

The Association Between Adiponectin with Lipid Profile and Troponin in Acute Myocardial Infarction Patients

Ammal Esmaeel Ibrahim* ,Hadeef Dhafer EL-Yassin*,
Hamid Kareem Sachit AL-Janabi**

ABSTRACT:

BACKGROUND:

Adiponectin is thought to be exclusively synthesized by adipocytes; however, a recent suggestion stated that adiponectin is also synthesized and secreted by human cardiomyocytes. Adipose tissue is increasingly recognized as a key regulator of energy balance, playing an active role in lipid storage and buffering, and synthesizing and secreting a wide range of endocrine products that may be directly involved in the pathogenesis of the complications associated with obesity. So obesity consider the major independent risk factor for atherosclerotic cardiovascular disease Acute Myocardial Infarction (AMI), is the interruption of blood supply to part of the heart, causing some heart cells to die. Insulin is a very important hormone as it regulates the level of glucose, in the blood. Troponin is a complex of three regulatory proteins that is integral to muscle contraction in skeletal and cardiac muscle.

OBJECTIVE:

To monitor adiponectin level and its effect on lipid profile and Troponin levels in Acute Myocardial infarction patients.

SUBJECTS AND METHODS:

The study included 50 patients with Acute Myocardial infarction and forty healthy subject as control group. This study designed to measure adiponectin, lipid profile and troponin levels.

RESULTS:

Levels of adiponectin, cholesterol, LDL-C and Troponin were significantly elevated with ($p < 0.001$), while HDL-C was significantly lower with ($p < 0.001$), There was negative correlation between adiponectin with , cholesterol LDL-C, triglyceride and VLDL, and there was positive correlation between adiponectin with HDL in acute myocardial infarction.

CONCLUSION:

The significant increase in adiponectin in AMI may be related to inflammation. From the relation of adiponectin with lipid profile, adiponectin can increase level of HDL and decrease level of triglyceride so this suggested that adiponectin have anti-atherosclerosis properties.

KEY WORD: Adiponectin, Lipid profile, Troponin and Acute Myocardial Infarction.

INTRODUCTION:

Adipose tissue is increasingly recognized as a key regulator of energy balance, playing an active role in lipid storage, buffering, synthesizing and secreting a wide range of endocrine products that may be directly involved in the pathogenesis of the complications associated with obesity. So obesity consider the major independent risk factor for atherosclerotic cardiovascular disease. Initially, adiponectin was thought to be exclusively synthesized by adipocytes; however, a recent study suggests that

adiponectin is also synthesized and secreted by human cardiomyocytes.⁽¹⁾ This may explain why adiponectin is increasing in obese subjects with AMI while it supposed to decrease in obese subjects, but how much this cardiomyocytes effect on the total concentration of adiponectin this needs more investigations. Acute

Myocardial Infarction (AMI), is the interruption of blood supply to part of the heart, causing some heart cells to die. This is most commonly due to occlusion of a coronary artery following the rupture of a vulnerable atherosclerotic plaque, which is an unstable collection of lipids and white blood cells in the wall of an artery. The resulting ischemia and oxygen shortage, if left

*Department of Physiology Chemistry, College of Medicine University of Baghdad.

**Department of Internal Medicine, Collage of Medicine, University of Baghdad.

untreated for a sufficient period of time, can cause damage or death of heart muscle tissue. ⁽²⁾

Insulin is a peptide hormone composed of 51 amino acids. It is produced in the islets of Langerhans in the pancreas. The name comes from the Latin *insula* for "island". Insulin is synthesized in significant quantities only in beta cells in the pancreas. The insulin mRNA is translated as a single chain precursor

called preproinsulin, and removal of its signal peptide during insertion into the endoplasmic reticulum generates proinsulin. ⁽³⁾

Proinsulin consists of three domains an amino-terminal B chain, a carboxy-terminal A chain and a connecting peptide in the middle known as the C peptide. Within the endoplasmic reticulum, proinsulin is exposed to several specific endopeptidases which excise the C peptide, thereby generating the mature form of insulin. Insulin and free C peptide are packaged in the Golgi into secretory granules which accumulate in the cytoplasm. When the beta cell is appropriately stimulated, insulin is secreted from the cell by exocytosis and diffuses into islet capillary blood. C peptide is also secreted into blood, but has no known biological activity ⁽³⁾.

