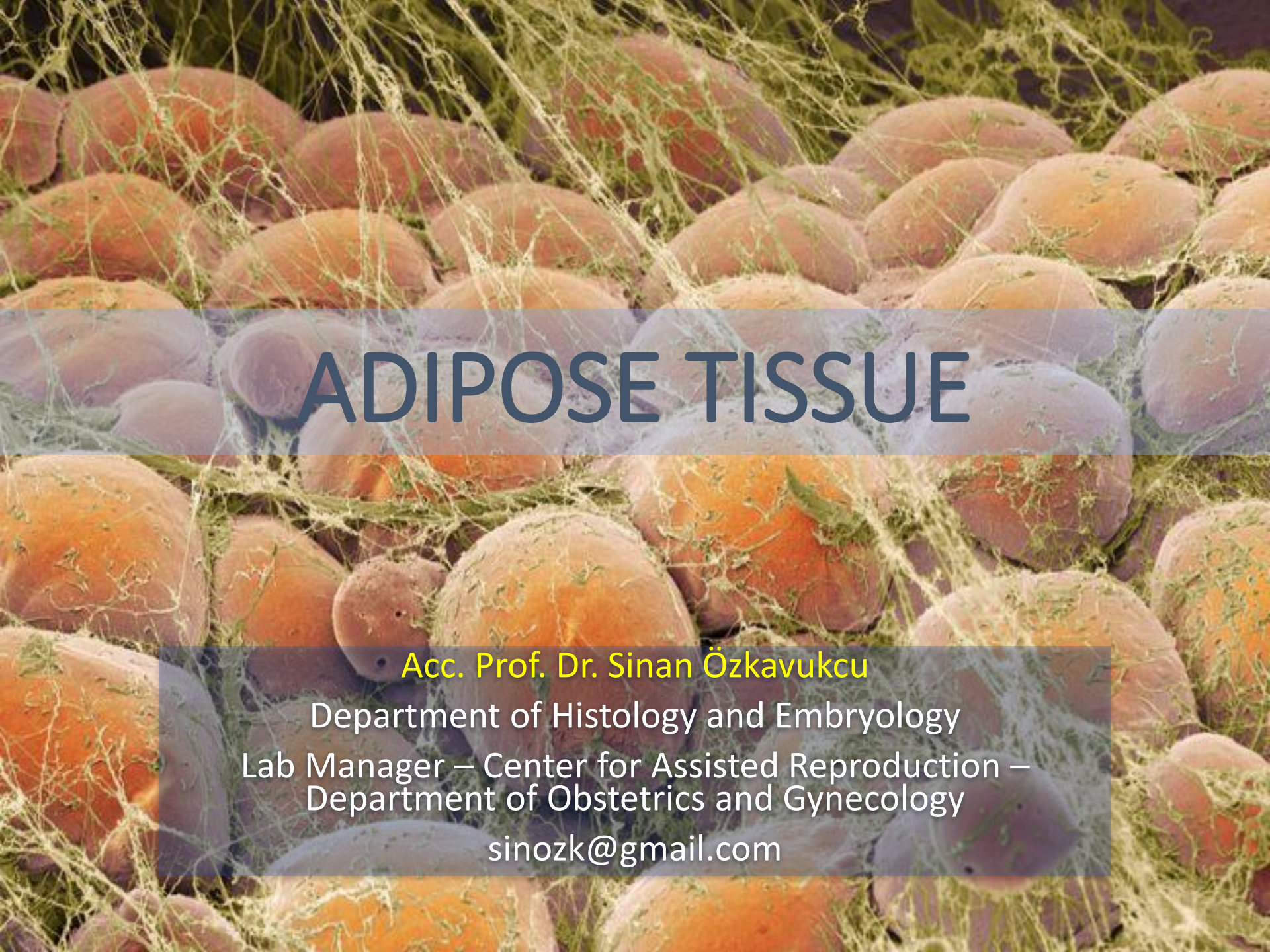


ADIPOSE TISSUE

Acc. Prof. Dr. Sinan Özkavukcu

Department of Histology and Embryology

Lab Manager – Center for Assisted Reproduction –
Department of Obstetrics and Gynecology

sinozk@gmail.com

Overview

- Adipose tissue is a specialized connective tissue that plays an important role in energy homeostasis and metabolism.
- Adipocytes are the primary cell type
- Individual **adipocytes** are found throughout loose connective tissue and groups of adipocytes make adipose tissue.
- Adipose tissue stores energy in order to meet the daily energy needs as required due to the varying nutrient intake.
- Storage of carbohydrate and protein is limited. Energy is therefore stored as triglycerides in the form of lipid droplets.

