Adipose Tissue

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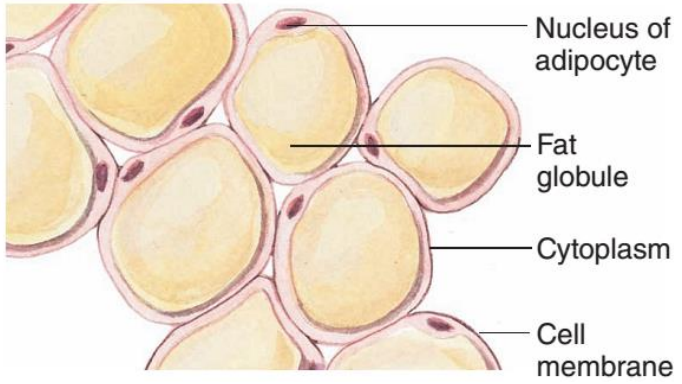
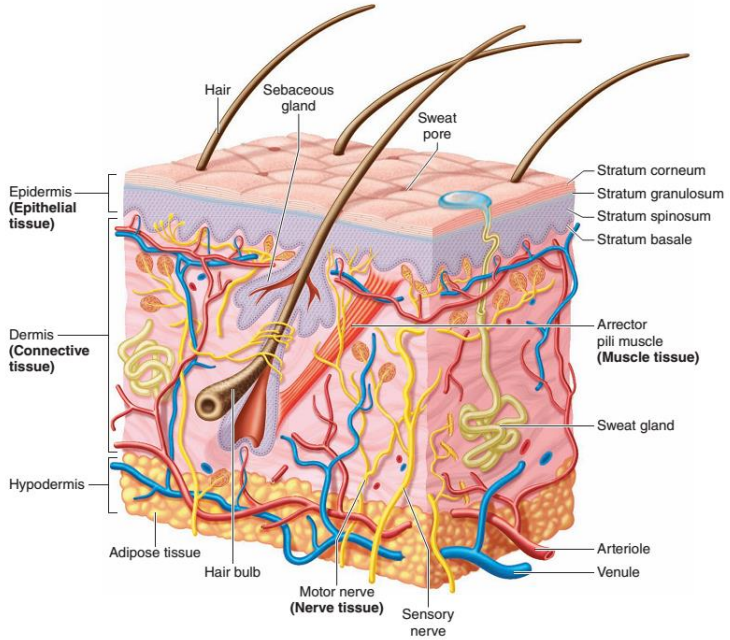
Adipose Tissue

- Loose connective tissue
- **Adipocyte:** adipose cell
- **Adipokines:** cytokines (cell signaling proteins) secreted by adipose tissue
- Cytoplasm is streched around a central globule fat
- Synthesis and breakdown of fat are accomplished by enzymes within the cytoplasm
- Adipose cells are grouped together to form the *hypodermis*
- Adipose tissue: masses of fat deposits throughout the body (e.g., subcutaneous fat, visceral fat)





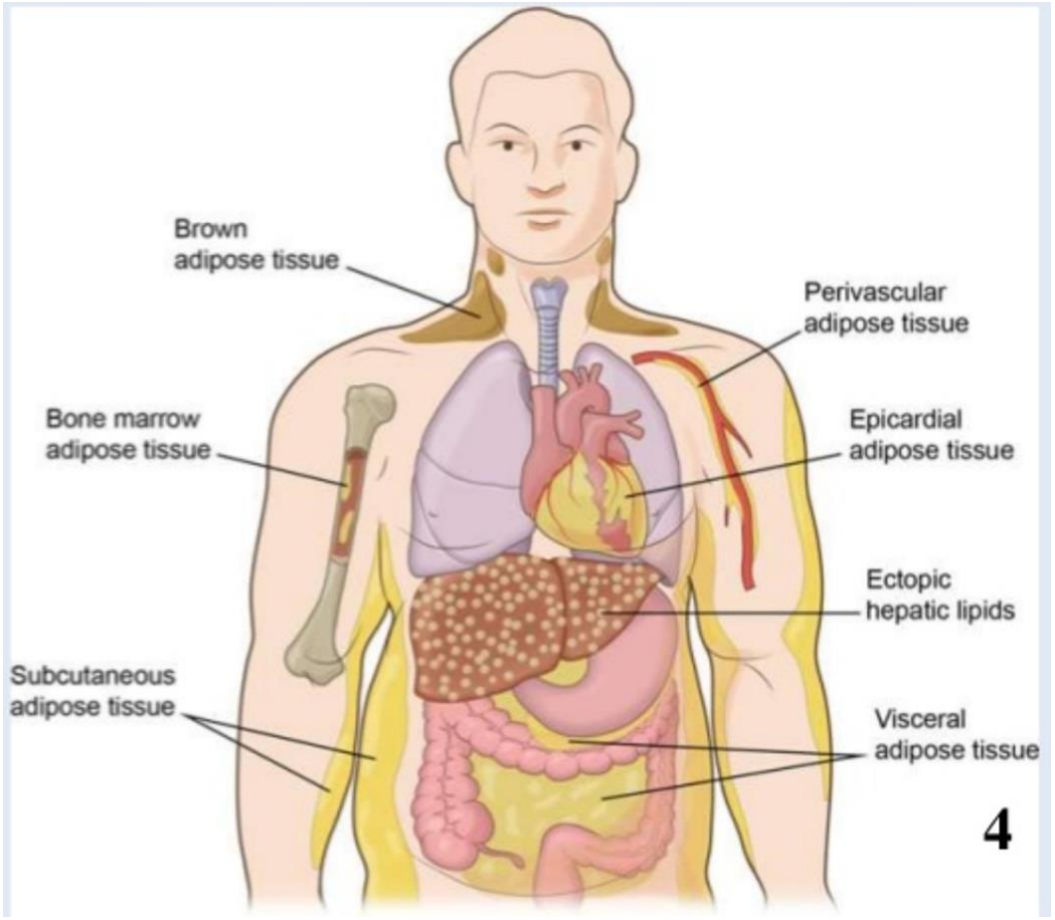
Functions of Adipose Tissue

- reserve of energy
- thermal isolation
- mechanical protection
- endocrine organ
- pro- and anti-inflammation (immune regulatory functions)

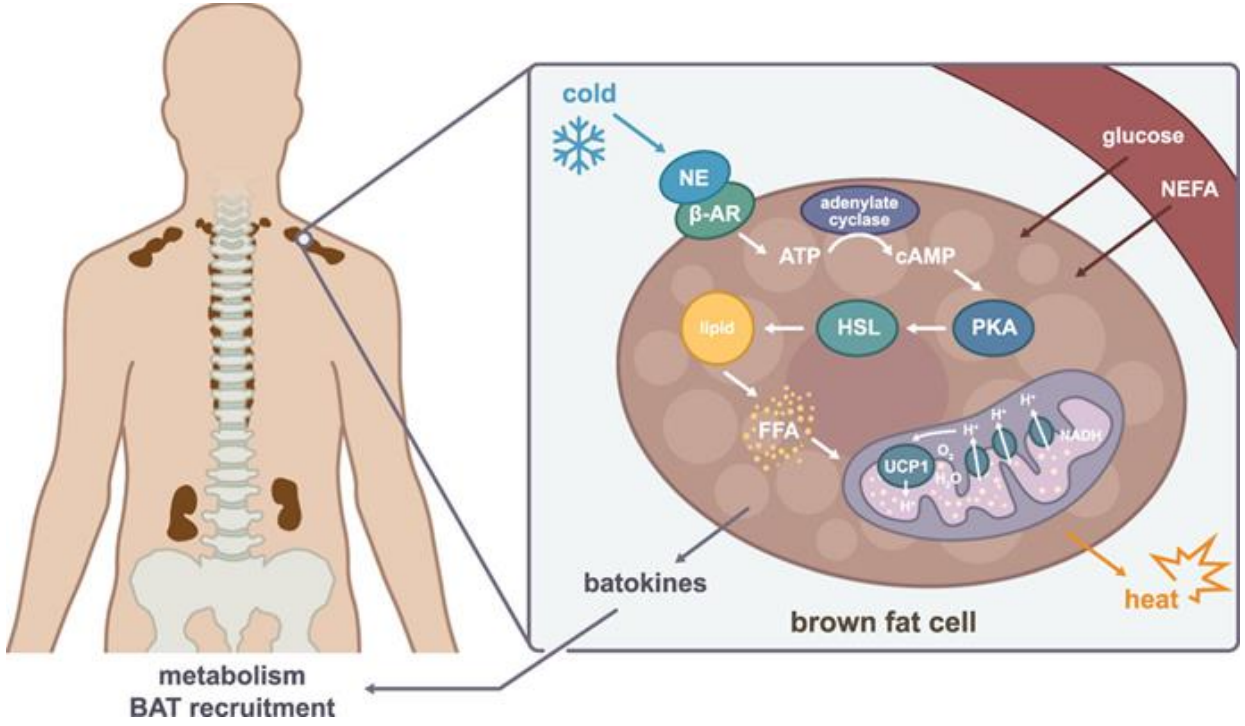
Adipose Tissue Types

- Brown adipose tissue (BAT)
- Beige adipose tissue
- White adipose tissue (WAT)

