

"Study the interplay of Sfrp5 and WISP1 in obesity and type 2 diabetes mellitus patients"

A thesis submitted by

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

"قَالُوا سُبْحَانَكَ لَا عِلْمَ لَنَا إِلَّا مَا عَلَّمْتَنَا إِنَّكَ
أَنْتَ الْعَلِيمُ الْحَكِيمُ"

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LIST OF ABBREVIATIONS



List of Abbreviations

ATP	Adenosine triphosphate
BMI	Body mass index
CCN	Cysteine rich 61 (CYR 61) Connective tissue growth factor (CTGF) Nephroblastoma overexpressed (NOV)
CTGF	Connective tissue growth factor
CYR 61	Cysteine rich 61
DM	Diabetes mellitus
FFAs	Free Fatty acids
FPG	Fasting plasma glucose
HbA_{1c}	Glycated haemoglobin
HDL-C	High density lipoprotein cholesterol
hs-CRP	High sensitivity C-reactive protein
HOMA	Homeostatic Model Assessment
IR	Insulin resistance
JNK	c-Jun N-terminal kinase
LDL-C	Low density lipoprotein cholesterol
Met	Metformin
NIDE	National institute of diabetes and endocrinology
NOV	Nephroblastoma overexpressed
OHA	Oral hypoglycemic agents
PI	Proinsulin
Sfrp	Secreted frizzled-related protein
Su	Sulphonylureas
T1DM	Type 1 diabetes mellitus
T2DM	Type 2 diabetes mellitus
TC	Total cholesterol
TCF7L2	Transcription factor 7-like 2
TG	Triglycerides
WC	Waist circumference
WISP	Wnt inducible signaling pathway protein
WHO	World Health Organization

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INTRODUCTION AND AIM OF THE WORK



1. Introduction and Aim of the Work

The global pandemic of obesity, insulin resistance (IR) together with numerous circulating plasma factors contribute in a vicious cycle ultimately leading to progression of type 2 diabetes mellitus (T2DM) and increasing its prevalence (*Tanabe et al., 2017*).

The association of obesity and T2DM is believed to be through biologically active molecules known as adipokines. Adipokines might have a pathophysiological role in IR and β -cell dysfunction which highlights the etiology for T2DM (*Neville et al., 2016; Tanabe et al., 2017*). Unravelling newly identified adipokines massively increases, however the molecular mechanisms by which adipokines affect the pathogenesis of T2DM are not well elucidated.

Secreted frizzled-related protein 5 (Sfrp5) is a recently identified anti-inflammatory adipokine (*Ouchi et al., 2010*). The circulating Sfrp5 level has been extensively studied in field of cancer, but interestingly some animal studies revealed its involvement in obesity, glucose metabolism (*Rulifson et al., 2014; Vincent and Postovit, 2017*) and β -cell proliferation (*Rebuffat et al., 2013*). However, limited human studies reported contradictory data about Sfrp5 in obesity, T2DM and its association with β -cell function and IR.

Wnt1 inducible signaling pathway protein 1 (WISP1), is another recently validated adipokine and a downstream target of Wnt signaling pathway (*Murahovschi et al., 2015*). The circulating WISP1 level has been studied in several fields including cancer (*Zuo et al., 2010*) and atherosclerosis (*Mill et al., 2012; Qi et al., 2016*). Being a target of Wnt1 in Wnt signaling pathways, it has been linked to metabolic disturbances (*Zhong*