Energy metabolism

- Triglycerides are the most concentrated form of metabolic energy storage available to humans.
- Because triglycerides lack water, they have about twice the energy density of carbohydrates and proteins.
- The energy density of triglycerides is approximately 37.7 kJ/g (9 cal/g), whereas the density of carbohydrates and proteins is 16.8 kJ/g (4 cal/g).
- In the event of food deprivation, triglycerides are an essential source of water and energy.
- Fatty-acid oxidation gives out water as the end product.
- The hump of a camel consists largely of adipose tissue and is a source of water and energy

Endocrine functions

- They also regulate energy metabolism by secreting paracrine and endocrine substances.
- Adipose tissue is now considered a major **endocrine organ**.

There are two types of adipose tissue

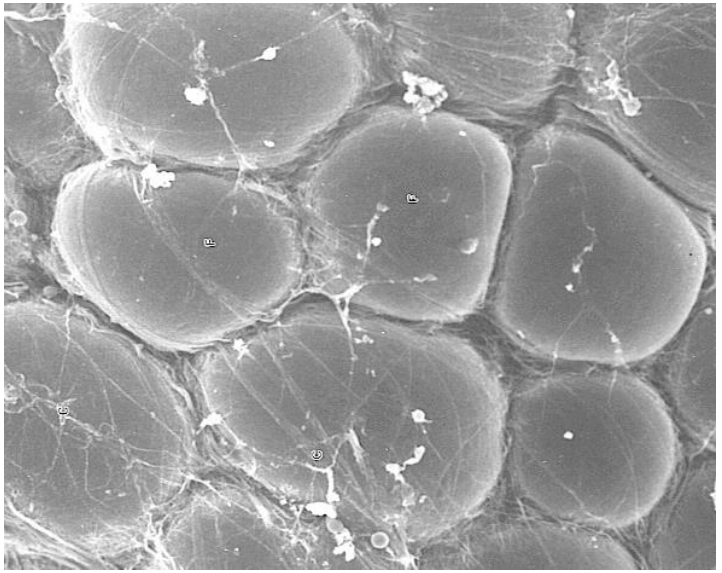
- White adipose tissue (unilocular)
  - predominant type in adult humans.
- Brown adipose tissue (multilocular)
  - present in humans during fetal life but diminishes during the first decade after birth.

White adipose tissue

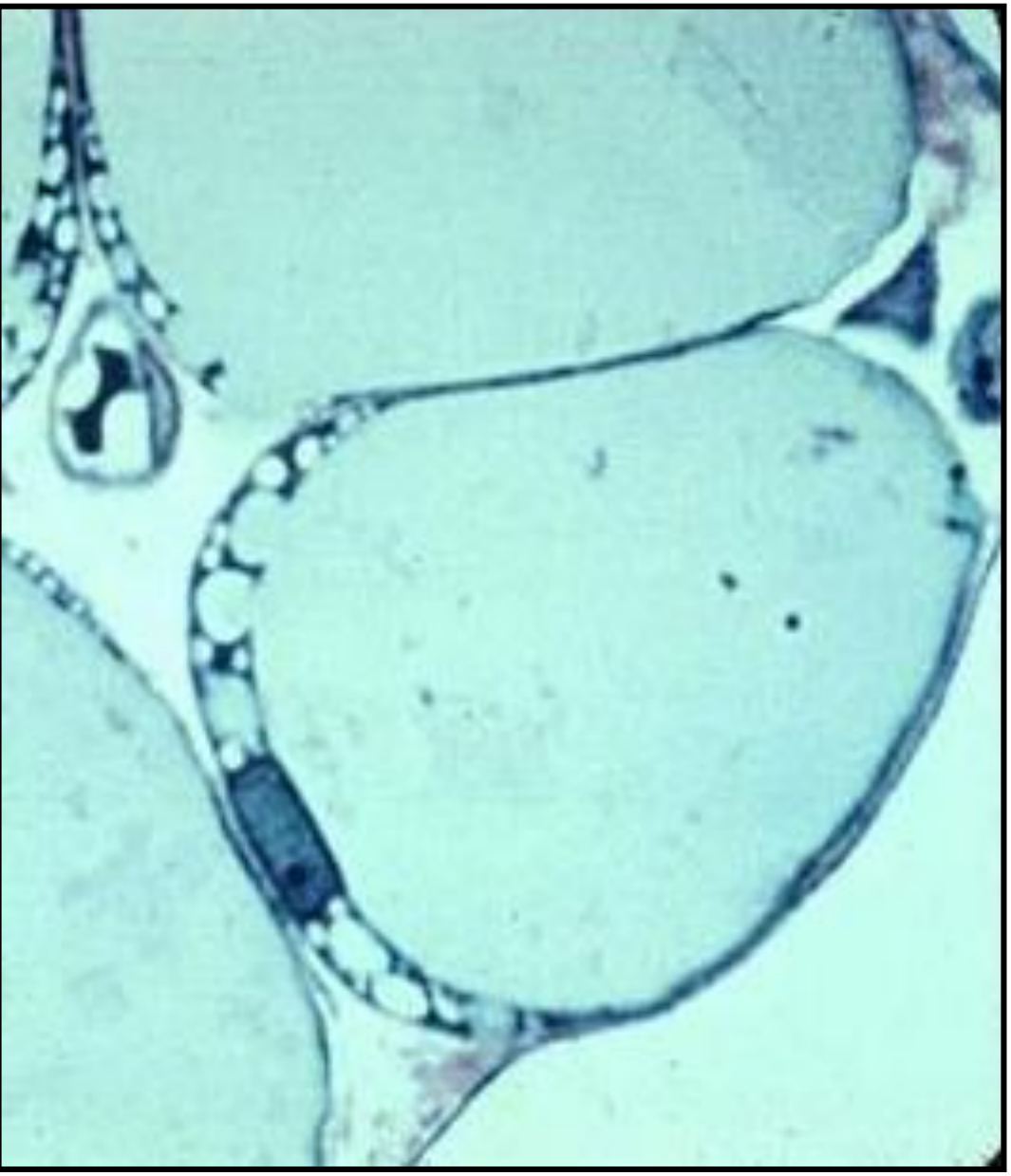
- Storage of energy
- Prevention of heat loss
- Protection of vital organs
- Hormone secretion