Troponin is a complex of three regulatory proteins that is integral to muscle contraction in skeletal and cardiac muscle. Troponin is attached to the protein tropomyosin and lies within the groove between actin filaments in muscle tissue. In a relaxed muscle, tropomyosin blocks the attachment site for the myosin crossbridge, thus preventing contraction. When the muscle cell is stimulated to contract by an action potential, calcium channels open in the sarcoplasmic reticulum and release calcium into the sarcoplasm. Some of this calcium attaches to troponin, causing a conformational change that moves tropomyosin out of the way so that the cross bridges can attach to actin and produce muscle contraction. Troponin is found in both skeletal muscle and cardiac muscle, but the specific versions of troponin differ between types of muscle. The main difference is that the TnC subunit of troponin in skeletal muscle has four calcium ion binding sites, whereas in cardiac muscle there are only three ⁽⁴⁾.

SUBJECTS:

This study was performed during the period from December 2009 to April 2010. This study include fifty patients with Acute Myocardial Infarction (AMI) were admitted to Cardiac Care Unit (CCU) at Medical City Teaching Hospital and

Ibn –ALbetar Hospital. Patients with age rang (20-78) years. Blood samples were taken from the patients after thorough examination. Subjects with a history of AMI or diabetes mellitus or any chronic diseases were excluded from the study. Forty healthy individuals were taken as a control group. They were comparable with patients group by their age, sex and BMI.

Blood collection and laboratory analysis

From each patients and control, five ml venous blood were aspirated from a suitable vein. Samples were collected between (8-9 A.M.) after 10 hours fast. Blood samples were divided into two parts, three ml transferred to a plain tube for lipid profile. The remaining of blood transferred to another sterile plain tubes for storage to measure the hormones. The non heparinized blood in the plain tubes were left to clot and then centrifuged at 4000 rpm for 5 minutes to separate the serum and dispensed into tightly closed Eppendorf tubes in 1.0 ml and stored at -20 C° until assayed. Each serum sample was analyzed for urea and creatinin to excluded kidney diseases. Other parameters included in this study: Lipid profile were measured by using standard methods with reagents from BioMaghreb Company – Tunisia, adiponectin and troponin were measured by using ELISA kits from United States Biological Company.

Statistical analysis

Statistical analysis was performed by statisticians with the SPSS 15.01 Statistical Package for Social Sciences and also Excel 2003. Data analysis was done using chi- square test for tables with frequencies, while we used independent sample t-test for tables with means and standard deviations. *p* value of ≤ 0.05 was used as the level of significance. Correlation coefficient used to find the correlation between studied markers by using Pearson correlation. Descriptive statistics for the clinical and laboratory results were formulated as mean and standard error.

RESULTS:

Lipid profile and troponin:

Serum levels of adiponectin, lipid profile and troponin were compared between patients groups and control group using analysis of variance t-test of significant as in table (2). Patients with MI were found to have significantly higher serum cholesterol, LDL, LDL/HDL, and troponin ($p < 0.001$) and significantly lower HDL ($p < 0.001$) compared with control group.

LIPID PROFILE AND TROPONIN IN ACUTE MYOCARDIAL INFARCTION

Table 1: Comparison between groups for (Adiponectin, lipid profile and troponin)

parameters	Female patients Mean±SR NO.=16	Female Control Mean±SR NO.=16	P-value	Male Patient Mean±SR NO.=24	Male Control Mean±SR NO.=34	p -value	Total Patients Mean±SR NO.=50	Total Control Mean±SR NO.40	P- value
Adiponectin g/ml	59.46 ±18.09	13.769±5 .095	<0.001	50.01 ±10.93	13.279 ±6.817	<0.001	54.68 ±13.88	13.48 ±2.09	<0.001
Total cholesterol mg/dl	183.76 ±49.20	99.478 ±25.225				<0.001	177.40 ±25.59	104.17 22.68±	<0.001
Triglyceride mg/dl	142.937±14.5 76	138.05 ±16.62	0.484	152.96 ±11.71	133.478 19.153	0.051	141.26 ±12.93	137.35 ±18.87	0.744
HDL mg/dl	37.71 ±3.06	59.777 ±10.458	<0.001	29.36 ±8.82	69.737± 8.249	<0.001	39.26 ±2.50	67.26 ±11.08	<0.001
LDL mg/dl	154.36 ±6.64	100.937 ±10.959	<0.001	156.80 ±12.04	119.852 ±8.753	<0.001	149.42 ±25.50	106.26 ±2.50	<0.001
LDL/HDL	3.82	0.361	<0.001	4.95	0.313	<0.001	4.56	0.350	<0.001
VLDL mg/dl	35.387 ±6.746	27.57 ±2.32	0.508	39.58 ±6.33	26.521± 5.737	0.051	38.23 ±8.58	27.28 ±8.64	0.744
Troponin ng/ml	34.63 ±6.51	-----	--	38.18 ±9.95	-----	--	30.21 ±8.36	0.0	-----

