

NSHRF PROJECT FACT SHEET

Understanding how the liver functions – and how to combat liver disease

Investigator: Christopher J. Sinal
Assistant Professor
Department of Pharmacology
Dalhousie University

The liver is one of the most important parts of the body. A complex organ with more than 500 functions, it is an essential chemical factory that works on a 24/7 shift. One of the liver's most important functions is to produce bile, which eliminates toxic substances from the body and aids digestion of fats and lipids. Sometimes the liver's ability to eliminate bile acids is impaired, which results in cholestasis (an accumulation of bile in the liver) and related liver diseases. Liver diseases afflict three million, or one in every 10, Canadians. Approximately 3,000 Canadians die each year from chronic liver disease and cirrhosis.

Dr. Christopher Sinal's groundbreaking research is leading to a greater understanding of how the liver functions. His team is investigating how bile acid is handled in the body. They have developed several novel mouse models lacking specific nuclear receptor genes crucial for normal bile acid equilibrium or homeostasis. Using these models, his lab has described the overlapping and complementary roles of various nuclear receptors in regulating normal bile acid metabolism. He determined that drugs that activate the constitutive androstane receptor, a protein that regulates liver toxicity, substantially reduce the toxicity associated with an excess accumulation of bile acid and cholestasis. Dr. Sinal's project has provided significant advances to understanding the mechanisms that contribute to bile acid metabolism in the liver. His long term goal is to identify molecular targets that can be altered by medications to treat cholestatic liver disease.

Dr. Sinal's research is also relevant for cardiovascular and heart disease. One of the receptors he's investigating is FXR – the farnesoid X receptor – mediates bile duct acid and also plays a role in regulating lipoproteins, a combination of a protein and a fat. Thus, it may be a factor in heart disease.

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Contact information:
Christopher J. Sinal
Department of Pharmacology
Dalhousie University
Phone: (902) 494-2347
Christopher.Sinal@Dal.ca