- In the connective tissue under the skin it forms a layer called panniculus adiposus or hypodermis
- Thermal conductivity of adipose tissue is only about half that of skeletal muscle so it provides a significant thermal insulation against cold.
- In the lactating female, mammary fat pad plays an important role in supporting breast function. It provides lipids and energy for milk production, also growth factors
- They are found as omentum in the abdomen, in the mesentery and retroperitoneally around the kidney. Abundantly in the bone marrow. Protective sheat around the eyes, pericardium, palms and soles.
- It is known that there is no fat accumulation in the eyelid, penis skin, scrotum and ear auricle.

- Histologically, fat cells come together tightly to form a lobular organization.
- Between these formed lobules, a surrounding fibrous septum can be seen
- Around the lobe-forming fat cells, there is a network of thin reticular fibrils.

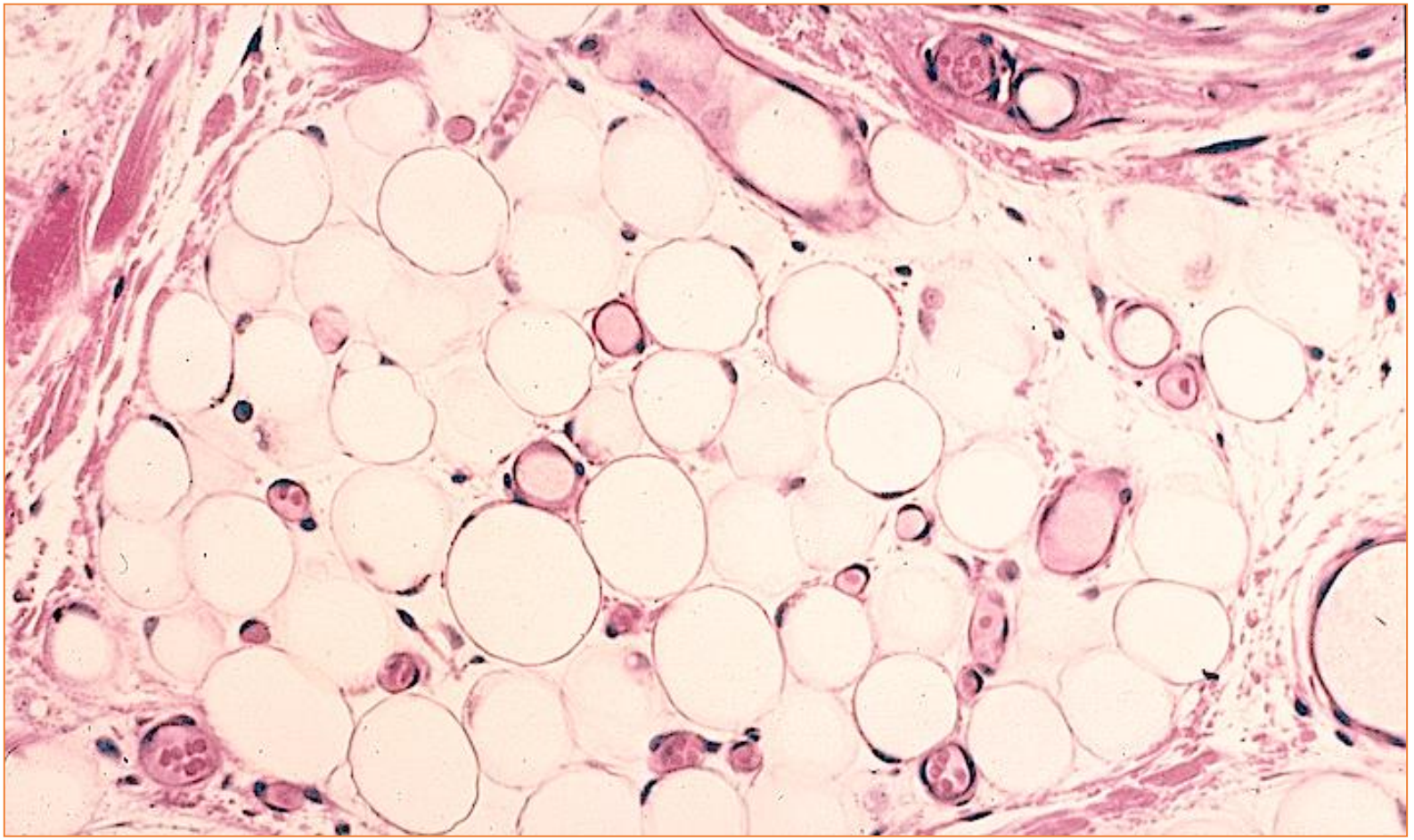


- Adipose cells.
- It is observed that the cell nuclei are pushed aside due to the accumulated fat.



Diamond ring appearance

- Another important feature is the presence of large number of blood capillaries in lobular spaces.

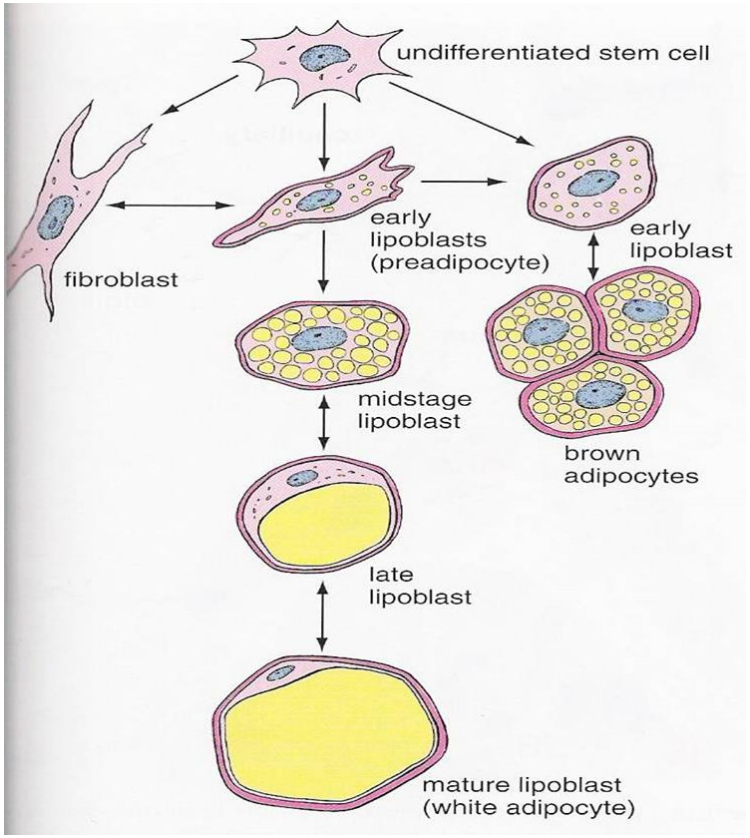


White Adipose Tissue

- Endocrine Functions;
  - Leptin: (Gr. *leptos* = fine)
    - 16 kd peptide hormone,
    - Secreted only from adiposides
    - Stops food intake, reduces body weight, increases metabolic rate
    - It is a factor that creates a feeling of satiety. Prevents nutrient intake while body energy level is sufficient
    - Communicates with the center of the brain that controls food intake
    - Specific receptors in the hypothalamus
  - Angiotensinogen: is the cause of HT as it increases in obesity
  - Adiponectin: improves insulin senstivity
  - Resistin
  - Steroid hormones (testosterone, estrogen, glucocorticoid)
  - TNF-α, TGF-b, IGF-I, cytokines (IL-6 and PGs), which are increasingly synthesized in obesity, may be triggering the development of diabetes.

