

6th Global Summit on

Toxicology & Applied Pharmacology

October 17-19, 2016 Houston, USA

Regulation of liver drug transporter MRP2 by LKB and *PTEN*

Bangyan Stiles

University of Southern California, USA

Liver kinase B 1 (LKB1 or *STK11*) and *PTEN* (phosphatase and tensin homologue deleted on chromosome 10) are two tumor suppressors that both regulate the mTOR signaling pathway. Deletion studies show that loss of either *Stk11* or *Pten* leads to liver injury. In this study, we investigated the molecular mechanisms underlying such toxicity. We show here that the hepatocyte transporter for bilirubin, multidrug resistant protein (MRP2) is significantly affected by LKB1 loss, correlating with the increases in plasma bilirubin levels. Both the levels and localization of MRP2 are altered by LKB1 loss. MRP2 levels are significantly reduced as a result of LKB1 loss in the liver of *Stk11* (LKO) or *Stk11/Pten* (LPKO) double deleted mice vs. the controls. MRP2 is a multi-drug resistant transporter localized to the canalicular membrane of hepatocytes in the control. MRP2 functions to transport various molecules across the apical membrane including bilirubin. In the LKO and LPKO livers, the canalicular localization of MRP2 is lost and became diffusely localized to both nucleus and the cytoplasm. This observed regulation of MRP2 by LKB1 likely contributed to the lack of cellular polarity and the early lethality phenotype associated with LKO mice.

Biography

Bangyan Stiles joined the faculty of the Department of Pharmaceutical Sciences to form the Department of Pharmacology and Pharmaceutical Sciences, at the USC School of Pharmacy in December 2005. She was promoted to Associate Professor with tenure in 2012. Over the past ten years, she has built a successful program that allows her team to explore the complicated pathogenesis of chronic disease and apply therapies to test the translational value of our discoveries. Her group is the leader in understanding the contribution of lipid metabolism to liver cancer targeting the phosphatidylinositol-3 kinase (PI3K) and related signaling pathway.

bstiles@usc.edu

Notes: