Adipocyte as we knew all these days was considered as a mere organ for deposition of fat however this view now is no longer tenable. We now know that adipocytes secrete a number of active hormones and is thus an important endocrinological organ. These hormones are loosely known as adipocytokines. Among the various “adipocytokines,” adiponectin, which is an abundant circulating protein synthesized solely in adipose tissue, appears to play a very important role in carbohydrate and lipid metabolism and vascular biology. Adiponectin appears to be a major modulator of insulin action and its levels are reduced in type 2 diabetes, which could contribute to peripheral insulin resistance. It has significant insulin-sensitizing as well as anti-inflammatory properties that include suppression of macrophage phagocytosis and TNF- alpha secretion and blockage of monocyte adhesion to endothelial cells in vitro. One of the important regulators of the adipocyte levels is the amount of body fat and thus the obesity. It has always been a practice to measure the amount of obesity and thus the risk of morbidity using anthropometric measures like body mass index, waist hip ratio or by measuring the body fat using bioimpedence methods. These methods in clinical practice have never been accurate and it is in this situation that we find serum adiponectin levels particularly important.

Obesity defined as “excess of body fat relative to weight”, is the sixth most important risk factor contributing to the overall burden of disease worldwide. Overweight refers to an excess body weight compared to set standards, which may come from muscles (lean body mass), bone, fat (adipose tissues), some time tumors and/or body water. The obesity epidemic that started in the middle of last century has now established itself in North America and Western Europe and has spread to developing countries of Asia, Latin America and Africa including India, where there is paradoxically a dual burden of obesity and malnutrition, often within the same families. Obesity develops because of a mis-match between energy intake and expenditure that results from behavior (feeding behavior and time spent in activities) and physiology (resting metabolism and expenditure when active). The availability of abundant energy rich processed foods in last few decades has contributed to the sharp rise of prevalence of obesity worldwide.

**INDIAN SCENARIO**

India is currently experiencing a rapid epidemiological transition which has resulted in increased life expectancy and decrease mortality due to communicable diseases. As a consequence of industrialization and urbanization there has also been an increase in the standard of living leading to nutritional transition with consumption of diets that are energy dense and high in fat and sugar content. Moreover with changes in occupation from predominantly agriculture based manual labor jobs to sedentary office type jobs; there is a perceptible decrease in physical activity. This is the basis for the rapid weight gain and obesity seen in several parts of the subcontinent. According to the Nutritional Foundation of India, the prevalence of obesity is one percent for males and four percent for females in slums while the corresponding figures for the middle socio-economic class was 32.2% and 50% respectively. Several reports suggest that for any given body mass index (BMI), Indians tend to have increased waist circumference. Further, Indians also tend to have excess body fat, abdominal and truncal obesity. For any given waist circumference; they have increased body fat accumulation and for any given body fat, they have increased insulin resistance. These features have been referred to as the “Asian Indian phenotype or Paradox”. Thus anthropometric measurements may not be of use when considering obese of Asian origin. This forces us to device newer markers for obesity the latest and the most accurate being adiponectin a adipokine with great prospects in research of obesity. The rising prevalence of obesity has several health consequences as obesity is a predecessor for many related conditions like diabetes, dyslipidemia, hypertension and coronary heart disease. A lot remains to be known about the effects of obesity like insulin resistance and hypertension the discovery of a new molecule adiponectin could throw some light on this.

**THE ADIPOCYTE AN ENDOCRINOLOGICAL ORGAN**

Adipose tissue is composed of the lipid-storing adipose cell and a stromal/vascular compartment in which preadipocytes reside. Adipose mass increases by enlargement of adipose cells through lipid deposition, as well as by an increase in the number of adipocytes. The process by which adipose cells are derived...
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Recent research has shown that adipose tissue is not simply an inert storage depot for lipids but is also an important endocrine organ that plays a key role in the integration of endocrine, metabolic, and inflammatory signals for the control of energy homeostasis. The adipocyte has been shown to secrete a variety of bioactive proteins into the circulation. These secretory proteins, which have been collectively named adipocytokines, include leptin, tumor necrosis factor (TNF)-alpha, plasminogen activator inhibitor type 1 (PAI-1), adipin, resistin, and adiponectin. Adiponectin, the gene product of the adipose most abundant gene transcript one (apM1), is a novel and important member of the adipocytokine family.