- Subcutaneous adipose tissue
- Visceral adipose tissue



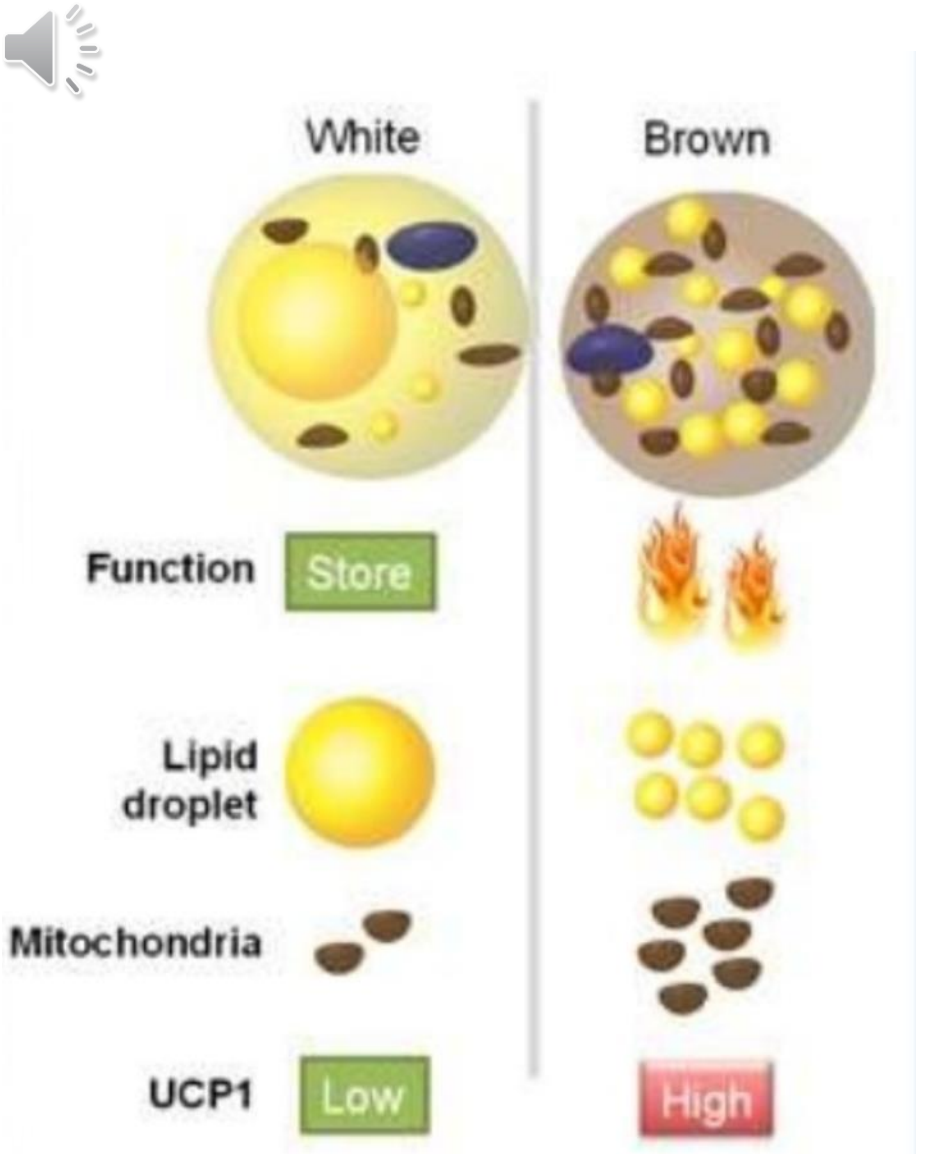
Brown Adipose Tissue



- Found in mammals
  - Supraclavicular region, deep neck, perirenal region, around spinal cord
  - More prominent in newborns
- Usually diminishes with age
- Can persist as an adaptation to cold-induced thermogenesis

Brown Adipose Tissue

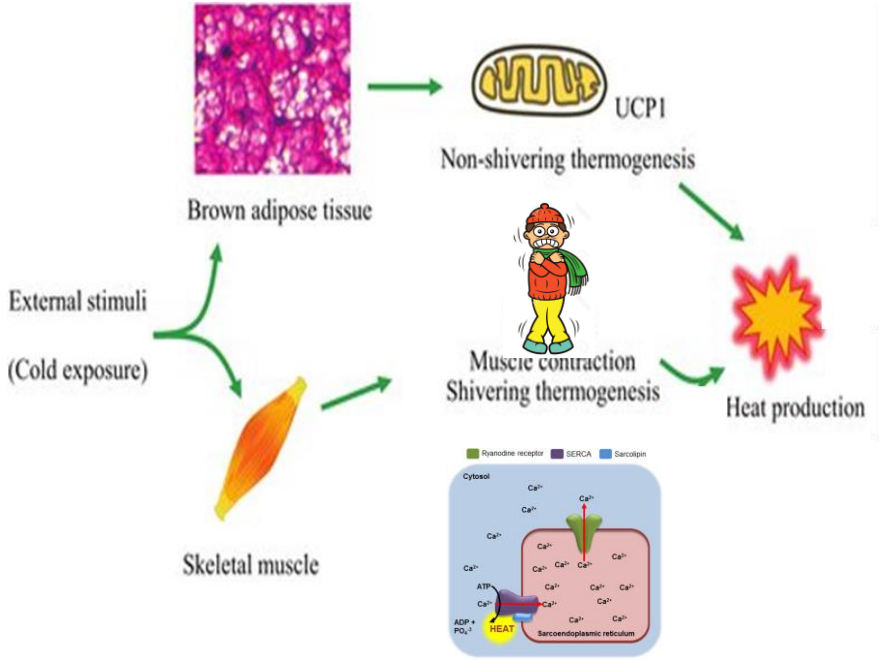
- Thermogenesis
  - release heat by oxidizing fatty acids within the adipocyte rather than supplying free fatty acids for use by other cell types
- Multiple number of lipit droplets of different sizes
- Numerous mitochondria (containing UCP1)
- Extensive vascularization
  - Deliver fuel for storage and oxidation
  - Disperse heat generated by the numerous mitochondria to other parts of the body



Non-shievering Thermogenesis

- Shievering thermogenesis → muscle
- Non-shievering thermogenesis → BAT

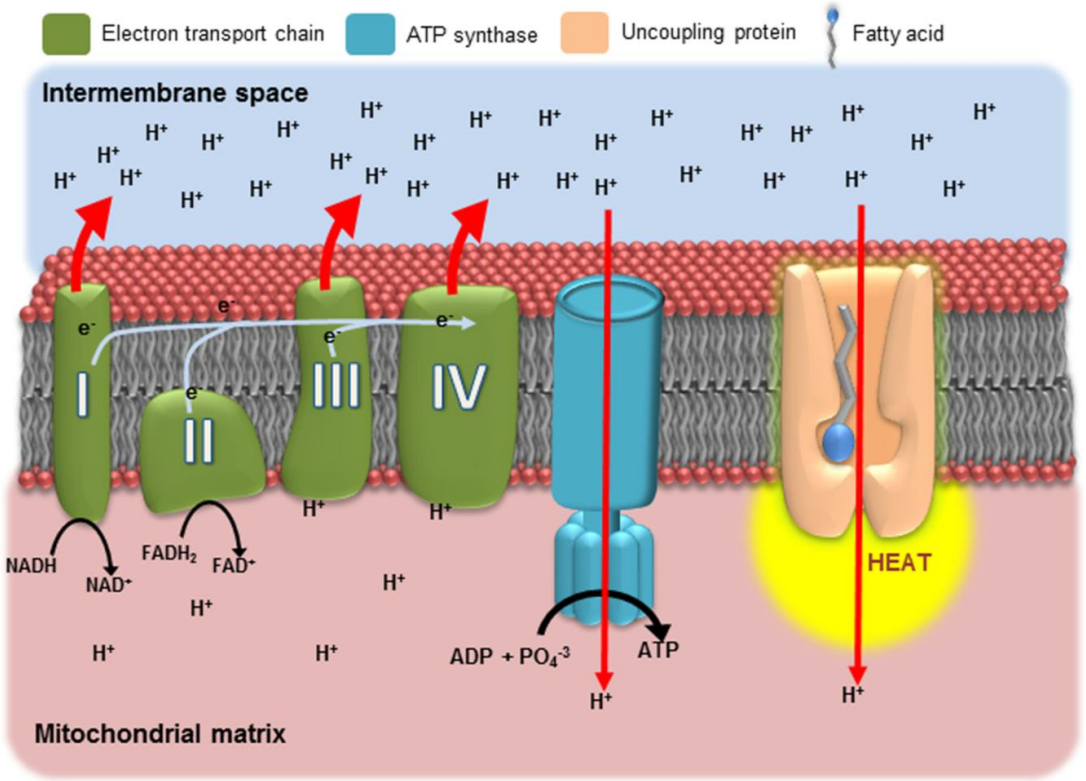
- Increase in metabolic rate not due to increased muscle activity
- Triggered by exposure to cold, increased sympathetic activity

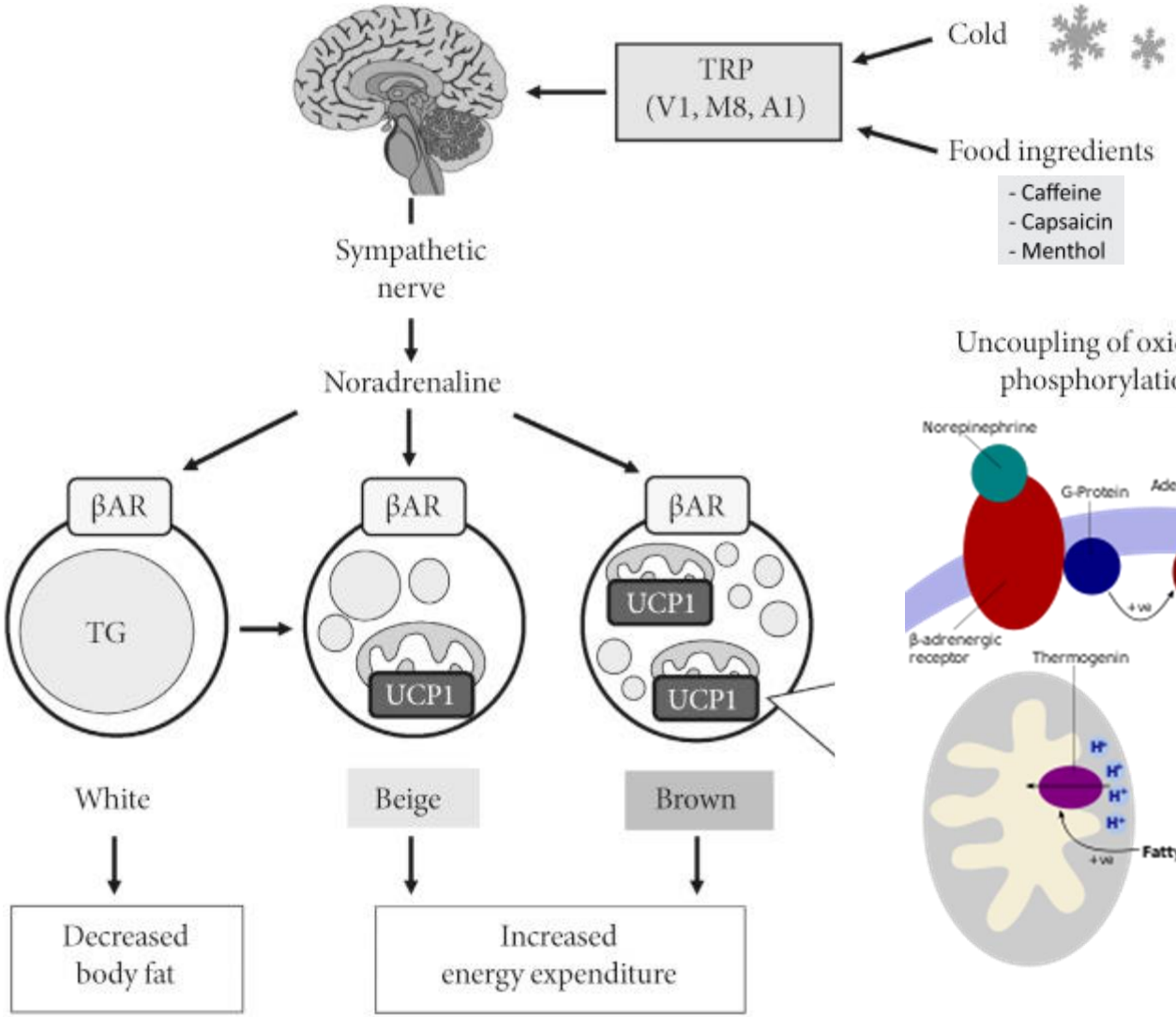


Non-shievering Thermogenesis

- UCP: *uncoupling protein* or *thermogenin*

- UCP1→ influx of H+ into mitochondrial matrix, bypasses ATP synthase, uncouples oxidative phosphorylation and energy is dissipated as heat instead of making ATP




TRP
(V1, M8, A1)
Cold
Food ingredients
- Caffeine
- Capsaicin
- Menthol
Sympathetic
nerve
Noradrenaline
βAR
TG
βAR
UCP1
βAR
UCP1
UCP1
White
Beige
Brown
Decreased
body fat
Increased
energy expenditure

Uncoupling of oxidative
phosphorylation
Norepinephrine
G-Protein
Adenylate cyclase
ATP
β-adrenergic
receptor
Thermogenin
cAMP
Protein
kinase A
ATP
ADP
Hormone-sensitive
lipase
Fatty acids
Triglycerides

