Kari Nejak-Bowen, MBA, PhD
Associate Professor of Pathology
Division of Experimental Pathology
University of Pittsburgh

“Therapeutic Implications of Enhancing Beta-Catenin Activation in Hepatocyte Reprogramming”
Thursday, June 23, 2022
12:00 – 1:00 PM EST
901 Biomedical Research Building
Zoom Link

KARI NEJAK-BOWEN’S RESEARCH INTERESTS
For the past 11 years, her research has been focused on understanding the cellular and molecular basis of liver health and disease. Specifically, she is interested in understanding the role of signaling pathways such as Wnt/β-catenin in liver inflammation, injury, and cholestasis. She has identified novel downstream targets of β-catenin in the liver such as regucalcin. She has also demonstrated the advantage of activating β-catenin signaling to enhance liver regeneration. She characterized an inhibitory interaction between β-catenin and the p65 subunit of NF-κB. More recently, she developed a significant interest in cholestatic liver disease, and has made several novel and important findings using models of bile duct injury and cholestasis. First, lack of β-catenin in hepatocytes led to lesser liver injury, fibrosis, and atypical ductular proliferation, as well as decreased total hepatic bile acids and enhanced farnesoid X receptor activation after bile duct ligation (BDL). She recently identified a novel association of β-catenin with FXR that is unresponsive to bile acids or FXR agonists but sensitive to β-catenin inhibition, which causes synergistic activation of FXR in combination with an FXR agonist. Secondly, she is elucidating the role of β-catenin in transdifferentiation of hepatocytes to cholangiocytes during chronic biliary injury, such as 3,5-diethoxycarbonyl-1,4-dihydro-collidine (DDC) diet. Her lab recently identified an upregulation of Wnt signaling after DDC and BDL, and that cholangiocyte markers are absent in hepatocytes of mice lacking Wnt signaling, which coincides with a decrease in survival. Conversely, transgenic mice expressing a S45-mutated non-degradable form of β-catenin in liver (TG) have a significant number of hepatocytes expressing cholangiocyte markers after exposure to DDC diet compared to wild-types (WT). These observations suggest a novel preclinical opportunity to treat intrahepatic cholestasis by stimulating hepatocyte transdifferentiation through activation of Wnt/β-catenin. Her long-term goal is to ultimately apply her knowledge to the development of improved diagnostics and clinically relevant therapies in the treatment of cholestatic liver disease, particularly to primary sclerosing cholangitis, a condition with a significant unmet clinical need.

The meeting will start promptly at 12:00 pm. Please be on time.
Everyone inside and outside of the division is welcome to attend.