Synthesis of Adiponectin

Adiponectin cDNA was first isolated by large scale random sequencing of the human adipose tissue cDNA library. It is a collagen-like protein that is exclusively synthesized in white adipose tissue, is induced during adipocyte differentiation, and circulates at relatively high (microgram/milliliter) concentrations in the serum. Once synthesized, mammalian adiponectin undergos posttranslational hydroxylation and glycosylation yielding eight isoforms. Six of the adiponectin isoforms are glycosylated.

Structure of Adiponectin

A description of the cDNA encoding adiponectin was first reported in 1995.1 Adiponectin is a protein of 247 amino acids consisting of four domains, an amino-terminal signal sequence, a variable region, a collagenous domain (cAd), and a carboxy-terminal globular domain (gAd). On the basis of both its primary amino acid sequence and its subunit domain structure, adiponectin is most similar to C1q, a member of the complement-related family of proteins. However, X-ray crystallography of the globular fragment of adiponectin also reveals a striking structural homology to TNF-alpha, suggesting an evolutionary link between the TNF-alpha family members and adiponectin. The basic building block of adiponectin is a tightly associated trimer, which is formed by association between three monomers at the globular domains. Monomeric (30-kDa) adiponectin has not been observed in the circulation and appears to be confined to the adipocyte. Four to six trimers associate through their collagenous domains to form higherorder structures, or oligomers, which circulate in plasma at concentrations of 5 to 30 g/ml.

General Properties of Adiponectin

Adiponectin has been postulated to play an important role in the modulation of glucose and lipid metabolism in insulin sensitive tissues in both humans and animals. Decreased circulating adiponectin levels have been demonstrated in genetic and diet-induced murine models of obesity, as well as in diet induced forms of human obesity. Low adiponectin levels have also been strongly implicated in the development of insulin resistance in mouse models of both obesity and lipoatrophy. In humans, plasma levels of adiponectin are significantly lower in insulin-resistant states including type 2 diabetes and can be increased upon administration of the insulin-sensitizing thiazolidinedione (TZD) class of compounds. Plasma adiponectin levels in diabetic subjects with coronary artery disease (CAD) are lower than in diabetic patients without CAD, suggesting that adiponectin may have anti-atherogenic properties. In studies done on human aortic endothelial cells, adiponectin has been shown to dose-dependently decrease the surface expression of vascular adhesion molecules known to modulate endothelial inflammatory responses. It also inhibits proliferation of vascular smooth muscle cells and concentrates within the vascular intima of catheter-injured vessels. In clinical studies, low adiponectin levels have been associated with an atherogenic lipid profile. The association of low adiponectin levels with obesity, insulin resistance, CAD, and dyslipidemia indicates that this novel protein may be an important new marker of the metabolic syndrome especially in the unique Asian phenotype.

Measurement of Adiponectin

The current methods available for measuring adiponectin in plasma include a radioimmunoassay (Linco, St. Charles, MO) that measures the multimeric form and an enzyme-linked immunosorbent assay (B-Bridge International, San Jose, CA) that recognizes the denatured monomer form. Circulating levels detected with either method appear to be similar.

