Characterization of Individual Bile Acid Signaling in Novel *In Vivo* Low Bile Acid Model

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Bile acids (BAs) are endocrine molecules essential in the absorption of lipids in the small intestine. Beyond its well known digestive functions, BAs are also critical signaling molecules in cholesterol and BA homeostasis in the gut-liver axis. BAs are endogenous ligands of nuclear receptors such as the Farnesoid X Receptor (FXR) and the purpose of this study is to characterize the role of individual BAs in FXR and other receptor activation. To generate a low BA model, mice were engineered to be deficient in two critical genes that encode enzymes in BA synthesis, Cyp7a1 and Cyp27a1. Deoxycholic acid (DCA) is well known to be increased in chronic liver diseases in humans, and ursoDCA (UDCA) has been used to treat cholestasis. We hypothesize that Cyp7a1 & Cyp27a1 double knockout (DKO) mice administered DCA and UDCA via diet will have altered BA levels and subsequent changes in molecular pathways involved in BA signaling and homeostasis compared to wild-type mice. Observed changes in molecular pathways will help elucidate the role of DCA and UDCA individually. Preliminary qPCR data suggest trends that show that feeding BA-low mice DCA increases, whereas feeding them UDCA decreases the expression of proinflammatory genes. Once individual BA signaling pathways are determined, the knowledge can be applied to better target mechanistic pathophysiology in liver diseases such as Nonalcoholic steatohepatitis (NASH) and Primary biliary cirrhosis (PBC). Supported by R25ES020721, R01GM135258, and the ASPET SURF Program.