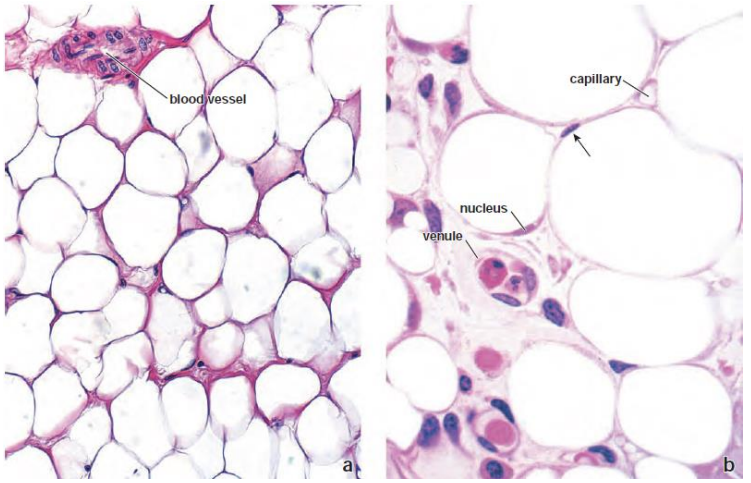
Adipocyte differentiation

- It is a unique type of cell originating from mesenchymal stem cells found in the adventitia of small venules.
- a transcription factor called peroxisome proliferator–activated receptor gamma (PPARγ) in complex with the retinoid X receptor (RXR) play a critical role in adipocyte differentiation and initiation of lipid metabolism
- Thus, triglycerides begin to accumulate in early lipoblasts (adipoblasts) or preadiposites.