The Mechanisms of Action of Adiponectin

The mechanisms of action are largely unknown and controversial. Adiponectin administration has been shown to increase insulin-induced tyrosine phosphorylation of the insulin receptor in skeletal muscle in association with increased whole-body insulin sensitivity.2 Stimulation of glucose utilization and fatty acid oxidation in skeletal muscle and liver by adiponectin may also occur through activation of 5-AMP kinase. 5-AMP–activated protein kinase is believed to play a crucial role in the regulation of energy expenditure and glucose and lipid metabolism. The tissue-specific effect of adiponectin on 5-AMP kinase has recently been demonstrated in mice. In these studies, both the globular and fulllength forms of adiponectin activated 5-AMP kinase in skeletal muscle, but only the full-length form stimulated phosphorylation and activation of AMP kinase in the liver. In skeletal muscle of mice, adiponectin has been shown to increase expression of the genes encoding proteins involved in fatty acid transport and oxidation, such as CD36, acyl-CoA oxidase, and uncoupling protein, resulting in enhanced fat combustion and energy dissipation. In the liver, low doses of adiponectin decreased the expression of proteins involved in fatty acid transport, such as CD36, leading to reduced fatty acid influx into the liver and hepatic triglyceride content. Improved hepatic insulin sensitivity occurs, leading to a postulation that the primary effects of adiponectin on muscle are to augment uptake and combustion of free fatty acids (FFAs), whereas decreased liver triglyceride content results from secondary reductions in serum FFA and triglyceride levels.
Adiponectin is secreted only from adipose tissue, its levels are paradoxically lower in obese than in lean humans. This is in contrast to most other adipocytokines, whose levels are increased in obesity in proportion to an increased total body fat mass. It is possible that although adiponectin expression is activated during adipogenesis, a feedback inhibition on its production may occur during the development of obesity. Levels are also lower in diabetic patients compared with nondiabetic subjects, and are particularly low in subjects with CAD. Decreased levels are found in men compared with women, and this may be androgen induced. Ethnicity seems to play a role, since one study showed significantly higher plasma concentrations of adiponectin in Caucasians compared with BMI-matched Indo-Asians. Several studies have reported a significant negative correlation between circulating adiponectin and triglyceride levels and a positive correlation between adiponectin and HDL cholesterol levels in type 2 diabetes. Others have also demonstrated that plasma adiponectin concentrations were not only inversely related to triglyceride levels, atherogenic index (total: HDL cholesterol) and apolipoproteins (apos) B and E, but also positively correlated to serum HDL cholesterol and apo A-1 in nondiabetic female patients. These declines in adiponectin in hypertriglycerideremic, high atherogenic index, and low HDL states were also observed after adjusting for BMI, body fat mass, age, and diastolic blood pressure. These findings suggest that the hypoadiponectinemia observed in dyslipidemia may accelerate the atherosclerotic changes seen in the metabolic syndrome.

ADIPONECTIN AND METABOLIC DISEASES

Adiponectin: The Missing Link Between Obesity and Insulin Resistance

Studies have documented that adiponectin concentrations are significantly related to various measures of body fat and that significant weight loss leads to a rise in adiponectin levels. However, it is possible that the relationship between obesity and adiponectin is due in part to metabolic changes frequently associated with obesity. For example, insulin resistance and hyperinsulinemia are frequently associated with obesity, and both decline with weight loss. Importantly, both in vitro and in vivo studies have demonstrated that insulin itself may lead to downregulation of adiponectin secretion from fat cells. Adiponectin as we know is a modulator of insulin action and exhibits anti-inflammatory and antiatherogenic properties. In humans, adiponectin levels are inversely related to the degree of adiposity and positively associated with insulin sensitivity both in healthy subjects and in diabetic patients. Plasma adiponectin concentrations have been reported to be decreased in some insulin-resistance states, such as obesity and type 2 diabetes mellitus, and also in patients with coronary artery disease. Moreover, plasma levels of adiponectin have been shown to correlate negatively with body mass index, insulin and TG levels, and positively with HDL-c in adult obese subjects. Adiponectin increases insulin sensitivity by enhancing tissue fat oxidation, which results in reduced circulating fatty acid levels and TG contents in liver and muscle. Adiponectin increases the tyrosine kinase activity of insulin receptor by enhancing the activity of the oxidative phosphorylation UCP3. Adiponectin knockout mice on a carbohydrate-rich diet develop insulin resistance and have a reduced PI-3K activity. Adiponectin may have a direct impact in the regulation of insulinemia as well as in lipoprotein metabolism, confirming that, not only in adults but also in prepubertal children, insulin and adiponectin are antagonist hormones reciprocally regulated. Low levels of adiponectin would decrease the interaction with its hepatic and skeletal muscle receptors and contribute to downregulate the insulin transduction signal cascade, resulting in a reduced fatty acid oxidation, activation of hepatic gluconeogenesis and reduced glucose uptake in both tissues. Thus adiponectin could be the missing link between the pathogenesis of insulin resistance in obesity. This could also throw light over the long standing debate of obesity first or insulin resistance first.

