## Dr. Jihong Lian Department of Pediatrics Supervisor: Dr. Richard Lehner

I obtained my PhD degree from the East China University of Science and Technology. My PhD research focused on the bioactive compounds screening for type 2 diabetes treatment. With potential pharmaceutical targets involved in lipid and glucose metabolism (PPAR, PTP1B, and GLUT4), *in vitro* drug screening models have been developed and several active compounds were identified in the screening work. An *in vivo* mouse model has also been established for the evaluation of these compounds against type 2 diabetes. I have two first-author papers on the related work published in professional journals.

For my research interest in metabolic syndromes, I have been trying to build up a research experience and knowledge in this area. In 2010, I had the opportunity to join Dr. Richard Lehner's



Laboratory at the University of Alberta as a postdoctoral fellow. My research has been focusing on the role of an enzyme Carboxylesterase 3/Triacylglycerol hydrolase (Ces3/TGH) in lipid and glucose homeostasis, and on the evaluation of whether this enzyme can be a pharmaceutical target for the treatment of metabolic diseases.

Ces3/TGH participates in hepatic very low-density lipoprotein (VLDL) assembly. Hyperlipidemia, elevated circulating levels of apolipoprotein B (ApoB)-containing lipoproteins, and insulin resistance are independent risk factors for the atherosclerosis. Ces3/TGH global knockout mice showed reduced plasma lipids and VLDL-size particles without liver steatosis, and improved insulin sensitivity, implicating Ces3/TGH as a potential pharmacological target for the treatment of cardiovascular disease. I have tested the hypothesis and it showed in our research that the inhibition of Ces3/TGH had protective effect against development of dyslipidemia and atherosclerotic plaques. This research has been published in *Circulation Research* and I am the first author.

Since Ces3/TGH also participates in the adipose tissue basal lipolysis, which affects circulating fatty acid contributing to hepatic lipid storage and VLDL secretion, in the current paper published in *Hepatology*, we wished to investigate what effect would liver Ces3/TGH has on lipid metabolism. With liver-specific Ces3/TGH deficient (L-TGH KO) mice, we found that the absence of hepatic Ces3/TGH is the primary cause for the reduced plasma lipids previously observed in global knockout animals. Meanwhile L-TGH KO mice only showed minor increment in hepatic TG content. Importantly, significantly decreased plasma lipid levels with reduced hepatic lipid content were observed in L-TGH KO mice challenged with high-fat, high-cholesterol diet. This work provided important information that pharmacological inhibition of hepatic Ces3/TGH might be sufficient to afford protection against dyslipidemia and fatty liver.

I also have co-author papers published in *Plos One* and *Arterioscler Thromb Vasc Biol* by contributing to other researches in our laboratory. I am currently researching the mechanism of Ces3/TGH deficiency protecting against the non-alcoholic fatty liver disease (NAFLD), and the role of Ces3/TGH in cholesterol homeostasis. For my research work, I have been awarded the Alberta Innovates – Health Solutions (AIHS) Training and Early Career Development Programs Postgraduate Fellowship. In the future, I plan to engage in the discovery and translational (therapy) research in metabolic diseases.