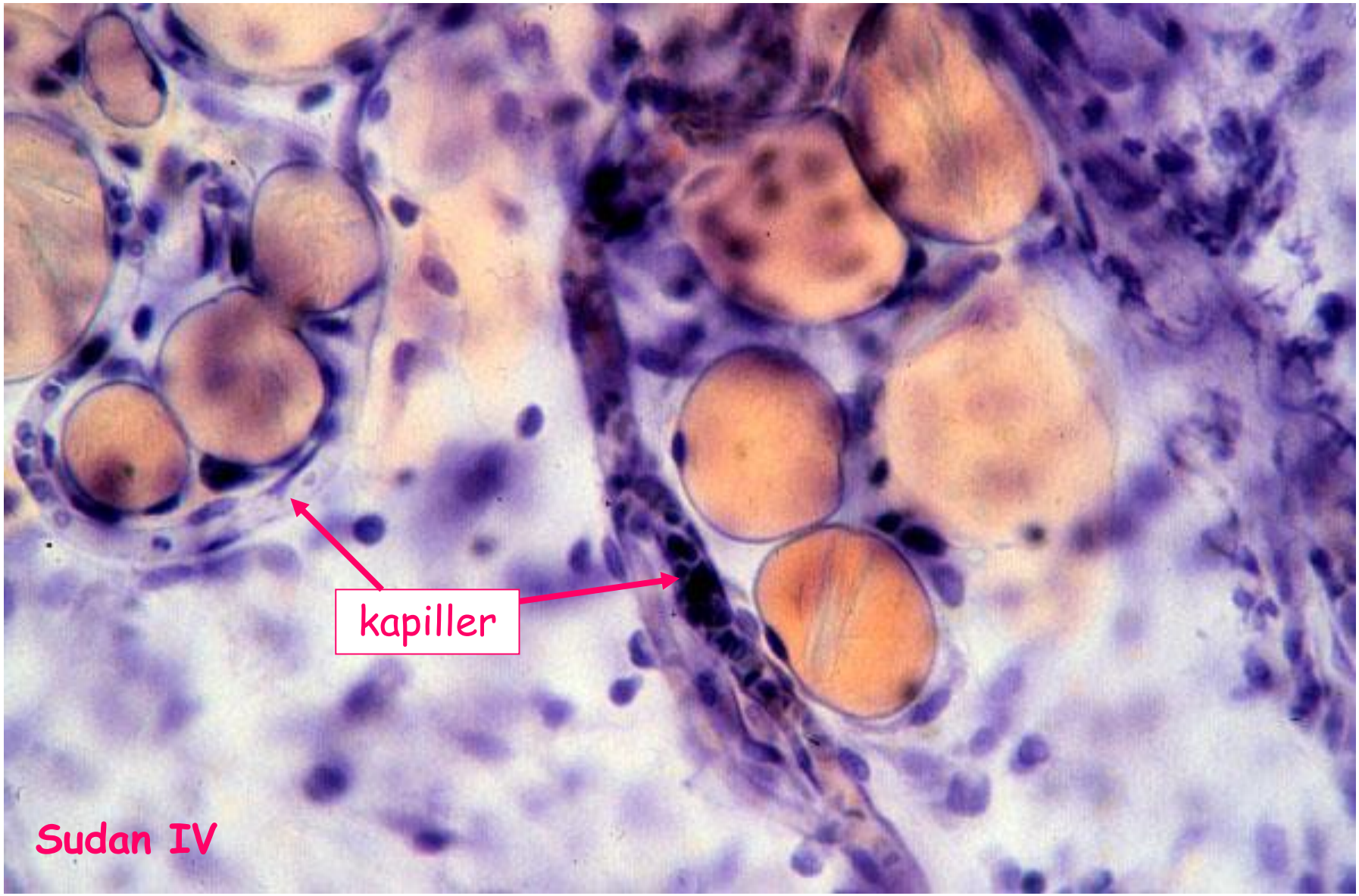
Mature adipocyte

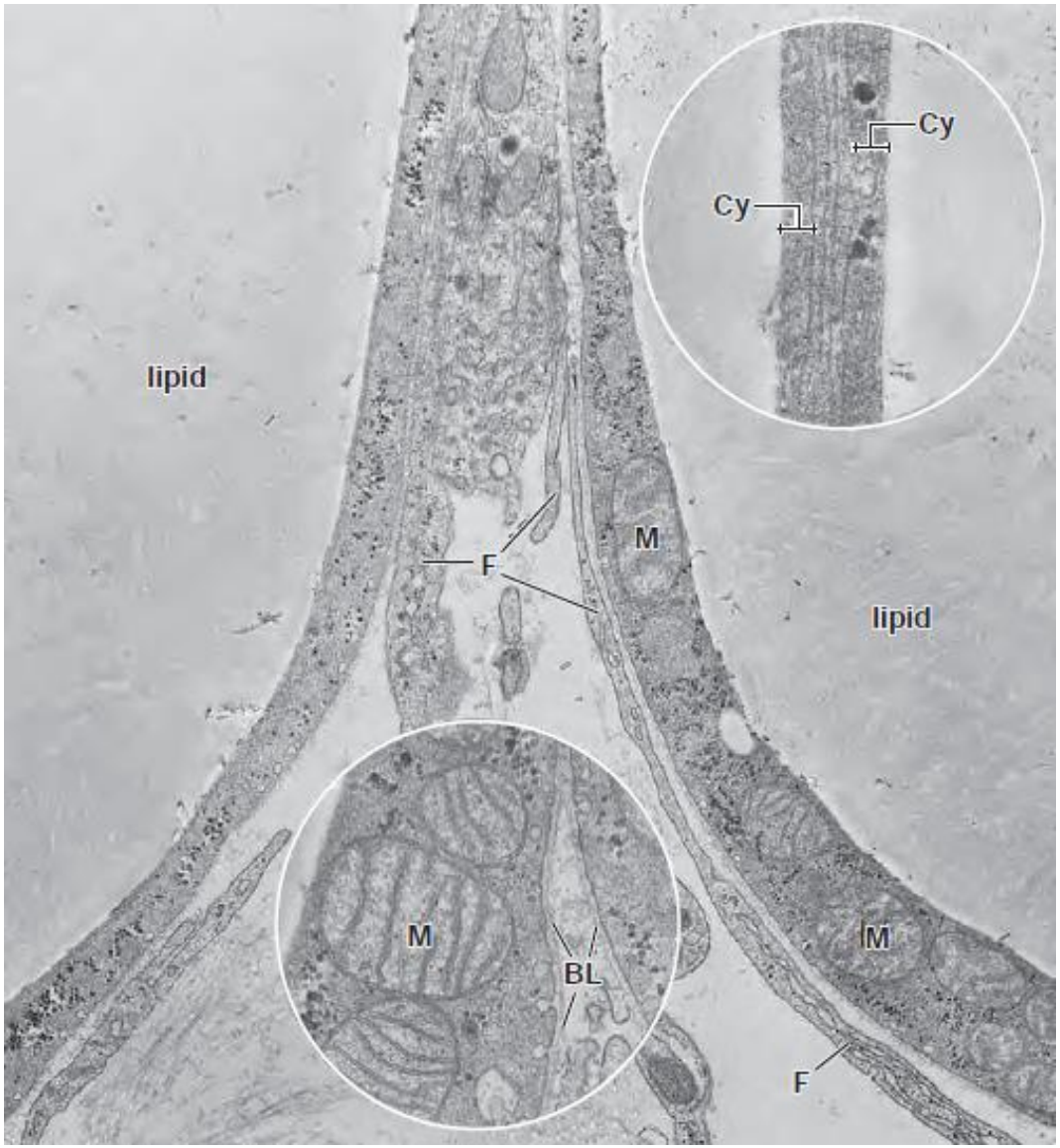
- The mature adipocyte is characterized by a single, large lipid inclusion surrounded by a thin rim of cytoplasm
- Smooth endoplasmic reticulum (sER) is abundant, whereas rER is less prominent
- The lipid mass compresses the nucleus to an eccentric position and flattened shape
- There is a single lipid droplet inside the cell, so called unilocular