ADIPONECTIN AND DIABETES MELLITUS

Type 2 diabetes results from an interaction between genetic and environmental factors. Genome-wide scans have mapped a susceptibility locus for type 2 diabetes, metabolic syndrome, and coronary heart disease to chromosome 3q27, where the gene encoding adiponectin is located. In some studies it was found that genetic variations resulting in reduced serum adiponectin levels are associated with increased risk for type 2 diabetes in the Japanese population. In another study, Japanese subjects carrying a missense mutation in the adiponectin gene associated with hypoadiponectinemia exhibited the phenotype of the metabolic syndrome, including insulin resistance and coronary artery disease. Thus genetic polymorphisms of the adiponectin gene that result in lower production and secretion of adiponectin may be responsible, at least in part, for the pathogenesis of the insulin resistance syndrome and diabetes. Conversely, increased baseline concentrations of adiponectin may be associated with a
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Reduced Risk of Developing Type 2 Diabetes.

The connection between adiponectin levels and insulin resistance has been further confirmed by data obtained from treatment with TZDs. The peroxisome proliferator–activated receptor (PPAR) gamma is a ligand-activated transcription factor thought to be a master regulator of adipocyte differentiation and multiple adipocyte genes. TZDs are specific synthetic ligand activators of PPAR-gamma that improve glucose tolerance and insulin sensitivity in type 2 diabetic patients and in animal models of insulin resistance through mechanisms that are incompletely understood. The administration of TZDs has been shown to increase the plasma adiponectin concentrations in insulin resistant humans and rodents and in subjects with type 2 diabetes. Thus, induction of adipose tissue adiponectin expression and consequent increases in circulating adiponectin levels could potentially represent a novel potential mechanism for PPAR-mediated enhancement of whole body insulin sensitivity. Furthermore, adiponectin may be a biomarker of in vivo PPAR-gamma activation. Studies reported an increase in adiponectin levels in normal subjects after only 14 days of treatment with rosiglitazone. The activation of PPAR-gamma by TZDs may promote weight gain by increasing adipocyte differentiation and the number of small adipocytes, as has been previously shown, as well as enhance adiponectin gene transcription in existing mature adipocytes, thus increasing adiponectin levels. Adiponectin has also been proposed by some investigators now as a reliable marker for insulin resistance in type 2 diabetes.

Adiponectin and Hypertension

Hypertension is a major risk factor for cardiovascular disease, and the latter is the leading cause of morbidity and mortality worldwide. In developed countries, hypertension ranks as the top contributing factor for mortality and third in causing disability-adjusted life years. Hypertension is a polygenic and complex disease with rising prevalence. More than 25% of the adult population is affected by hypertension, and two thirds of those individuals reside in developing countries. Mechanistically, endothelial dysfunction, increased renin-angiotensin system (RAS) activity, and sympathetic nervous system (SNS) hyperactivation have been considered as important risk factors of hypertension and hint at important events taking place at the interface of the endothelium, kidney, and SNS. Adiponectin has been proved to effect all three of these factors and thus may have a role to play in the pathophysiology of hypertension.