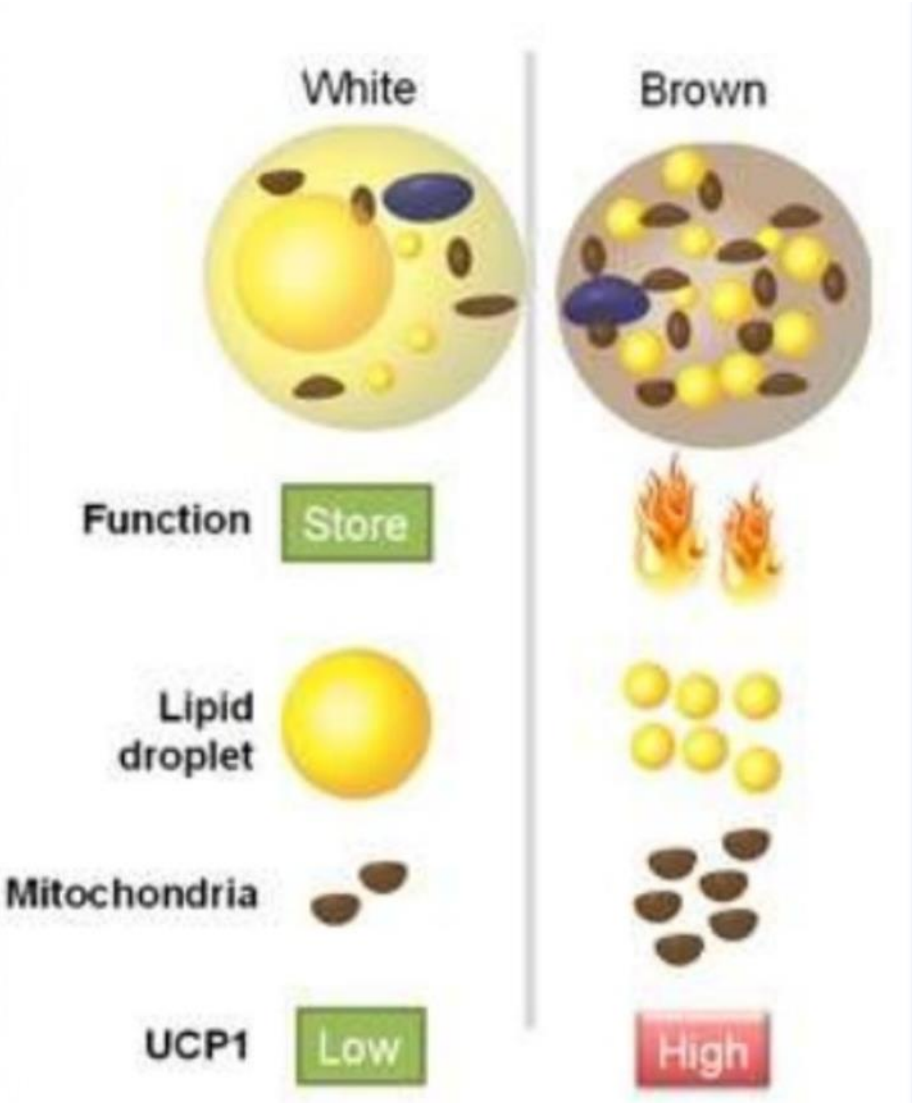
Beige Adipose Tissue

- Resembles brown fat by morphology and function but is developmentally more related to White fat
  - ability to thermogenesis
  - derives from precursors of white adipocytes
- Found in clusters scattered within the areas of white adipose tissue as opposed to occurrence of BAT in separate and distinct depots
- Exhibit low basal expression level of UCP1 and other thermogenesis related genes that are inducible upon stimulus, such as cold stimulation

	WHITE ADIPOSE TISSUE	BROWN ADIPOSE TISSUE	BEIGE ADIPOSE TISSUE
Localization	• Subcutaneous • Intra-abdominal • Epicardial • Gonadal	• Interscapular • Paravertebral • Perirenal • Cervical • Supraclavicular	Emerges in white adipose tissue depots with appropriate stimuli
Morphology	Spherical	Elliptical and smaller than white	Spherical
Cell composition	• Single lipid droplet • Few mitochondria • Flattened peripheral nucleus • Little endoplasmic reticulum	• Multiple small lipid droplets • Large number of mitochondria • Oval central nucleus	• Unilocular morphology but small lipid droplets after stimulation • Mitochondria appear after stimulation
Function	Storing energy	• Expending energy and heat production (non-shivering thermogenesis)	Thermogenic potential
Uncoupling protein	Undetectable	Positive	Positive after stimulation

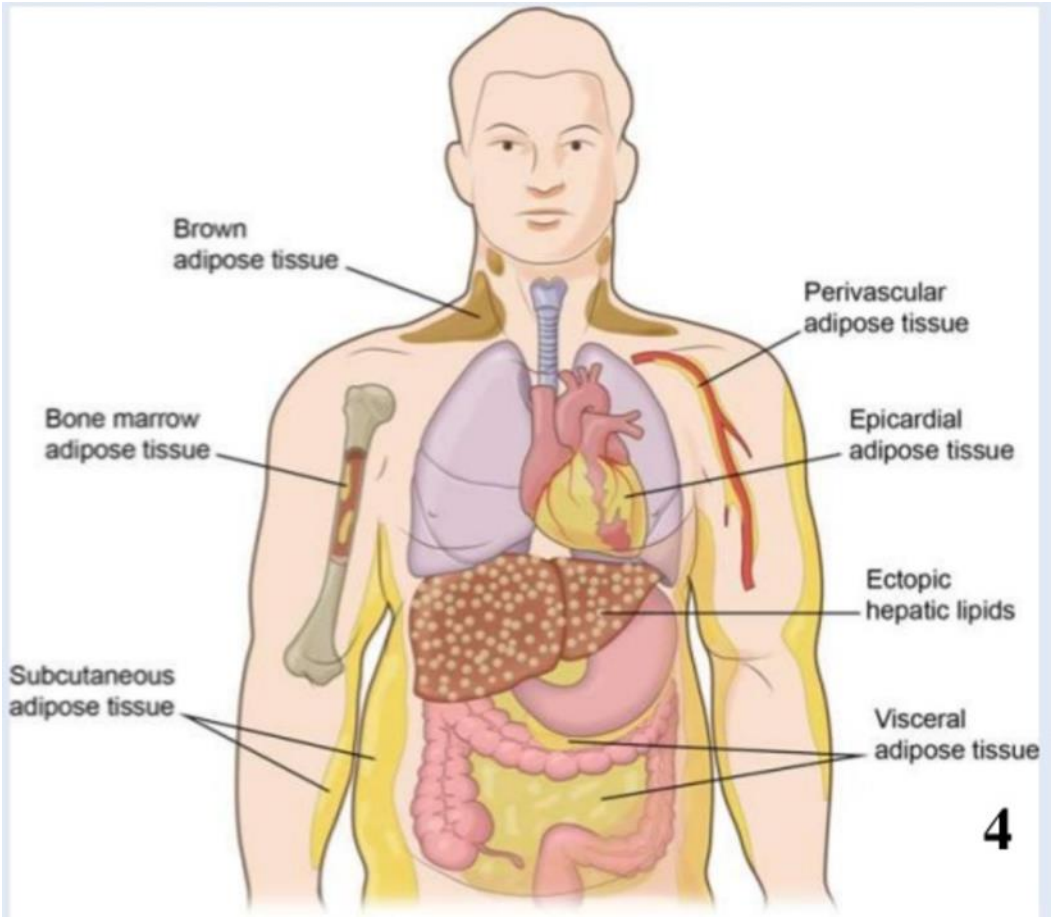
White Adipose Tissue

- Main site of energy storage in the body
- Adipocytes are the predominate cell type
- Low amounts of mitochondria



White Adipose Tissue

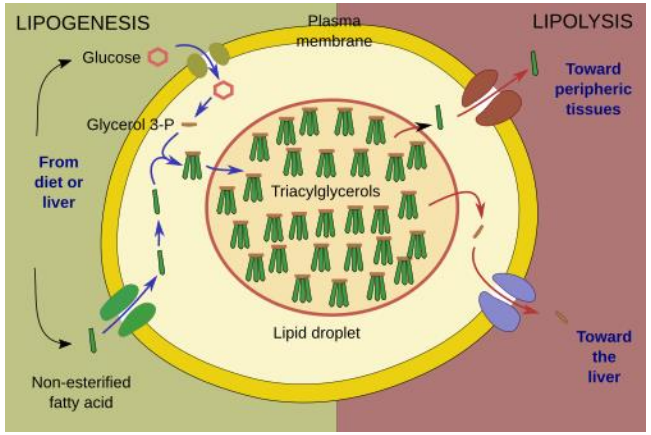
- Extensive distribution in the body
  - Mechanical protection
  - Softening the impact of shocks
  - Allowing appropriate sliding of muscle bundles
  - Thermal insulation (maintaning body temperature)
  - Buffering system for lipid energy balance



Lipogenesis and Lipolysis

Lipogenesis: Fat synthesis

- Synthesis of fatty acids
- Adipose tissue (+ liver)
- Responsive to changes in diet
  - Stimulated by high carbonhydrate diet
  - Inhibited by polyunsaturated fatty acids and fasting