- They can be 100 µm or larger
- Because of the chemicals used in the preparation of histological preparations (xylen), lipid dissolves in the cell, the cells appear clear (diamond ring)
- Reticular fibers (type III collagen) around adipocytes can be shown by silver staining
- They contain mast cells, unmyelinated nerve fibers and abundant blood vessels.

- If they are stained with lipid dyes through special processes, the oil content they contain is easily observed.





- The lipid inside the cell is not wrapped by a membrane
- At the junction of the cytoplasm and lipid droplet, the 5 nm thick condensed lipid layer is supported by parallel viment filaments.

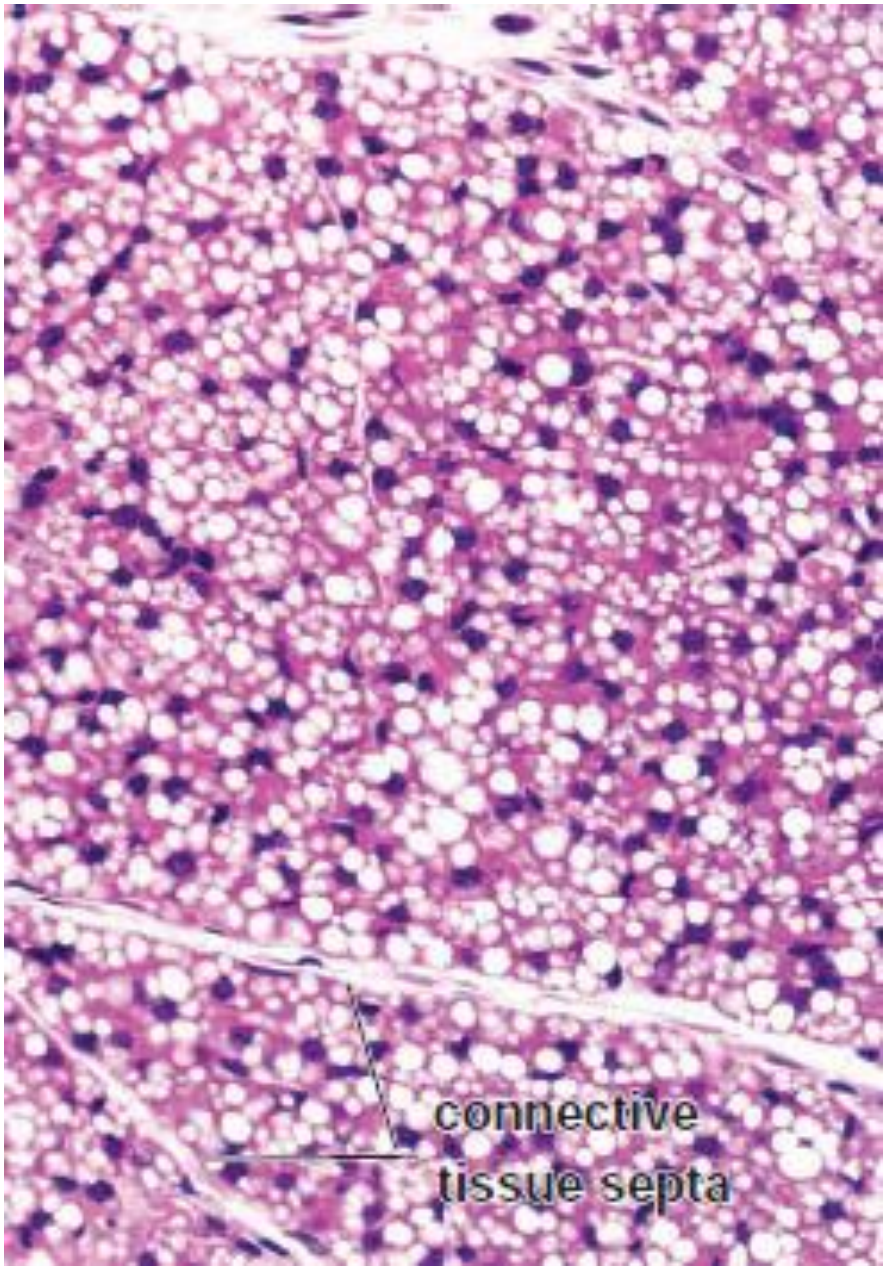
Brown (multilocular) Adipose Tissue

- The high number of mitochondria of brown adipocytes contain a large amount of cytochrome that is why the tissue is observed in brown color.
- Although white adipose tissue is common in the body, brown or brown adipose tissue is located in very specific areas.
- Brown adipose tissues are more developed in hibernating animals.
- It is also called the hibernating gland as this tissue regulates body temperature during hibernation.