A growing body of evidence shows that hypoadiponectinemia is associated with endothelial dysfunction. By measuring forearm blood flow in response to reactive hyperemia, Ouchi et al found that plasma adiponectin levels are correlated with an endothelial vasodilation response. Similarly, another study showed that hypoadiponectinemia is associated with a lower vasodilation response in diabetic patients. The same group found that adiponectin administration increases NO production in human aortic endothelial cells. The dysregulated production of adiponectin may be one of the critical factors mediating obesity-associated NO decrease, endothelial dysfunction, and cardiovascular disease. Adiponectin regulates eNOS enzymatic activity and NO production by several mechanisms. Both adiponectin receptors are expressed in human endothelial cells. Knockdown of either receptor decreases the production of NO and phosphorylation of eNOS after adiponectin treatment (full-length and globular) in human umbilical vein endothelial cells.

The well-established role of adiponectin as an insulin sensitizer prompted further studies into the relation between angiotensin II receptor blocking and adiponectin production. Growing evidence from clinical studies shows that exposure to angiotensin II receptor blockers increases circulating levels of adiponectin. The angiotensin II receptor blocker–mediated increase of adiponectin may contribute to the additional beneficial effects that these drugs exhibit in hypertensive patients. Several mechanisms have been proposed to explain the stimulatory effect of angiotensin II receptor blocking on circulating adiponectin levels. Angiotensin II inhibits adiponectin production through angiotensin II receptor subtype 1, and angiotensin II receptor blockers may elicit their effect by inhibiting angiotensin II receptor subtype 1 signaling. In rats, angiotensin II infusion for 2 weeks significantly decreases adiponectin circulating levels. Neither an antagonist nor an agonist of angiotensin II receptor subtype 2 treatment has any effect on the suppression of adiponectin by angiotensin II. Interestingly, the decrease of adiponectin by angiotensin II infusion occurs before the blood pressure increase.

The SNS is an autonomous regulatory system responsive to physiological stress situations. The disproportionate activation of SNS in the obese state is proposed to play important roles in obesity-associated metabolic dysfunction. The hyperactivation of SNS increases heart rate and peripheral vascular resistance and eventually causes hypertension. With these methods, SNS activity has been shown unequivocally to correlate with the hypertensive state, and the SNS is, therefore, intricately involved with the initiation, maintenance, and progression of hypertension. More recently, SNS overdrive has been shown to suppress adiponectin expression. Hypertensive patients, 6 months of treatment with SNS blockers improved blood pressure control and increased circulating adiponectin by 30%, independent of insulin resistance. Because adiponectin has been found in cerebrospinal fluid and administration of adiponectin centrally affects energy homeostasis, it is tempting to speculate that adiponectin may be involved in the regulation of SNS activity from the brain. The action of adiponectin on SNS activation in the brain may be indirect and mediated via an interaction with leptin signaling. Recently, it was demonstrated that adiponectin reverses leptin-mediated suppression of food intake in the hypothalamus. Considering the important role of leptin on SNS activation and blood pressure control, it is tempting to suggest that adiponectin may regulate SNS activity by inhibiting leptin action in the brain.

Adiponectin thus modifies the endothelial function, effects the RAAS and has effect on the SNS thus it may play a major role
in future research concerning pathophysiology and treatment of hypertension.

