Study of the Adipocytokine visfatin in Obesity and Type 2 Diabetes Mellitus

Thesis

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List of Abbreviation

ACC	**Acetyl-CoA carboxylase**
ADIPO R2	**Adiponectin receptor 2**
AGTR	**Agouti Related peptide**
AIDS	**Acquired immune deficiency syndrome**
AKT	**Members of Protein kinase B**
ALI	**Acute lung Injury**
AMPK	**5' adenosine monophosphate-activated protein kinase**
APOA-IV	**Apo-lipoprotein A- IV**
AR	**Adrenergic Receptors**
ATP	**Adenosine Tri Phosphate**
ATP III	**Adult treatment panel III**
BAT	**Brown Adipose Tissue**
BDNF	**Brain-Derived Neurotrophic Factor**
BMI	**Body Mass Index**
BMR	**Basal Metabolic Rate**
BNP	**Brain Naturetic Peptide**
BP	**Blood Pressure**
CCL2	**Chemokine (C-C motif) ligand 2**
CGRP	**Calcitonin Gene Related peptide**
CHD	**Coronary Heart Disease**
CNS	**Central Nervous System**
CPE	**Carboxy Peptidase E**
CRH	**Cortico trophin Releasing Hormone**
CRP	**C-Reactive Protein**
CT	**Computerized tomography**
CVS	**Cardiovascular disease**
DBP	**Diastolic Blood Pressure**
DBP	**Diastolic blood pressure**
DM	**Diabetes mellitus**
DoHaD	**Developmental origins of health and disease**
EDHF	**Endothelium Derived Hyperpolarizing Factor**

EGIR	**European Group for the study of Insulin Resistance**
ELISA	**Enzyme Linked Immune Assay**
ENPP1	**Ectonucleotide pyrophosphatase/phosphodiesterase 1**
ERKs	**Extracellular Signal-Regulated kinases**
ETC	**Electron Transport Chain**
FFA	**Free Fatty Acid**
FIZZ3	**Found in inflammatory zone 3**
G6Pase	**Glucose 6 phosphatase**
G6PDH	**Glucose 6 phosphate dehydrogenase**
GDM	**Gestational diabetes**
GH	**Growth Hormone**
GLP-1	**Glucagon like peptide 1**
GLUT	**Glucose transporter**
HAART	**Highly Active Antiviral Therapy**
HDL	**High Density Lipoprotein**
HIV	**Human immunodeficiency virus**
HNF4A	**Hepatocyte nuclear factor 4 alpha**
HOMA	**Homeostatic Model Assessment of insulin**
HOMA(IR)	**Homeostatic Model Assessment of Insulin Resistance**
HPA	**Hypothalamo Pituitary Axis**
HSC	**Hepatic Stellate Cells**
HSL	**Hormone Sensitive Lipase**
HTN	**Hypertension**
IAPP	**Islet Amyloid Poly Peptide**
IBW	**Ideal Body weight**
IDF	**International Diabetes Federation.**
IFG	**Impaired Fasting Glucose**
IFG	**Impaired fasting glucose**
IGT	**Impaired Glucose Tolerance**
IHD	**Ischemic Heart Disease**
IKK	**Inflammatory Kinase inhibtor Кβ Kinase**
IKβ	**Inhibitor of Ķ β**
IL	**Interleukin**
IR	**Insulin Resistance**
IRS-1	**Insulin Receptor Substrate-1**

IUGR	**Intra Uterine Growth Retardation**
JNK	**c-Jun NH3 terminal kinase**
KCNJ11	**ATP-sensitive potassium channel**
KIR 6.2	**Potassium Inward rectifier 6.2**
KO	**Knock Out**
LC-CoA	**long-chain coenzyme A**
LDL	**Low Density Lipoprotein**
LDLR	**Low Density Lipoprotein Receptor**
LPL	**Lipoprotein lipase**
LVH	**Left Ventricular Hypertrophy**
LVM	**Left Ventricular Mass**
MAPK	**Mitogen activated Protein Kinase**
MC	**MelanoCortin**
MCF-7	**Michigan Cancer Foundation - 7**
MCP-1	**Monocyte chemotactic protein-1**
MCR	**Melanocortin Receptor**
MODY	**Maturity onset diabetes of the young**
MRS	**Magnetic Resonance Spectroscopy**
MSH	**Melanocyte Stimulating Hormone**
MSX	**Metabolic Syndrome**
NAD	**Nicotin amide dinucleotide**
NAFLD	**Non Alcholic Fatty Liver Disease**
NAM	**Nicotine amide mononucleotide**
NamPRTase	**Nicotine amide phoshop ribosyl transferase**
NASH	**Non Alcoholic Steatohepatitis**
NCEP	**National Cholesterol Education program**
NEFA	**Non Esterified free fatty acid**
NF-Κβ	**Nuclear Factor- Kappa Beta**
NGF	**Nerve Growth Factor**
NGT	**Normal Glucose Tolerance**
NIY5	**Neuron peptide Y 5**
Ob	**Obese gene**
OGTT	**Oral Glucose Tolerance Test**
OLETF	**Otsuka Long Evans Tokushima Fatty**
OSA	**Obstructive Sleep Apnea**