Table 2: The correlation between adiponectin with(lipid profile and troponin) for studied groups.

parameters	Female Patients NO.=16	Female Control NO.=16	Male Patients NO.=34	Male Control NO.=24	Total Patients NO.50	Total Control NO.=40
Cholesterol	-0.550	-0.361	-0.597	-0.396	-0.561	-0.379
Triglyceride mg/dl	-0.633	-0.391	-0.504	-0.355	-0.512	-0.372
HDL	0.532	0.427	0.609	0.503	0.509	0.409
LDL mg/dl	-0.489	-0.461	-0.438	-0.256	-0.408	-0.366
LDL/HDL	-0.497	-0.416	-0.522	-0.406	-0.425	-0.401
VLDL	-0.552	-0.434	-0.566	-0.367	-0.513	-0.471
Troponin	-0.641	---	-0.619	--	-0.637	----

Relation between adiponectin with (lipid profile and troponin):

The results showed that there was strong positive correlation between adiponectin with HDL in female patient group ($r=0.532$), in male patient group ($r=0.609$) and in total patient ($r=0.509$). While the positive correlation was found between adiponectin with HDL in female control group ($r=0.427$) and in total control ($r=0.409$).

The strong negative correlation was found between adiponectin with cholesterol in female patient group ($r=-0.550$), in male patient group ($r=-0.597$) and in total patient ($r=-0.561$), also with triglyceride in female patient group ($r=-0.633$), in male patient group ($r=-0.504$) and in total patient ($r=-0.521$), also with LDL/HDL in male patient group ($r=-0.522$), with VLDL in female patient group ($r=-0.566$) and total patient ($r=-0.513$), with troponin in female patient group ($r=-0.641$) in male patient group ($r=-0.619$) and in total patient ($r=-0.637$).

DISCUSSION:

Kobayashi in 2009⁽⁵⁾ demonstrated that adenovirus mediated increase of plasma adiponectin significantly suppressed the progression of atherosclerotic lesions in apoE ob/ob mice. These mice develop hyperlipidemia and vascular lesions similar to human atherosclerosis. Adenovirus-derived adiponectin accumulated in the fatty streak lesions composed of macrophages and foam cells in apoE ob/ob mice⁽⁵⁾

Animal data support adiponectin as a cardiovascular protective molecule. In a mouse model of acute MI, adiponectin null mice responded with larger infarct sizes, greater myocardial cell apoptosis, and increased tumour necrosis factor expression when compared with wild-type controls. Rescue attempts with adiponectin delivered by adenovirus, and recombinant adiponectin infusion prior to or during the ischaemia-reperfusion procedure, ameliorated all the associated damaging effects, suggesting that exogenous adiponectin protects the heart against ischaemic insults⁽⁶⁾. That agree with our notice that the patients with higher levels of adiponectin have good prognosis.

Adiponectin was also demonstrated to inhibit strongly the expression of adhesion molecules, including intracellular adhesion molecule-1, vascular cellular adhesion molecule-1, and E-selectin. Adiponectin was also shown to inhibit TNF- α -induced nuclear factor- κ B activation through the inhibition of κ B phosphorylation .

Suppression of nuclear factor- κ B by adiponectin might be a major molecular mechanism for the inhibition of monocyte adhesion to endothelial cells (VCAM-1 play a pivotal role in the development of atherosclerosis. The expression of VCAM-1 localized over the surface of endothelial cells in lesion-prone sites). Adiponectin also inhibits the expression of the scavenger receptor class A-1 of macrophages, resulting in markedly decreased uptake of oxidized low-density lipoprotein by macrophages and inhibition of foam cell formation. In addition, in cultured smooth muscle cells, adiponectin attenuated DNA synthesis induced by growth factors including platelet-derived growth factor, heparin-binding epidermal growth factor (EGF)-like growth factor, basic fibroblast growth factor, and EGF, as well as cell proliferation and migration induced by heparin binding EGF-like growth factor.⁽⁷⁾