**Adiponectin and Atherosclerosis**

Experimental studies have indicated that adiponectin has potential antiatherogenic and anti-inflammatory properties. Monocyte adhesion to the vascular endothelium and subsequent differentiation to macrophages and foam cells is considered crucial for the development of vascular disease. In certain studies it was found that adiponectin had effects on monocyte adhesion to endothelium, myeloid differentiation, and macrophage cytokine production and phagocytosis. Adiponectin has been shown to inhibit both the production and action of TNF-alpha, a cytokine that has direct effects on the adhesion molecules. Although its receptor has not been identified, adiponectin modulates signaling of nuclear factor beta (NF Beta) (a transcription factor involved in the inflammatory response), at least partly through a cAMP-dependent pathway. It has been shown that adiponectin suppressed macrophage to foam cell transformation in vitro. Thus adiponectin probably serves as a modulator for macrophage foam cell formation and could provide an answer to the fundamental mechanism for the link between vascular inflammation and atherosclerosis. Furthermore, adiponectin mediated signaling has been shown to inhibit growth factor–induced human aortic smooth muscle cell proliferation and migration. These in vitro studies demonstrate that adiponectin may act as an antiatherosclerotic factor through a direct effect on endothelial cells. Severe neointimal thickening and increased proliferation of vascular smooth muscle cells has been demonstrated in mechanically injured arteries of adiponectin knockout mice. Supplementation of adiponectin in this mouse model attenuated the neointimal proliferation. This has been the first in vivo evidence that adiponectin might serve as a critical link bridging the adipose tissue–vascular axis. Amelioration of atherosclerosis associated with decreased expression of class A scavenger receptor and TNF-alpha has been demonstrated in globular adiponectin transgenic (gAd Tg) apo E–deficient mice. This appears to be the first in vivo demonstration of a protective role of adiponectin against atherosclerosis. High-sensitive C-reactive protein (hs-CRP) is a well-known marker and risk factor for coronary artery disease. It was recently shown that CRP mRNA is expressed in human adipose tissue. A significant inverse correlation has been observed between CRP and adiponectin mRNA levels in subcutaneous adipose tissue of human subjects with angiographically demonstrated coronary atherosclerosis. The same negative correlation exists between plasma hs-CRP and adiponectin levels. This reciprocal association between adiponectin and CRP levels in both human adipose tissue and plasma is supportive of a role for adiponectin against the development of atherosclerosis and vascular inflammation.

**Adiponectin and Coronary Artery Disease**

When the vascular endothelium is injured, adiponectin accumulates in the subintimal space of the arterial wall through its interaction with collagens in the vascular intima. Adiponectin attenuates TNF-a–induced expression of adhesion molecules in endothelial cells, which is an initial step of atherosclerosis. In a study it was shown that Plasma adiponectin concentrations in diabetic women without CAD were significantly lower than those in nondiabetic women (7.6 versus 11.7 μ gm/dl, P = 0.001). Diabetic women with CAD exhibited even lower plasma adiponectin concentrations (6.3μ gm/dl). In men, diabetic subjects without CAD also showed lower plasma adiponectin levels compared with nondiabetic subjects (6.660.4 versus 7,960.5 μ gm/dl). Plasma adiponectin levels in diabetic men with CAD were even lower and statistically significant when compared with diabetic men without CAD (4.060.4 versus 6.660.4 μ gm/dl, P=0.001).

**Adiponectin in HIV and HCV**

Adipose tissue expression and circulating adiponectin concentrations have also been found to be significantly decreased in HIV-positive patients with lipodystrophy treated with highly active antiretroviral therapy. Thus adiponectin may be used as a marker and predictor of lipodystrophy on patients of HIV infection. The link between viral factors and adiponectin was recently established. A positive association of serum adiponectin and HCV load, independent of IR, was found. Patients with HCV genotype 1 infection had a higher IR than those with genotype 2 infection and lower serum adiponectin levels. These findings suggest HCV genotype specific differences in inducing IR and adiponectin levels. There are two possible explanations: the influence of the degree of hepatic pathological changes (inflammation or fibrosis) on serum adiponectin levels or the existence of HCV specific differences in AdipoR1 and AdipoR2 gene expression. Although we did not study the response of adiponectin to antiviral treatment, two findings must be mentioned: the basal levels of adipocytokines are independent from treatment outcome, and the kinetic analysis of adipocytokines during and after therapy revealed an increase in serum adiponectin levels at the end of follow-up. Insulin resistance evaluated by HOMA-IR also decreased at the end of followup in patients with virological response.

