The role of the Ron receptor tyrosine kinase in regulating bile acid metabolism in a diet induced steatohepatitis model

Abstract

Nonalcoholic steatohepatitis (NASH) is quickly becoming one of the most prominent liver diseases in the nation and worldwide. The surge in steatohepatitis incidences is strongly linked to the obesity epidemic and subsequent metabolic derailments associated with it. With currently no specific treatments for steatohepatitis, this common liver disease is becoming a major burden, contributing to the rise in morbidity and mortality rates in the nation. Consequently, extensive efforts have gone into elucidating mechanisms and causes of the disease. These efforts have answered some questions but much remains unclear about steatohepatitis. Our lab has demonstrated that the Ron receptor tyrosine kinase plays a protective role in steatohepatitis development and progression by restraining macrophage mediated inflammation. Here, I propose that this restraint of inflammation encourages bile acid dependent lipid efflux and thus attenuates hepatic lipid accumulation and inflammation. My overall goal is to determine the mechanism underlying the protective role of the Ron receptor in diet induced steatohepatitis. The specific aims of this project are (1) To determine whether Ron receptor mediated suppression of hepatic inflammation regulates bile acid synthesis using a diet induced steatohepatitis mouse model; (2) To determine whether Ron receptor mediated suppression of hepatic inflammation regulates the expression of transporter proteins that facilitate bile acid export, re-absorption, secretion into the circulation and uptake into the liver. Results from this project will give insight on potential novel therapeutic options for treating uncontrolled lipid metabolism and elevated inflammation linked to NASH.