(Wolfgang Koenig, et al, 2009)⁽⁸⁾ study on adiponectin-deficient mice have shown a 2-fold increase in neointimal thickening and increased proliferation of vascular SMCs in arteries after mechanical injury. That agree with what we noticed with patients, that the thickness of artery in ECO monitoring may be associated negatively with adiponectin level. In addition, adiponectin knockout mice showed high levels of TNF- α mRNA in adipose tissue. Thus suggest an antidiabetic and antiatherogenic role of increased concentrations of adiponectin and that hypoadiponectinemia, in particular in combination with low HDL-C, therefore might be associated with a strongly increased risk of T2DM and atherosclerotic disease. The effects of both, low adiponectin and low HDL-C on endothelial dysfunction, and their enhancement of an inflammatory response may represent plausible arguments for their additive effect on risk.⁽⁸⁾

Atul Singhal⁽⁹⁾ studied adiponectin in vitro and suggested that adiponectin reduced the development of atherosclerosis by stimulating the production of nitric oxide from vascular endothelial cells⁽⁹⁾

On the other hand, low adiponectin levels are associated with reduced expression of nitric oxide, and increased expression of angiotensin II and cellular adhesion molecules from the endothelium.⁽¹⁰⁾

In humans, there are many offensive factors, including oxidized LDL (as our results showed

that there was significantly higher level of LDL in our patients as in table (2), inflammatory stimuli, and chemical substances that may induce vascular injuries. At that time, adiponectin secreted from adipose tissues

may go into the injured arteries and protect against the development of atherogenic vascular changes. Therefore, adiponectin might be likened firefighters who put out the fire of the vascular walls while it is still small. When the plasma levels of adiponectin are decreased in the subjects with visceral fat accumulation, the small fire may become bigger and bigger because of the shortage of firefighters⁽¹¹⁾.

The mortality rate was also inversely related to BMI, most probably reflecting the known association of cardiac 'wasting' with increased mortality, suggesting that the paradoxical increase of adiponectin levels in those with the highest mortality may have been secondary to weight loss, a known stimulator of adiponectin.

Despite all the counter-regulatory mechanisms that are mobilized in the high-risk patients, including up-regulation of plasma adiponectin levels, it is intuitive that the reparative processes of the body may be overwhelmed, translating into higher cardiovascular morbidity. The anti-inflammatory effects of adiponectin indicate that it is an interesting protective factor for atherosclerosis development, particularly in those clinical situations associated with low plasma concentrations of adiponectin. It is conceivable that the use of recombinant adiponectin may become beneficial in the prevention of cardiovascular disease in selected patients. That suggest the increasing plasma adiponectin might be useful in preventing vascular restenosis after vascular intervention⁽¹²⁾. This suggestion agrees with our results because adiponectin is negatively correlated with cholesterol, triglyceride and VLDL-C, the most important with LDL-C, while positively correlated with HDL as shown in tables(3) and these relations make adiponectin act as cardio-protective factor.

Further investigations in patients with the above-mentioned states and other hypo adiponectinemic conditions are required to clarify these aspects of the potential therapeutic applications of this adipocytokine⁽¹³⁾

Osamu et al 2009⁽¹⁴⁾ demonstrated a novel effect of natriuretic peptides (ANP and BNP) on the production of adiponectin by adipocytes in both experimental and clinical studies. By:

-First, they clearly demonstrated that pathophysiological and pharmacological concentrations of either ANP or BNP increased adiponectin synthesis by primary cultured human adipocytes.

-Second, they showed that administration of recombinant ANP increased the plasma adiponectin level.

Adiponectin with lipid

This study showed negative correlation between adiponectin with (Cholesterol and LDL-C) in table (1). Adiponectin has been shown to regulate weight reduction as well as free fatty acid oxidation in mouse muscle and liver. The full-length recombinant adiponectin protein is apparently less potent at mediating these effects. The mechanism underlying the role of adiponectin in lipid oxidation may involve the regulation of production or activity of proteins associated with triglyceride metabolism, including acyl CoA oxidase, activated protein kinase, and peroxisome proliferator- activated receptor γ (PPAR γ). A negative correlation between obesity and circulating adiponectin has been well established, and adiponectin concentrations increase concomitantly with weight loss.⁽¹³⁾

Magnetic resonance spectroscopy has demonstrated that intracellular lipid content in human muscle negatively correlates with adiponectin concentrations, potentially because of adiponectin-induced fatty acid oxidation.⁽¹³⁾

Adiponectin with HDL

This study showed a positive correlation between adiponectin with HDL in table (2). High levels of adiponectin are associated with high levels of HDL-cholesterol indicating a protective risk profile.

