

# **Study of Some Novel Adipokines in Type 2 Diabetes Mellitus**

**By**

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## **LIST OF ABBREVIATIONS**

<b>AAP</b>	Amino antipyrine
<b>AGE</b>	Advanced glycation end-products
<b>ALT</b>	Alanine aminotransferase
<b>ANOVA</b>	Analysis of variance
<b>ATP</b>	Adenosine triphosphate
<b>BAT</b>	Brown adipose tissue
<b>BMI</b>	Body mass index
<b>BUN</b>	Blood urea nitrogen
<b>CBC</b>	Complete blood count
<b>CCR</b>	Chemokine receptors
<b>CE</b>	Cholesterol esterase
<b>CETP</b>	Cholesteryl ester transfer protein
<b>CO</b>	Cholesterol oxidase
<b>CRP</b>	C-reactive protein
<b>DEA-HCl/AAP</b>	N,N-diethylaniline-HCl/4-aminoantipyrine
<b>DM</b>	Diabetes mellitus
<b>DSBmT</b>	N,N-bis-(4-sulphobutyl)-m-toluidine-disodium
<b>ELISA</b>	Enzyme linked immunosorbent assay
<b>ER</b>	Endoplasmic reticulum
<b>FAO</b>	Fatty acid oxidation
<b>FFA</b>	Free fatty acids
<b>FPG</b>	Fasting plasma glucose
<b>GK</b>	Glycerol kinase
<b>GLDH</b>	Glutamate dehydrogenase
<b>GLUT-4</b>	Glucose transporter
<b>G-6-PDH</b>	Glucose-6-phosphate dehydrogenase
<b>GPO</b>	Glycerol-3-phosphate oxidase
<b>GSIS</b>	Glucose stimulated insulin secretion
<b>HbA<sub>1C</sub> %</b>	Glycated hemoglobin

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*List of abbreviations*

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<b>HDL-C</b>	High density lipoprotein cholesterol
<b>HK</b>	Hexokinase
<b>H<sub>2</sub>O<sub>2</sub></b>	Hydrogen peroxide
<b>HOMA-IR</b>	Homeostasis model assessment for insulin resistance
<b>HPLC</b>	High performance liquid chromatography
<b>HSL</b>	Hormone sensitive lipase
<b>ICAM-1</b>	Intercellular cell adhesion molecule
<b>IDDM</b>	Insulin dependent diabetes mellitus
<b>IDF</b>	International diabetes federation
<b>IGT</b>	Impaired glucose tolerance
<b>IKK-<math>\beta</math></b>	Inhibitory kappa kinase- $\beta$
<b>IL-1</b>	Interleukin-1
<b>IL-1R</b>	Interleukin-1 receptor
<b>IL-6</b>	Interleukin-6
<b>IRS</b>	Insulin receptor substrate protein
<b>JAK/STAT</b>	Janus kinase/signal transducer and activator of transcription
<b>K<sub>ATP</sub></b>	ATP dependent potassium channel
<b><math>\alpha</math>-KG</b>	$\alpha$ -Ketoglutarate
<b>LDH</b>	Lactate dehydrogenase
<b>LDL-C</b>	Low density lipoprotein cholesterol
<b>LPL</b>	Lipoprotein lipase
<b>MAPK</b>	Mitogen activated protein kinase
<b>MCP-1</b>	Monocyte chemoattractant protein-1
<b>NAD</b>	Nicotinamide adenine dinucleotide
<b>NADH</b>	Reduced nicotinamide adenine dinucleotide
<b>NADP</b>	Nicotinamide adenine dinucleotide phosphate
<b>Nampt</b>	Nicotinamide phosphoribosyl transferase
<b>NF-<math>\kappa</math>B</b>	Nuclear factor kappa B
<b>NIDDM</b>	Non-insulin dependent diabetes mellitus