PAI-I	**Plasminogen Activator Inhibitor 1**
PASP	**Pulmonay Artery Systolic Pressure**
PBEF	**Pre Beta colony Enhancing Factor**
PCOS	**Polycystic Ovarian Syndrome**
PDX-1	**Pancreas Duodenum Homeobox-1**
PET	**Positron Emission Tomography**
PGC1	**Peroxisome proliferator-activated receptor Gamma coactivator 1**
PI 3-kinases	**Phosphoinositide 3-kinases**
PI-3K	**Phosphatidyl Inositol 3 Kinase**
PKCE	**Protein Kinase Carboxy Peptidase E**
POMC	**ProOpioMelanoCortin**
PPARγ	**Peroxisome Proliferators Activator Receptor γ**
PTP1B	**protein tyrosine-phosphatase 1B**
RBP -4	**Retinol Binding Protein -4**
RIA	**Radio Immuno Assay**
RMR	**Resting Membrane Rate**
RNS	**Reactive Nitrogen Species**
ROS	**Reactive oxygen Species**
RXR	**Retinoid X Receptor.**
SBP	**Systolic blood pressure**
SHBG	**Sex Hormone Binding Globulin**
Sir2	**sirtuin genes**
SNPs	**Single nucleotide polymorphism**
SOCS	**Suppressor of cytokines signaling**
SPARC	**Secreted Protein Rich in Cysteine**
STAT	**Signal Transducer and activator of transcription**
SUR 1	**Sulfonylurea Receptor1**
TAG	**Tri Acyl Glycerol**
TCF7L2	**Transcription factor 7-like 2**
TG	**Triglycerides**
THP1	**Human acute monocytic leukemia cell line**
TNFα	**Tumor necrosis Factor α**
TrkA	**Tyrosine Kinase A**
Trp 64 Arg	**Tryptophan in position 64 to Arginine**

TZDs	**Thiazolidinediones**
UCP-1	**Uncoupling Protein -1**
UCP-2	**Uncoupling Protein -2**
UTI	**Urinary tract infection**
VLDL	**Very low Density Lipoprotein**
vWF Ag	**Von –Willebrand factor antigen**
WAT	**White adipose tissue**
WC	**Waist Circumference.**
WHO	**World Health Organization**
WHR	**Waist Hip Ratio**
WT	**Wild Type**
α AR	**Alpha 1 adrenergic receptor**
β 2 AR	**Beta 2 adrenergic receptor**
β 3 AR	**Beta 3 adrenergic receptor**

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Introduction

Excess Adiposity is the most important risk in the development of insulin resistance and type 2 diabetes mellitus **(Bloomgarden, 2002).** Adipose tissue produces several proteins (adipocytokines) such as leptin, adiponectin, resistin, TNF α , and IL-6, that modulate insulin sensitivity and appear to play an important role in the pathogenesis of insulin resistance, diabetes, dyslipidemia, inflammation, and atherosclerosis **(Kershaw et al., 2004)**.
Several adipokines including adiponectin, leptin, and interleukin (IL)-6, have been linked to the development of diabetes **(Thorand et al., 2005)**.

In most studies, low adiponectin **(Lindsay et al., 2002; Kanaya et al., 2006)** and elevated IL-6 have been associated with the development of subsequent diabetes independent of obesity, and some have shown the associations to be independent of measures of insulin **(Duncan et al., 2004)**.
However, the mechanisms by which fat tissue induces insulin resistance and the role of adipocytokines in the pathogenesis of Type 2 Diabetes Mellitus has not been well established **(Chen et al., 2006).**

In 2004, Fukuhara et al., identified a molecule that is expressed at much higher levels in visceral than in subcutaneous fat which was named Visfatin **(Fukuhara et al., 2005)**.

Visfatin, also known as pre-B cell colony-enhancing factor, is a cytokine that is highly expressed in visceral fat and was originally isolated as a secreted factor that synergizes with IL-6 and stem cell **(Kralisch et al., 2005b)**.

Visfatin was reported to be expressed almost exclusively in visceral adipose tissue and has insulin-like metabolic effects **(Fukuhara et al., 2005).**

It turns out that the molecule was previously identified as a growth factor for early B-lymphocytes termed pre-B cell colony enhancing factor (PBEF) **(Samal et al., 1994)**.

The visfatin gene is expressed in adipocytes, where it is subject to regulation **(Kralisch et al., 2005b)**.

Furthermore, in humans the gene is expressed predominantly in visceral adipose tissue as compared with subcutaneous adipose tissue human adipose tissue, this fact could provide a novel mechanism by which visceral fat accumulation can promote the development of Type 2 Diabetes Mellitus **(Sethi et al., 2005).**

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Aim of work

The aim of the work is to study the role of plasma Visfatin in Obesity and type 2 DM.

Obesity

Definition:

In its most simplistic definition, obesity means an excess body fat. Excess weight per se, is an inadequate definition because weight can increase as a result of increased mass, fluid retention, pregnancy leading to a state of overweight in which weight exceeds a standard based on height. It is possible to be obese at a weight within normal, according to standard tables, just as it possible to be overweight without being obese. However, in most people, overweight and obesity tend to parallel to each other ***(Fetissov, 2009).*** Obese individuals differ in the amount of excess fat they store, and also in the regional distribution of that fat within the body. The distribution of fat induced by weight gain affect the risk associated with obesity and the kind of the disease that result **(WHO, 2000).**

Measurement:

Overweight and obesity are assessed in a variety of ways depending on the necessity for accuracy.

I-Weight for height: the tables of the Metropolitan Life Insurance Company are widely used to establish a standard of ideal body weight (IBW). The term overweight refers to an excess of body weight and usually determined by comparing a person's weight against the standard height and weight chart. If a person's weight is 10 percent greater than the standard, he or she is considered to be overweight, and obese if the weight is 20 percent or more than the standard weight for height, morbid obesity when one weighs in excess of 30 percent of the standard. A person is underweight if he or she is 10 percent below recommended weight for height **(Fetissov, 2009).**

2- Body mass index (BMI): the more preferred methods include body mass index (BMI), or Quetelet index (W/H2), the formula used for the BMI was developed over a hundred years ago by a