

Session/Poster#

Presenter

**B53**

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### **Design and Validation of Collagen-Targeted Protein Nanomicelles for the Imaging of Non-Alcoholic Steatohepatitis (NASH)**

NASH is a condition defined by inflammation and progressive fibrotic collagen deposition in the liver, primarily of type I. Currently, there are few effective methods of monitoring the progression of NASH, with biopsy remaining the gold standard. However, biopsy is invasive and not preferable for longitudinal tracking in patients. Furthermore, current imaging methods involving elastography can be unreliable due to increased hepatic stiffness in conditions lacking fibrosis. Thus, direct molecular imaging of type I collagen is a sensitive and relatively noninvasive alternative. We have designed and characterized a unique protein-based imaging probe called Col1-TRAP-Vivo that self-assembles into micellar structures and multivalently binds to type I collagen with high affinity ( $K_d = 100$  nM). Col1-TRAP was recombinantly expressed in *E. coli* and labeled with the near-infrared fluorescent dye VivoTag 680 with a high degree of efficiency (68%) and purity. Dye-labeled protein was assessed for its self-assembled structure, and ability to bind to collagen type I in vitro in assembled vs denatured form. Col1-TRAP-Vivo was also evaluated for its ability to track to fibrotic liver in vivo. Cohorts of C57BL mice were fed either a high fat high sugar NASH diet or a chow diet for 16 weeks. Col1-TRAP-Vivo was then injected intravenously and serum samples were collected over 4 hours post-injection. Afterwards, subjects were sacrificed, and their organs were imaged for fluorescent accumulation before being sectioned and histologically graded for fibrosis. Results show a significant ( $p < 0.05$ ) increase of fluorescence in the fibrotic livers of mice fed the NASH diet compared to the chow diet, and significantly decreased recirculation time of the protein in the serum of NASH mice. These encouraging results represent the only self-assembled protein-based probe for collagen in literature and point to future longitudinal imaging studies visualizing fibrosis regression with treatment.