Lipolysis (fatty acid oxidation): Fat breakdown

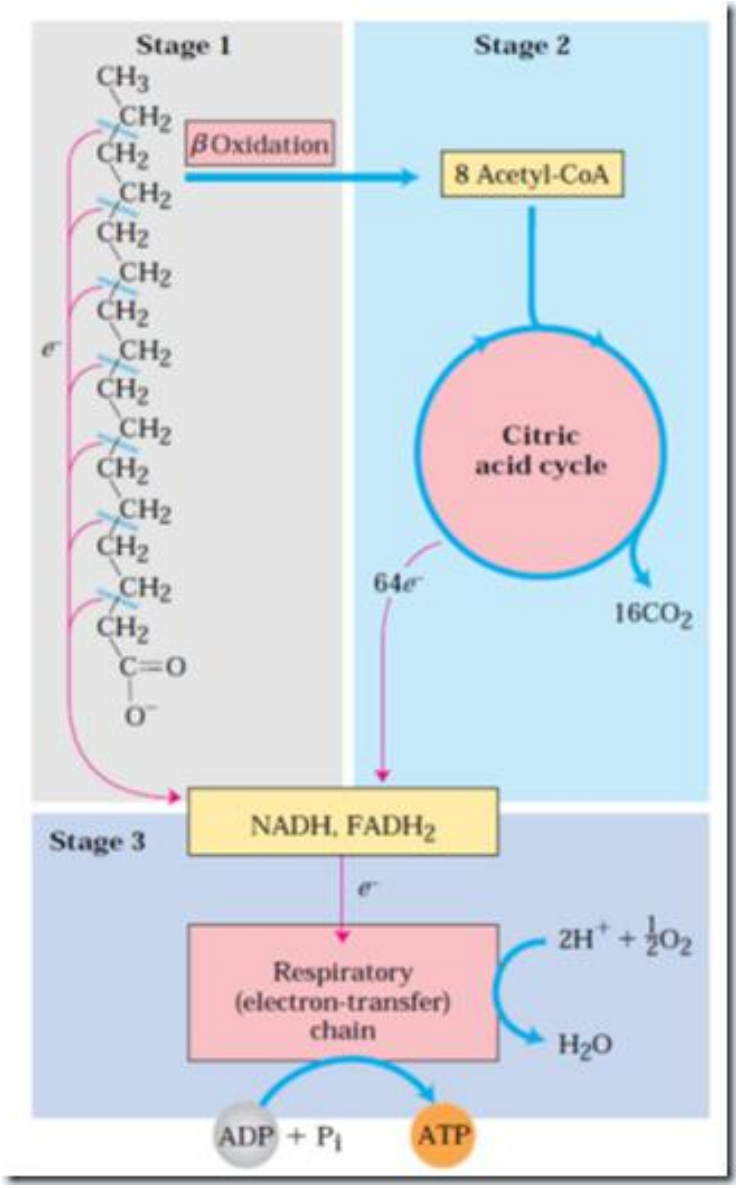
- Adipose tissue
- Triacylglycerol = 3 free fatty acids + glycerol
  - Hormone-sensitive lipase
    - Inhibited by insulin
    - Favored by the presence of glucagon and epinephrine
- Monoacylglycerol lipase

Lipolysis

- Glycerol effluxed out of adipocytes via an aquaporin type of transport molecule
  - Shuttled back to liver for use in gluconeogenesis

- Fatty acids are immediately bound to albumin and carried in the bloodstream to the liver, muscle and other tissues for oxidation

- *Beta-oxidation*: catabolic process in which the free fatty acids resulting from lipolysis are used by the body as a source of energy.

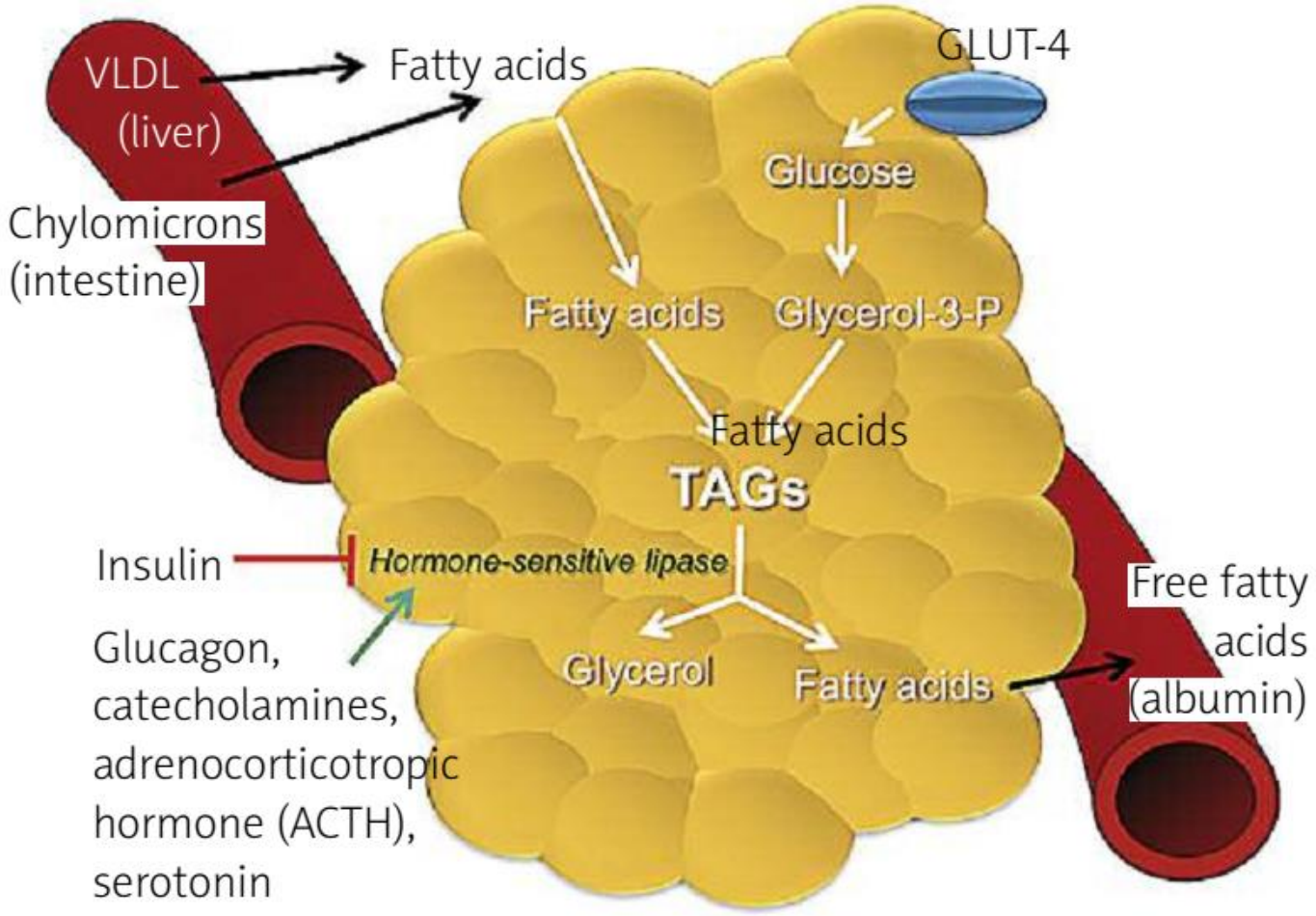


Lipogenesis and Lipolysis

- After a meal, white adipocytes take up fatty acids carried, convert into triglycerides and store these in a large intracellular lipid droplet
  - insulin inhibits lipolysis and causes the uptake of fatty acids
  - During periods of calorie surplus, WAT mass expands by increasing both the size (hypertrophy) and the number of adipocytes (hyperplasia)

- Between meals and in other catabolic states, WAT releases free fatty acids (FFAs) liberated by intracellular lipolysis into the bloodstream to provide other organs with energy
  - Sympathetic nervous system activation is the major lipolytic signalling and increase hormone sensitive lipase levels by stimulating β-adrenergic receptors.