**The pharmacological effects of adiponectin**

Adiponectin as a pharmacological agent has been studied at animal, tissue, and cellular levels using a variety of recombinant adiponectin products. Studies investigating the bioactivity of full length adiponectin versus that of the globular domain alone have produced mixed results. The globular head domain of adiponectin has been shown to be more potent than the full-length form in ameliorating hyperglycemia and hyperinsulinemia in diet-induced and genetic forms of murine obesity and in decreasing elevated plasma free fatty acids in mice fed a high-fat meal or given intravenous intralipid injections.

Adiponectin might have therapeutic implications as an anti-obesity drug, although there have been no studies in humans so far. In a study, administration of adiponectin slightly but not significantly reduced weight gain induced by a high-fat diet in mice. It remains to be determined whether adiponectin can be effectively and safely used as a pharmacologic means to treat obesity in humans. It is also important to note that although low concentrations of plasma...
Adiponectin are observed in obese individuals, a prospective study done in Pima Indians found that circulating adiponectin levels did not predict future weight gain and thus did not appear to play an etiologic role in the development of obesity in these individuals. Improvement in insulin sensitivity by weight reduction in obese subjects with gastric bypass surgery has been reported to increase adiponectin levels. However, there has been conflicting data on whether improvement in insulin sensitivity with exercise training is associated with increased adiponectin levels.

Replenishment of adiponectin might represent a novel treatment strategy for insulin resistance and type 2 diabetes. Adiponectin might have several therapeutic advantages over antidabetic drugs now used clinically. First, in addition to hypolipidemic and antidiabetic effects, adiponectin has potential anti-inflammatory properties that might prevent or retard atherosclerosis. Second, adiponectin appears to exert these effects without increasing body weight.

Circulating concentrations of adiponectin decreased significantly following chronic consumption of high-fat ethanol-containing food. Delivery of recombinant adiponectin into these mice dramatically alleviated hepatic steatopyg and steatosis (fatty liver) and also significantly attenuated inflammation and the elevated levels of serum alanine aminotransferase. These therapeutic effects resulted partly from the ability of adiponectin to increase carnitine palmitoyltransferase I activity and enhance hepatic fatty acid oxidation, while it decreased the activities of two key enzymes involved in fatty acid synthesis, including acetyl-CoA carboxylase and fatty acid synthase. Furthermore, adiponectin treatment could suppress the hepatic production of TNF-alpha and plasma concentrations of this proinflammatory cytokine. Adiponectin was also effective in ameliorating hepatic steatopyg, steatosis, and alanine aminotransferase abnormality associated with nonalcoholic obese, ob/ob mice. These results demonstrate a novel mechanism of adiponectin action and suggest a potential clinical application of adiponectin and its agonists in the treatment of liver diseases.

Studies have show that local Ad-APN (recombinant adiponectin) treatment through intima or adventitia reduces atherosclerotic plaque area, although the exact mechanism needs further investigation. This elucidates the protective mechanism of adiponectin in atherosclerosis. Adiponectin has been shown to reduce atherosclerosis through attenuating endothelial inflammatory response and macrophage-to-f0am cell transformation. Adiponectin also suppresses the expression of NF-κ B-inducible genes, including VCAM-1, in endothelial cells and class A scavenger receptor expression in monocyte-derived macrophages. This local administration of adiponectin could help in plaque regression in atherosclerosis.

CONCLUSION

In conclusion we find that adiponectin may be the missing link in many a metabolically altered pathways in our body. The role of adiponectin in relating obesity with insulin resistance, diabetes and hypertension may open up new avenues in metabolic research. Possible therapeutic roles for adiponectin the molecule of this decade are under investigation and whether it has a potential benefit only future will tell. This fact together with the promising results of experimental studies suggests the possibility that adiponectin replacement might become a new pharmacological approach to treatment of insulin resistance and/or atherosclerosis. Despite this promising implication, there is still a number of crucial steps to be performed to fully understand the biology of adiponectin, e.g. identification of the adiponectin receptor and the exact mechanism of adiponectin action. From the clinical point of view, human studies with recombinant adiponectin administration will be necessary in order to test the effectiveness of this compound in the treatment of insulin resistance and/or atherosclerosis in clinical medicine.

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