# Research Theme: Metabolic Diseases and Drug Discovery

## Research Project Title: NR4A Nuclear Receptors in Insulin Signaling and Fatty Liver Diseases

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**Co-supervisor/ Collaborator(s) (if any):**

### Project Description

#### a) Background:
Diabetes Mellitus, a metabolic disease characterized by high blood sugar and other chronic symptoms, is a public health concern affecting more than 400 million people worldwide. Pathophysiology of diabetes is focused on the regulator hormone insulin, where Type 1 diabetes signifies an autoimmune destruction of insulin secreting cells, and Type 2 diabetes indicates other cases including insulin resistance and dysfunctional insulin secretion. Although many medications have been introduced to the market, patients develop resistance to available treatments. Insulin resistance is highly associated with nonalcoholic fatty liver diseases such as nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH).

#### b) Proposed work:
In recent years, NR4A subfamily of nuclear receptors, which comprises three members (NR4A1/Nur77, NR4A2/Nurr1 and NR4A3/Nor1), has emerged as important regulatory molecules in the brain and metabolic tissues. Intriguingly, accumulating evidences corroborate that Nor1 plays a key role in beta cell signaling, where it is shown that Nor1 is involved in direct expression of insulin peptide, release of insulin vesicles, and survival of insulin secreting beta cells. Currently, the biological roles of Nor1 in other metabolic diseases such as NAFLD and NASH remain largely unknown. This proposal aim to investigate the biological roles of hepatic Nor1 on fatty liver-related diseases in connection with insulin resistance. In particular, the study will aim to delineate the molecular roles of lipids, inflammatory signaling molecules, and mitochondrial function involved in the disease process.

### Supervisor contact:
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