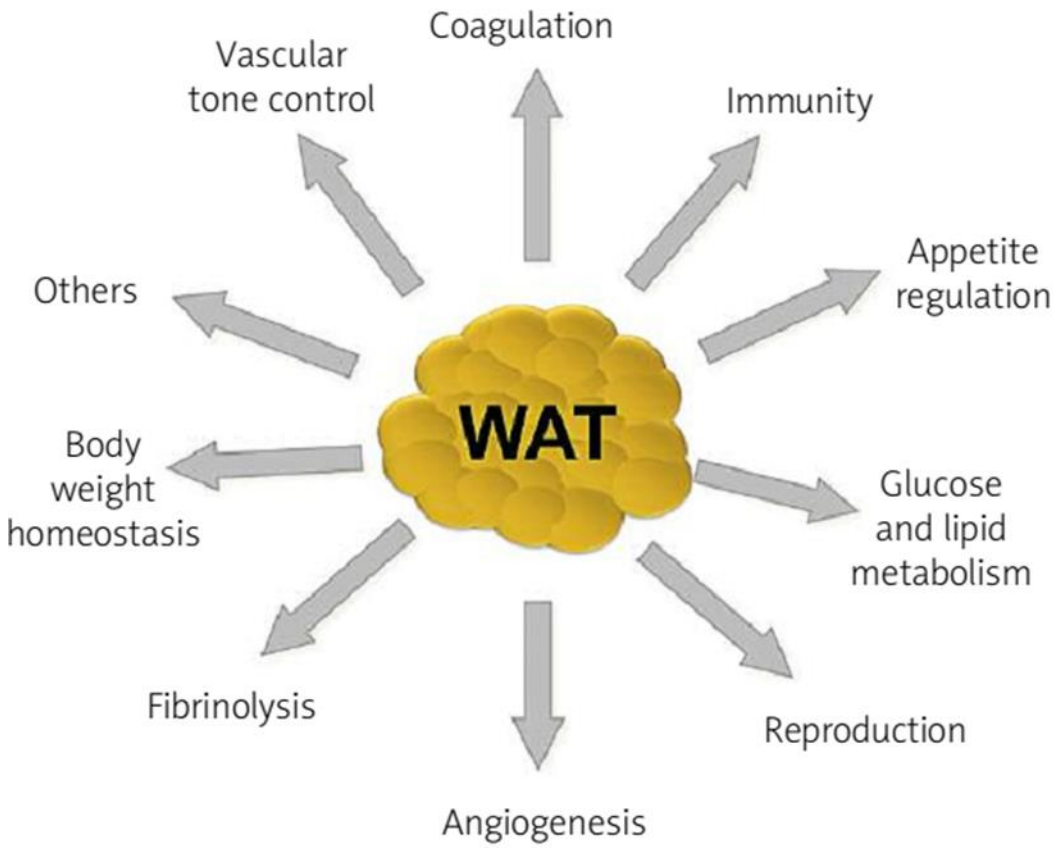
Primary metabolic role of adipose tissue



Secretory Organ

- White adipose tissue is the largest endocrine tissue of humans
- Release and have receptors for;
  - Growth factors
  - Enzymes
  - Cytokines
  - Complement factors
  - Matrix proteins

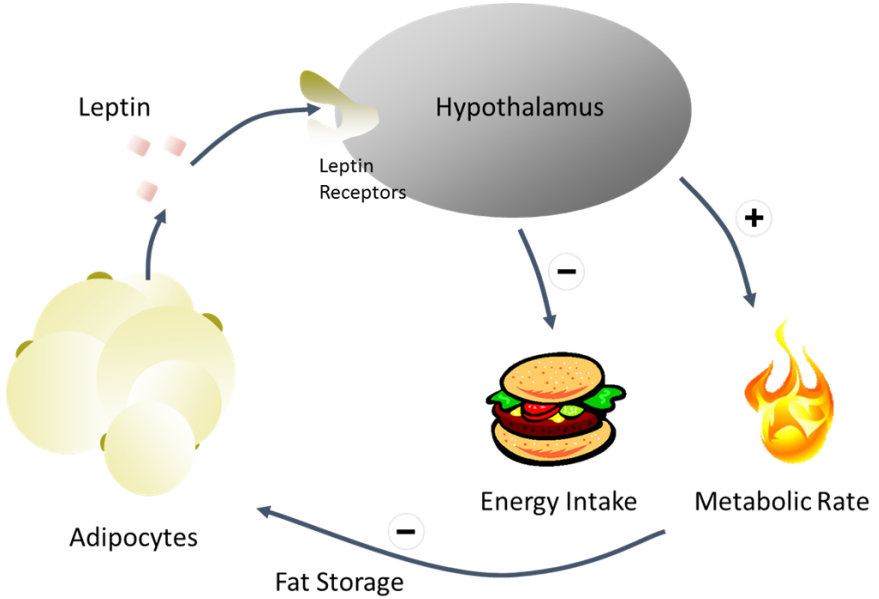
- Takes place in the regulation of;
  - Food intake
  - Energy expenditure
  - Metabolism homeostasis
  - İmmunity and blood pressure homeostasis



Leptin

- Signals satiety (fullness), Anorexigenic peptide
- Expressed mainly by adipose tissue
- Increases energy expenditure
- *ob* gene

- Leptin decreases in response to low insulin levels and increases with feeding or in response to insulin stimulation
- Increased by glucocorticoids, acute infection and proinflammatory cytokines
- Decreased by cold exposure, adrenergic stimulation, growth hormone (GH), thyroid hormone, melatonin



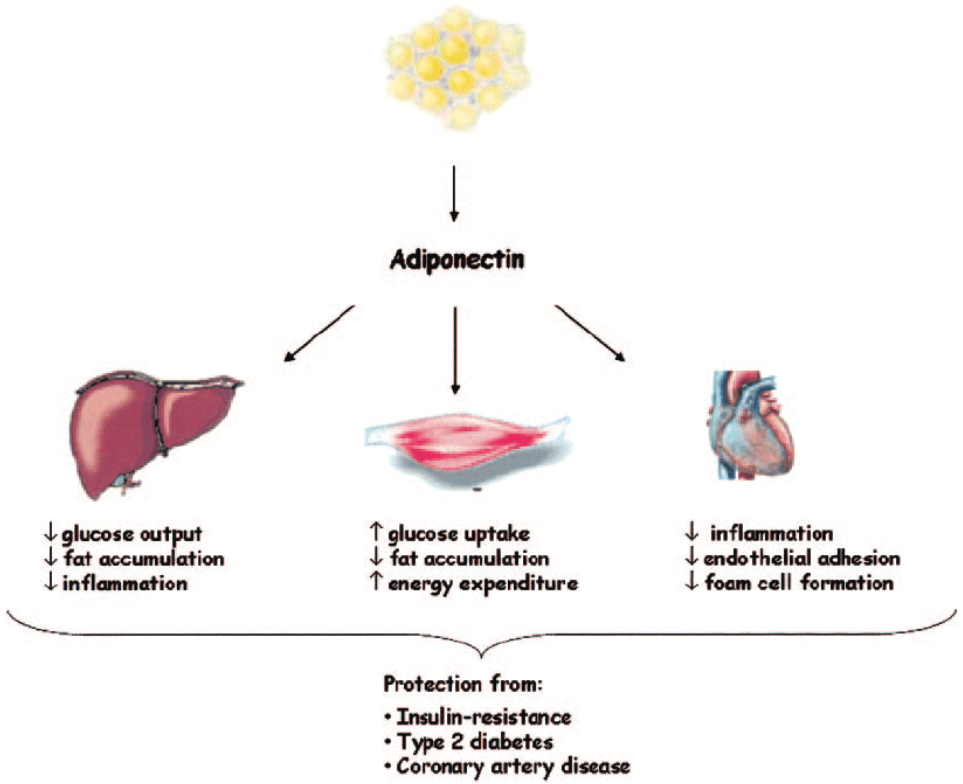
Ob/Ob Mouse

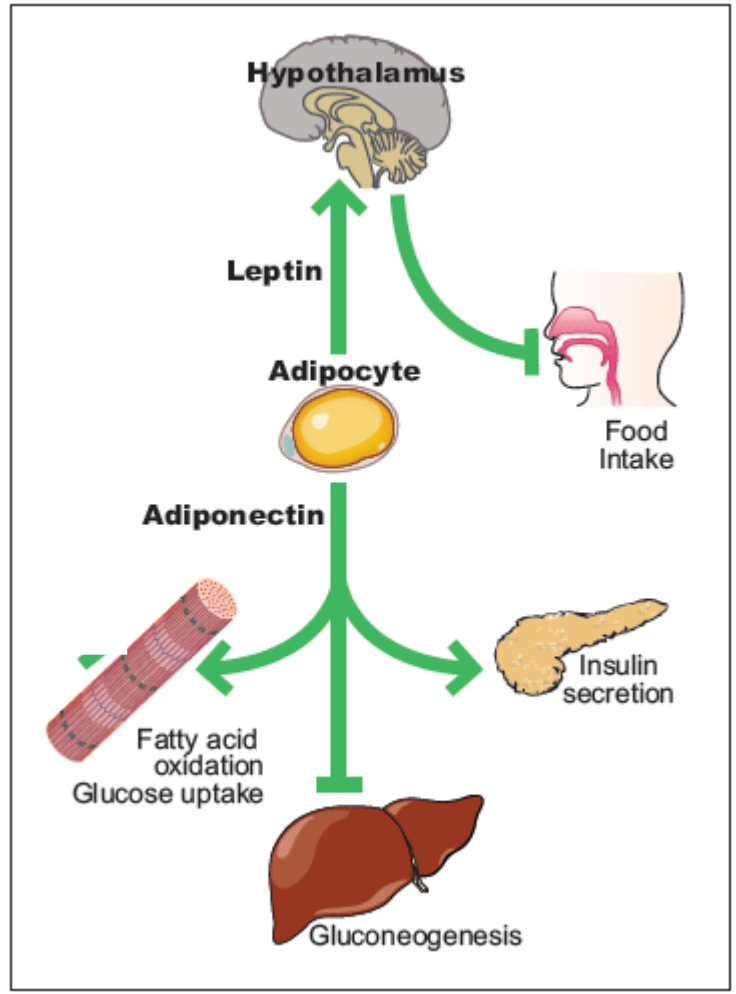
- Mutation on the Ob gene
- Unable to express leptin
- Normal weight at birth, but gain weight rapidly throughout its life (3x unaffected mouse)

