#106 Andrew Wang Advisor(s): Jin Montclare

Theranosis of Non-Alcoholic Fatty Liver Disease (NAFLD) with Collagen-Targeted Thermoresponsive Assembled Protein

Non-alcoholic fatty liver disease (NAFLD) is the leading cause of chronic liver disease worldwide, especially in Western nations due to its association with obesity and diabetes. The pathogenesis of NAFLD is known to progress from steatosis to non-alcoholic steatohepatitis (NASH) to cirrhosis. One important metric of disease progression is thus fibrotic collagen deposition in the liver, but this is difficult to measure with traditional methods. Furthermore, although there are no currently approved medical treatments beyond diet and lifestyle modifications, there is evidence that pharmacological therapy may improve outcomes when initiated at an early to moderate stage of the disease. Therefore, there is a need for improved diagnostic monitoring of disease progression in vivo, coupled with the capacity for controlled intervention at desired timepoints.

Thermoresponsive assembled protein (TRAP) is a versatile protein construct that self-assembles into micelles engineered to release drug cargo above body temperature at 37°C. We have recombinantly expressed a collagen-targeting nonapeptide tag on the micellar surface that will target TRAP toward fibrotic deposits in the liver. In addition, iron oxide nanoparticles conjugated to non-canonical azidohomoalanine residues will enable MRI visualization of particle accumulation. Computational modeling will be used to determine the optimal arrangement of moieties on the micellar surface. TRAP will be injected into mouse models of NAFLD with comorbid diabetes at predetermined time points to study disease progression and response to treatment, which will be initiated through locally applied high-intensity focused ultrasound (HIFU).