 complex in the liver over the first 24h and filtration with 72h. This result suggests an extended circulation and retention time in vivo that may benefit other Hep@PGEA based gene therapies.