- Type II diabetes
  - High blood sugar
  - Enlargement of pancreatic islet cells
  - Increased level of insulin

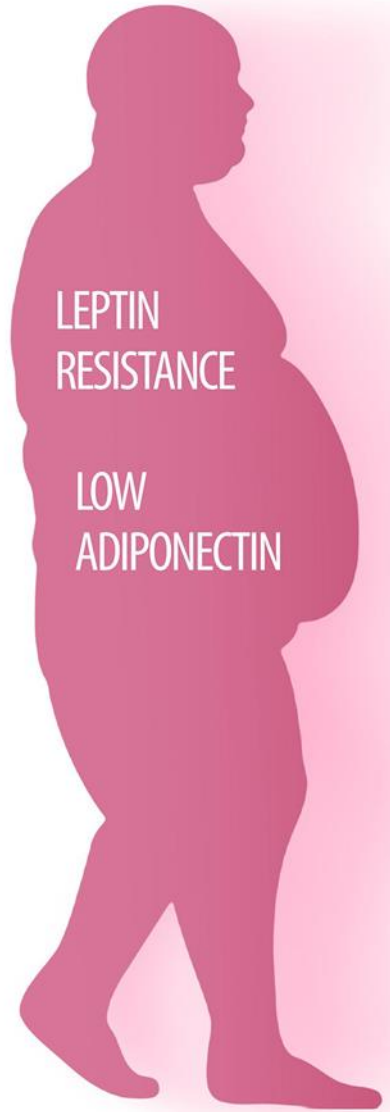
Adiponectin

- Secreted exclusively from adipose tissue
- Strong negative correlation between plasma adiponectin concentration and fat mass
- Adiponectin is associated with type 2 diabetes
  - increase whole body insulin sensitivity
  - stimulate fatty acid oxidation and glucose uptake in skeletal muscle and adipose tissue
  - suppression of hepatic glucose output
- Regulates energy expenditure through activation of AMPK in the hypothalamus





OBESITY/ OVERWEIGTH

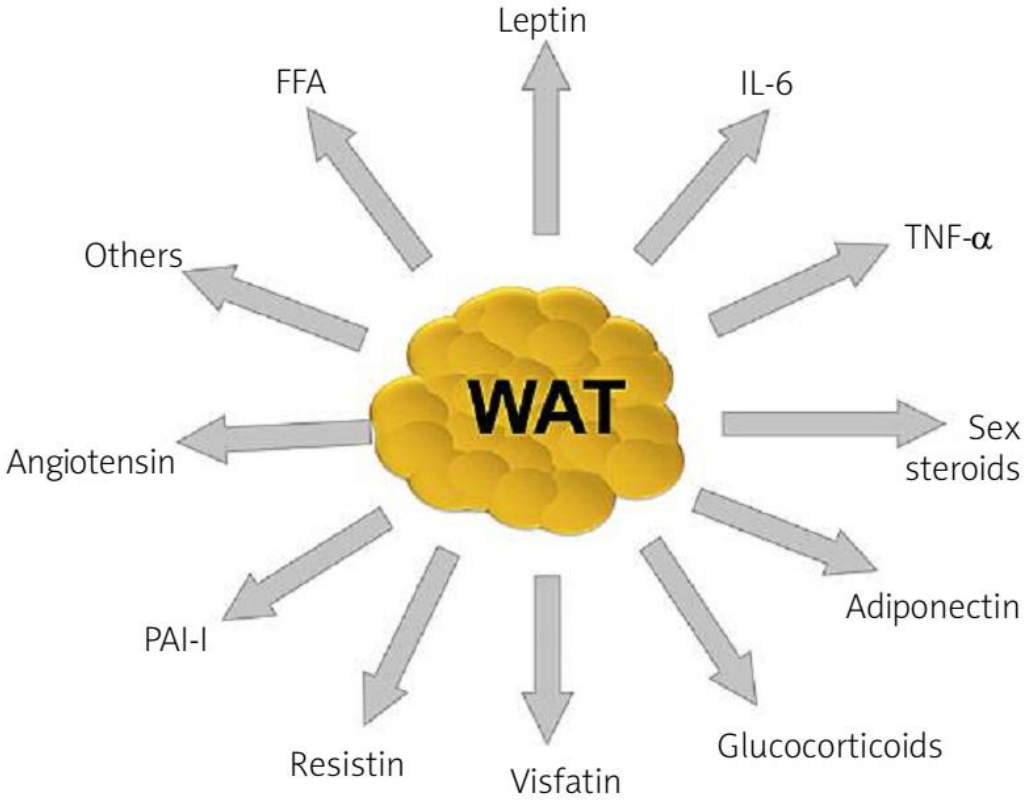


Endocrine factor	Regulation of secretion	Molecular signalling (receptor)	Physiological functions
Adipocyte-enriched endocrine factors			
Leptin	• Increased by fat mass • Decreased by β-adrenergic signalling • Decreased by prolonged fasting	Receptor ligand (LEPR)	CNS signalling • Increased starvation response • Decreased appetite • Increased energy expenditure • Decreased heat loss • Increased hepatic gluconeogenesis • Decreased insulin resistance Peripheral signalling • Decreased insulin secretion • Decreased atherogenesis
Adiponectin	• Increased by β-adrenergic signalling • Decreased by endoplasmic reticulum stress • Decreased by oxidative stress • Decreased by obesity	Receptor ligand (ADIPOR1, ADIPOR2)	• Decreased inflammation • Increased insulin sensitivity • Increased fatty acid catabolism • Decreased gluconeogenesis

Factors secreted by white adipose tissue

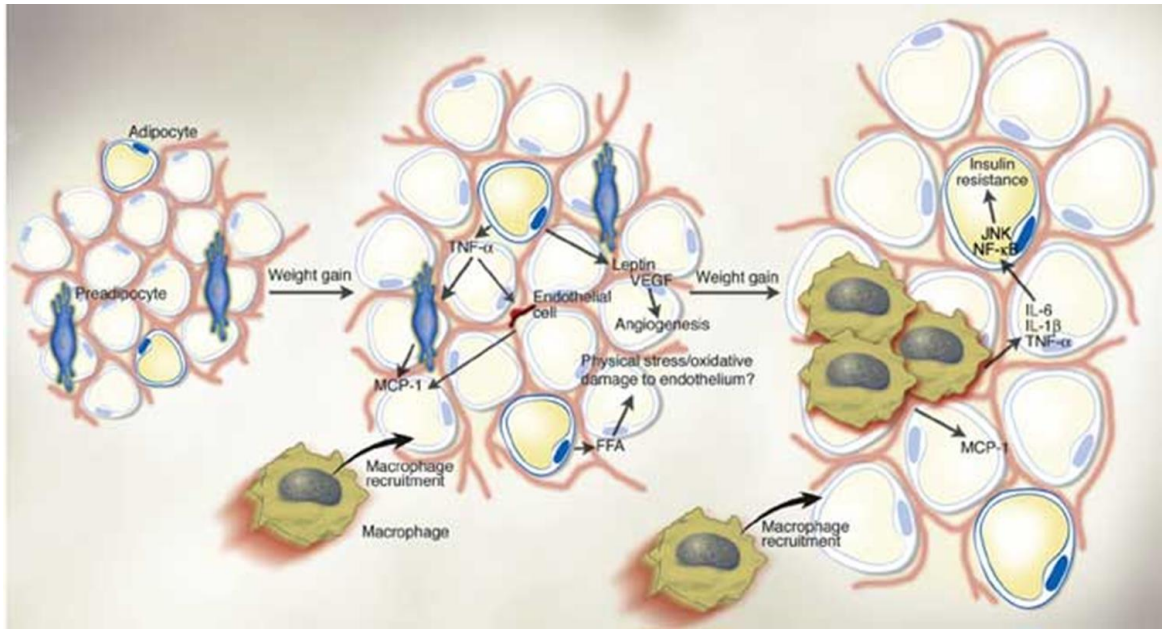
Molecule	Function/effect
Leptin	Signals to the brain about body fat stores. Regulation of appetite and energy expenditure. Wide variety of physiological functions
Adiponectin	Plays a protective role in the pathogenesis of type 2 diabetes and cardiovascular disease
Resistin	Hypothetical role in insulin resistance
TNF-α	Affects insulin receptor signaling, possible cause of the development of insulin resistance in obesity
IL-6	Pro-inflammatory, lipid and glucose metabolism, regulation of body weight
PAI-1	Inhibitor of the fibrinolytic system by inhibition of activation of plasminogen
Angiotensinogen	Precursor of angiotensin II; regulator of blood pressure and electrolyte homeostasis
FFA	Oxidized in tissues to produce local energy. Serve as a substrate for triglyceride and structural molecular synthesis. Involved in the development of insulin resistance
ASP	Influences the rate of triacylglycerol synthesis in adipose tissue
VEGF	Stimulation of angiogenesis
Adipsin	Potential relation between the complement pathway and adipose tissue metabolism
Glycerol	Structural component of the major classes of biological lipids and gluconeogenic precursor
IGF-1	Stimulates proliferation of a wide variety of cells and mediates many cells and many of the effects of growth hormone