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*List of abbreviations*

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<b>NIDE</b>	National institute of diabetes and endocrinology
<b>NMN</b>	Nicotinamide mononucleotide
<b>Nmnat</b>	Nicotinamide/nicotinic acid mononucleotide adenylyl transferase
<b>OLETF</b>	Otsuka Long-Evans Tokushima fatty rat
<b>PAI-1</b>	Plasminogen activator inhibitor-1
<b>PBEF</b>	Pre-B-cell colony enhancing factor
<b>PDK-1</b>	Phosphoinositide-dependent kinase-1
<b>PI3K</b>	Phosphatidyl inositol-3-kinase
<b>PKB</b>	Protein kinase B
<b>PKC</b>	Protein kinase C
<b>POD</b>	Peroxidase
<b>PPAR-<math>\gamma</math></b>	Peroxisome proliferator activated receptor-gamma
<b>P5P</b>	Pyridoxal-5-phosphate
<b>RAGE</b>	Receptor for advanced glycation endproducts
<b>RBP-4</b>	Retinol binding protein-4
<b>RLUs</b>	Relative light units
<b>ROS</b>	Reactive oxygen species
<b>R.P.M</b>	Rotation per minute
<b>SAA</b>	Serum amyloid A
<b>SA-HRP</b>	Streptavidin-horseradish peroxidase
<b>S.E.M.</b>	Standard error of mean
<b>Serpin</b>	Serine protease inhibitor
<b>SIRT-1</b>	Sirtuin-1
<b>SOCS</b>	Suppressor of cytokine signaling
<b>SREBP-2</b>	Sterol regulatory element binding protein-2
<b>STAT</b>	Signal transducer and activator of transcription
<b>TC</b>	Total cholesterol
<b>TCA</b>	Tricarboxylic acid cycle
<b>T2DM</b>	Type 2 diabetes mellitus



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*List of abbreviations*

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<b>TG</b>	Triglycerides
<b>TLR</b>	Toll like receptor
<b>TMB</b>	3,3',5,5'- tetramethylbenzidine
<b>TNF- <math>\alpha</math></b>	Tumor necrosis factor alpha
<b>TNFR</b>	Tumor necrosis factor receptor
<b>UCP-1</b>	Uncoupling protein-1
<b>Vaspin</b>	Visceral adipose tissue derived serine protease inhibitor
<b>VCAM-1</b>	Vascular cell adhesion molecule
<b>VLDL</b>	Very low density lipoprotein
<b>WAT</b>	White adipose tissue
<b>WHO</b>	World health organization
<b>WHR</b>	Waist to hip ratio

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## **PUBLICATION RELATED TO THE THESIS**

Vaspin and visfatin/Nampt are interesting interrelated adipokines playing a role in the pathogenesis of type 2 diabetes mellitus. *Metabolism*, In Press, Corrected Proof.

# **1. Introduction and aim of the work**

Type 2 diabetes mellitus (T2DM) is a complex metabolic disorder that affects more than 150 million people worldwide. Its prevalence is expected to increase exponentially around the world particularly in developing countries (*Stumvoll et al., 2005; IDF, 2009*). Insulin resistance and inflammation play a major role in the development of T2DM (*Mlinar et al., 2007*). In addition, increased abdominal/visceral fat is associated with insulin resistance and T2DM (*Antuna-Puente et al., 2008*). Vigorous efforts have been made to delineate the relationship between increased adiposity and insulin resistance. However, the molecular mechanisms that lead to the development of insulin resistance and T2DM are far from complete elucidation.

The realization that adipose tissue acts as an endocrine gland affecting whole-body energy homeostasis was a major breakthrough towards a better molecular understanding of T2DM (*Kershaw and Flier, 2004; Trujillo and Scherer, 2006*), and growing evidence implicates adipocyte-derived factors (adipokines) as major regulators of insulin resistance (*Fasshauer and Paschke, 2003*). Among these adipokines, the inflammatory regulator interleukin-6 (IL-6) has emerged as one of the potential mediators that link obesity-derived chronic inflammation with insulin resistance (*Kim et al., 2009*). A growing body of evidence has established IL-6 as an important player in metabolic disease states, such as diabetes (*Pradhan et al., 2001; Hu et al., 2004; Kim et al., 2009*).

Interestingly, *Hida and co-workers (2005)* isolated a unique insulin-sensitizing adipokine termed visceral adipose tissue-derived serine protease inhibitor (vaspin) from the visceral adipose tissue of an animal model of visceral obesity