



## INTRODUCTION

Adipose tissue is a specialized form of connective tissue consisting of fat-storing cells (adipocytes) associated with a rich blood supply. There are two types of adipose tissue: white (or unilocular) and brown (or multilocular) (*Naporitano , 1993*).

Adipocytes are highly specialized cells that play critical roles in energy regulation and homeostasis (*Brun et al., 1996*).

Adipose tissue has long been considered to be a passive, inactive tissue. However, research in the past decade has demonstrated that adipose tissue plays an important role in energy regulation via endocrine, paracrine and autocrine signals. Several hormones and other factors are secreted from adipocytes (*Flier & Maratosflier, 1998; Mohamed Alli et al.,2004*).

### **Adipocyte secrets (*Kershaw and Flier , 2004*):**

- 1- Hormones: leptin, resistin, adiponectin, angiotensinogen and sex steroid hormone.
- 2- Prostaglandins: PGE<sub>2</sub> (prostaglandin E<sub>2</sub>), and PGI<sub>2</sub> (prostaglandin I<sub>2</sub>).
- 3- Growth factors: HGF (Hepatocyte growth factor).
- 4- Enzymes: cytochrome P450 aromatase, 17 $\beta$  Hsd (17 $\beta$  hydroxyl steroid dehydrogenase), 11 $\beta$  hsd1 (11  $\beta$  hydroxyl steroid dehydrogenase 1), PAI-1 (plasminogen activator inhibitor-1), LPL (lipoprotein lipase), CETP (cholesterol ester transfer protein), and ACE (Angiotensin converting enzyme).
- 5- Free fatty acid.



- 6- Complement factors: adipsin, complement factor B, and ASP (acylation stimulating protein).
- 7- Cytokines: TNF- $\alpha$  (tumor necrosis factor-  $\alpha$ ), IL-6 (interleukin-6), IL-8 (interleukin-8), IL-10 (interleukin-10), and MCP-1 (monocyte chemoattractant protein-1).

Leptin is a hormone that plays a central role in the regulation of food intake and energy expenditure. Circulating leptin is transported to the cerebrospinal fluid where it is available to bind and activate specific receptors on the hypothalamus that mediate regulation of energy balance. Leptin, in vitro, has been found to have proinflammatory properties, leptin improved Insulin sensitivity with lipodystrophy (*Tartaglia, 1997*).

Resistin was originally reported as an adipose tissue specific hormone that provided a link between obesity and diabetes. Resistin is part of a new class of cysteine rich secreted proteins. In vitro studies have shown that resistin mRNA expression is increased by proinflammatory cytokines in human mononuclear cells and that resistin has a direct proinflammatory effect, probably mediated through nuclear factor- $\kappa$ B (NF- $\kappa$ B) signaling pathway on vascular endothelial human cells (*Kaser et al., 2003*).

Adiponectin is the anti-inflammatory adipokine that is produced exclusively by white adipocytes. Adiponectin has been related to insulin resistance and diabetes not only because of its AMP-activated protein kinase effects on FFA metabolism and glucose uptake but also because of its anti-inflammatory properties. Inhibition of phagocyte activity and TNF- $\alpha$  production by macrophages and inhibition of the TNF- $\alpha$  induced expression of adhesion molecules (through NF- $\kappa$ B signaling pathways)



are some of the known mechanisms by which adiponectin mediate its anti-inflammatory effects (*Weyer et al., 2004*).

Angiotensin -II is a well known hypertensive hormone, generated in the rennin angiotensin system (RAS) (*Campbell, 1997*).

Adipose tissue is an important peripheral site for the generation of All (angiotensin II), suggesting significant function of adipocyte derived All in adipose tissue development and metabolism and possibly obesity linked hypertension (*Crandall et al, 1994; Darimont et al., 1994 and Jones et al., 1997*).

Several studies have demonstrated that arachidonate metabolites modulate positively or negatively differentiation and maturation of adipose tissue (*Shillabeer et al., 1998*). Prostaglandin E<sub>2</sub> (PGE<sub>2</sub>) and prostaglandin I<sub>2</sub> (PGI<sub>2</sub>) are the two major PG produced from rodent and human adipocytes (*Hyman et al., 1992 and Richelsen, 1992*).

Among the proinflammatory adipokines, TNF- $\alpha$  and IL-6 have been studied most extensively. The effects of TNF- $\alpha$  on glucose metabolism may be mediated in an autocrine/paracrine manner by regulating secretion of other adipokines or by promoting lipolysis and raising serum free fatty acid (FFA) levels (*Hotamisligil et al., 1993*).

Comorbid conditions linked to obesity includes:

- Metabolic syndrome,
- Cardiovascular diseases,
- Respiratory diseases,
- Gastrointestinal diseases,
- Hepatobiliary diseases,
- Hematological disorders,



- Immunological diseases,
- Neurological diseases,
- Infertility,
- Varicosities,
- and cancer. (*Wang et al., 2004*).