TNF-α – tumor necrosis factor α, IL-6 – interleukin-6, PAI-1 – plasminogen activator inhibitor 1, FFA – free fatty acids, ASP – acylation stimulating protein, VEGF – vascular endothelial growth factor, IGF-1 – insulin-like growth factor 1



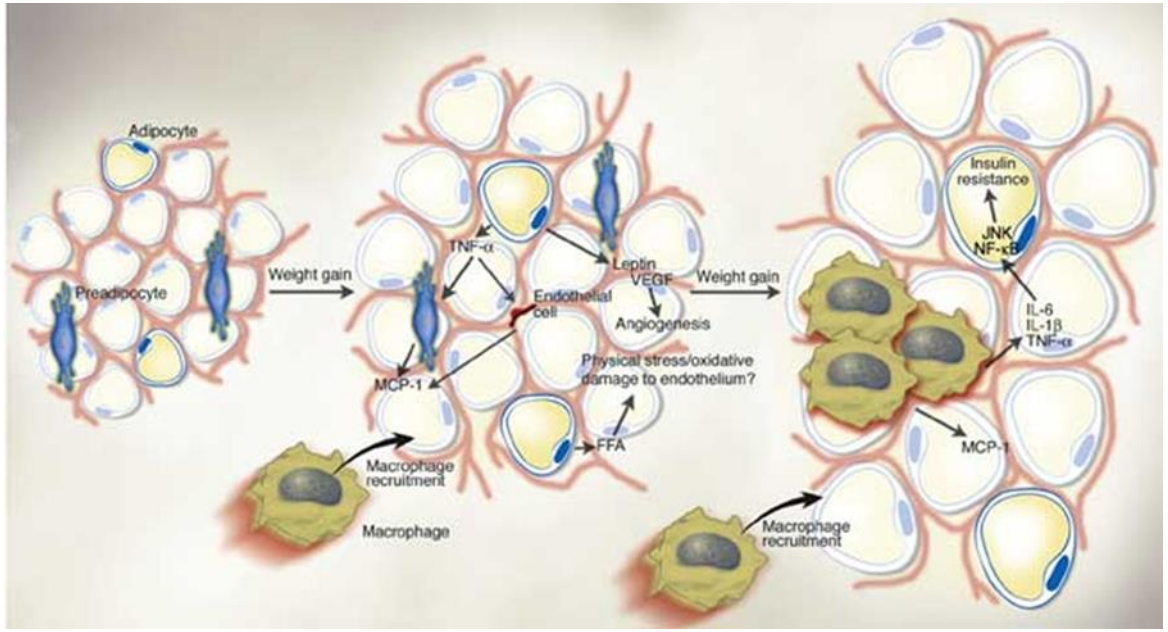
Tumor necrosis factor α (TNF- α)

- Systemic inflammation, regulates immune cells
- Adipocytes are capable of producing TNF-α but macrophages are the primary source of adipose derived TNF-α
- Macrophages are abundant visceral adipose tissue than in subcutaneous adipose tissue
- TNF-α can impair insulin signaling in hepatocytes and adipose tissue (insulin resistance)
    - possible cause of obesity



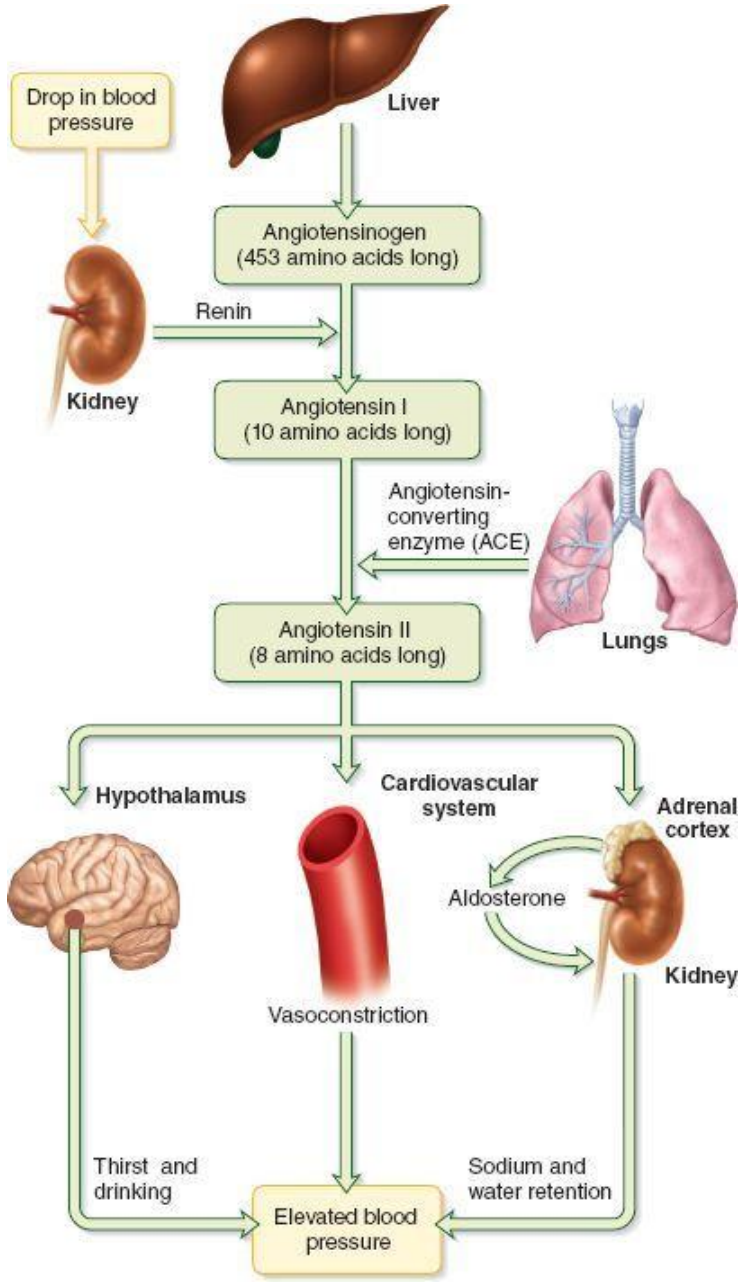
Interleukin-6 (IL-6)

- Pro-inflammatory (promotes inflammation)
- 30% of circulating IL-6 originates from adipose tissue
- Concentrations are higher in visceral fat as compared to subcutaneous fat
- IL-6 inhibits lipase lipoprotein, induces lipolysis and increases glucose uptake



Angiotensin

- Angiotensin II stimulates adipocyte differentiation and lipogenesis
- Adipose tissue expresses all components of the renin-angiotensin-aldosterone system (RAAS)
  - RAAS peptides secreted by adipose tissue act on the vasculature and distant targets to regulate blood pressure and cardiovascular responses in obese individuals



Adipose Tissue