Also some studies showed a relation between the adiponectin and Coronary heart disease risk factors, these results collectively indicate that plasma HDL cholesterol levels and visceral fat masses are independently associated with plasma adiponectin concentrations.⁽¹⁵⁾

Adiponectin with triglyceride

In this study there was negative correlation between adiponectin with (triglyceride and VLDL-C) in table (2).

Adiponectin increased fatty-acid combustion and energy consumption, presumably via PPAR γ activation at least in part, which led to decreased TG content in the liver and skeletal muscle and

thus coordinately increased *in vivo* insulin sensitivity.⁽¹⁶⁾

Interestingly, in skeletal muscle, adiponectin increased expression of molecules involved in fatty-acid transport such as CD36, in combustion of fatty-acid such as acylcoenzyme A oxidase, and in energy dissipation such as uncoupling protein. These changes led to decreased tissue TG content in skeletal muscle. Increased tissue TG content has been reported to interfere with insulin-stimulated

phosphatidylinositol (PI) 3-kinase activation and subsequent glucose transporter translocation and glucose uptake, leading to insulin resistance. Thus, decreased tissue TG content in muscle may contribute to improved insulin signal transduction. This was demonstrated in skeletal muscle of lipoatrophic mice treated with adiponectin, in which increases in insulin-induced tyrosine phosphorylation of insulin receptor and insulin receptor substrate-1 and insulin-stimulated phosphorylation of Akt.⁽¹⁷⁾

Adiponectine with VLDL

As shown in table (2) there was negative correlation between adiponectin and VLDL-C I could not find agree or disagree study for this relation between adiponectin and VLDL-C Adiponectin decreases the plasma concentration of very low-density lipoprotein (VLDL) apolipoprotein (Apo)-B in middle-aged men by increasing its rate of catabolism, this association is independent of the effect of insulin resistance on hepatic VLDL ApoB secretion and may result principally from the effect of adiponectin on lipid metabolism in skeletal muscle. This may explain why low plasma adiponectin levels are associated with atherogenic dyslipidemia [*i.e.* elevated triglycerides, low high-density lipoprotein cholesterol, and a preponderance of small dense low-density lipoprotein (LDL) particles].⁽¹⁸⁾

Adiponectin with troponin

To our knowledge we are the first in our country who report a relationship between adiponectin and troponin, as table (2) shows that there is a negative correlation between adiponectin with troponin, as troponin referred to the infarction size this negative correlation give a good idea about adiponectin as it may have good effect (as it explained previously in adiponectin and its effect on artery wall by increasing NO production in addition to its ability to decreasing ICAM) on heart by decreasing the infarction area size.

CONCLUSION:

- There are significant increase of adiponectin level in AMI patients, the negative association between adiponectin with troponin suggests a protective effect of adiponectin on heart.
- The relation of adiponectin with lipid profile shows that adiponectin can increase the level of HDL and decrease the level of triglyceride so this suggests that adiponectin have anti-atherosclerosis properties.

REFERENCES:

1. Yulin Liao, Wanling Xuan, Jing Zhao, Jianpin Bin, Hui Zhao, Masanori Asakura, Tohru Funahashi, Seiji Takashima, Masafumi Kitakaze. "Antihypertrophic effects of adiponectin on cardiomyocytes are associated with the inhibition of heparin-binding epidermal growth factor signaling". *Biochemical and Biophysical Research Communications*:2010:393:519-25.
2. Kosuge, M; Kimura K, Ishikawa T et al. "Differences between men and women in terms of clinical features of ST-segment elevation acute myocardial infarction". *Circulation Journal*. 2006;70:222–26.
3. Ivanova MI, Sievers SA, Sawaya MR, Wall JS, Eisenberg D. "Molecular basis for insulin fibril assembly". *Proc. Natl. Acad. Sci. U.S.A.* November 2009;106:18990–19005.
4. Ammann P, Pfisterer M, Fehr T, Rickli H. "Raised cardiac troponins." *BMJ*. 2004;328:1028-29.
5. Kobayashi, Naoki Terasaka, Toshimori Inaba, Tohru Funahashi and Yuji Matsuzawa Masahiro Kumada, Koji Ohashi, Naohiko Sakai, Ichiro Shimomura, Hideki Yoshihisa Okamoto, Shinji Kihara, Noriyuki Ouchi, Makoto Nishida, Yukio Arita."Adiponectin Reduces Atherosclerosis in Apolipoprotein E-Deficient Mice." *American Heart Association. Circulation* 2009;106:2767-70.
6. Subodh Verma."adipoinectin and therosclerosis." *European Heart Journal* :2006;27,2266–68.
7. Ouchi N, Kihara S, Arita Y, et al." Adipocyte-derived plasma protein, adiponectin, suppresses lipid accumulation and class A scavenger receptor expression in human monocyte-derived macrophages". *Circulation*.2010;110:1057–63.

