Study of Some Novel Adipokines in Type 2 Diabetes Mellitus

By

Dina Hamada Mahmoud Kassem

Demonstrator of Biochemistry, Faculty of Pharmacy, Ain Shams University
B.Ph.Sci., Ain Shams University, 2005

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Under supervision of

Dr. Hala Osman El-Mesallamy
Professor of Biochemistry
Head of Biochemistry Department
and Ex-Vice Dean for Community and Environmental Affairs
Faculty of Pharmacy
Ain Shams University

Dr. Ashraf Ismail Amin
Professor of Clinical Pathology
Head of Clinical Pathology and Laboratory Department
National Institute of Diabetes and Endocrinology (NIDE)

Dr. Ebtehal El-Demerdash Zaki
Assistant Professor of Pharmacology and Toxicology
Acting Head of Pharmacology and Toxicology Department
Faculty of Pharmacy
Ain Shams University

Biochemistry Department
Faculty of Pharmacy
Ain Shams University
(2010)

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LIST OF ABBREVIATIONS

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

HDL-C	High density lipoprotein cholesterol
HK	Hexokinase
H_2O_2	Hydrogen peroxide
HOMA-IR	Homeostasis model assessment for insulin resistance
HPLC	High performance liquid chromatography
HSL	Hormone sensitive lipase
ICAM-1	Intercellular cell adhesion molecule
IDDM	Insulin dependent diabetes mellitus
IDF	International diabetes federation
IGT	Impaired glucose tolerance
IKK-β	Inhibitory kappa kinase-β
IL-1	Interleukin-1
IL-1R	Interleukin-1 receptor
IL-6	Interleukin-6
IRS	Insulin receptor substrate protein
JAK/STAT	Janus kinase/signal transducer and activator of transcription
K_{ATP}	ATP dependent potassium channel
α-KG	α-Ketoglutarate
LDH	Lactate dehydrogenase
LDL-C	Low density lipoprotein cholesterol
LPL	Lipoprotein lipase
MAPK	Mitogen activated protein kinase
MCP-1	Monocyte chemoattractant protein-1
NAD	Nicotinamide adenine dinucleotide
NADH	Reduced nicotinamide adenine dinucleotide
NADP	Nicotinamide adenine dinucleotide phosphate
Nampt	Nicotinamide phosphoribosyl transferase
NF-κB	Nuclear factor kappa B
NIDDM	Non-insulin dependent diabetes mellitus

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

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