8. Wolfgang Koenig, MD, FACC, Natalie Khuseyinova, MD, Jens Baumert, PHD, Christa Meisinger, MD, MPH, Hannelore Löwel, MD ."Serum Concentrations of Adiponectin and Risk of Type 2 Diabetes Mellitus and Coronary Heart Disease in Apparently Healthy Middle-Aged Men Results From the 18-Year Follow-Up of a Large Cohort From Southern Germany." (J Am Coll Cardiol ;2009;52:13:69–77.
9. Atul Singhal, Nigel Jamieson, Mary Fewtrell, John Deanfield, Alan Lucas, and Naveed Sattar ."Adiponectin Predicts Insulin Resistance But Not Endothelial Function in Young, Healthy Adolescents.". The European Society of Cardiology;2009;112:1050–62.
10. Wolfgang Koenig, MD, FACC, Natalie Khuseyinova, MD, Jens Baumert, PHD, Christa Meisinger, MD, MPH, Hannelore Löwel, MD ."Serum Concentrations of Adiponectin and Risk of Type 2 Diabetes Mellitus and Coronary Heart Disease in Apparently Healthy Middle-Aged Men Results From the 18-Year Follow-Up of a Large Cohort From Southern Germany." (J Am Coll Cardiol ;2009;52:13:69–77.
11. Yuji Matsuzawa, Tohru Funahashi, Shinji Kihara, Iichiro Shimomura."Adiponectin and Metabolic Syndrome." Arterioscler Thromb Vasc Biol; January 2007;27:1276-82.
12. Amir Elokely, Amira Shoukry, Tarek A. Ghonemy*, Marwan Atia ."Association between Low Adiponectin Level and Cardiovascular Complications in Diabetic and non Diabetic Patients with End Stage Renal Disease". Arab Journal of Nephrology and Transplantation. 2010;3:15-21.
13. Ursula Meier and Axel M. Gressner ."Endocrine Regulation of Energy Metabolism: Review of Pathobiochemical and Clinical Chemical Aspects of Leptin, Ghrelin, Adiponectin, and Resistin." *Clinical Chemistry* : 2009:1511–25.
14. Osamu Tsukamoto, Masashi Fujita, Mahoto Kato." Natriuretic Peptides Enhance the Production of Adiponectin in Human Adipocytes and in Patients With Chronic Heart Failure."JACC; 2009;53 :105-125 .
15. Hanif Wasim, Nasser M Al-Daghri, Raja Chetty, Phillip G McTernan, A H Barnett and Sudhesh Kumar."Relationship of serum adiponectin and resistin to glucose intolerance and fat topography in south-Asians." Cardiovascular Diabetology :2009;10:1475-2840.
16. Mohammad Shojaie, Abdoreza Sotoodah and Ghafar Shafaie." Is adiponectin associated with acute myocardial infarction in Iranian non obese patients? Lipids in Health and Disease 2009;8:17-20.
17. Qiong L. Zhou, Zhen Y. Jiang, Allan S. Mabardy, Claudia M. Del Campo, David G. Lambright, John Holik, Kevin E. Fogarty, Juerg Straubhaar, Sarah Nicolero, Anil Chawla, and Michael P. Czech." A Novel Pleckstrin Homology Domain-containing Protein Enhances Insulin-stimulated Akt Phosphorylation and GLUT4 Translocation in Adipocytes". The journal of biological chemistry: 2010;285:27581–89.
18. Arya M. Sharma and Bart Staels ."REVIEW: Peroxisome Proliferator-Activated Receptor and Adipose Tissue—Understanding Obesity-Related Changes in Regulation of Lipid and Glucose Metabolism." The Journal of Clinical Endocrinology & Metabolism;2009;92:386–95.