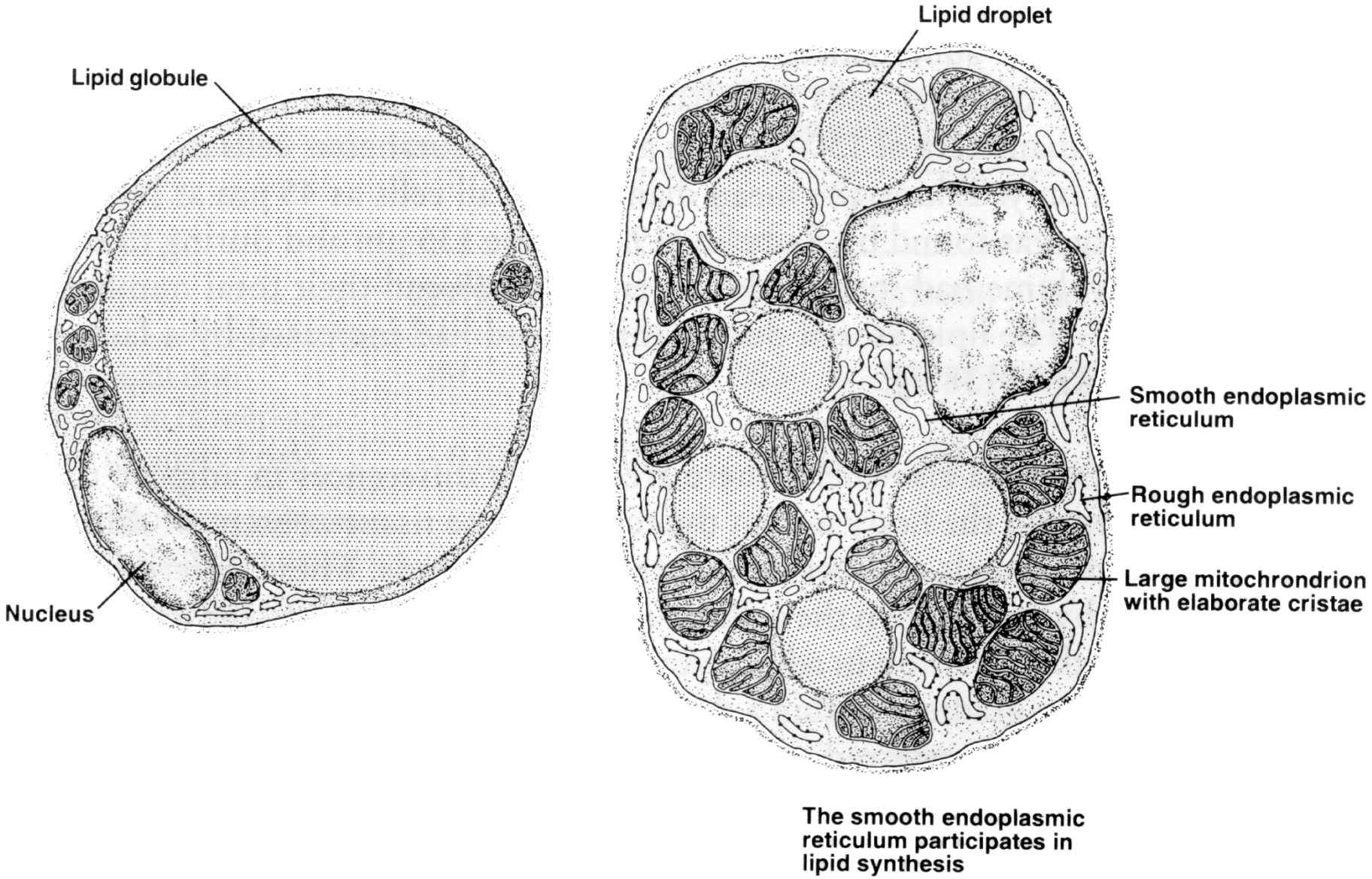
- Brown adipose tissue is quite common in fetus and newborns;
- They maintain their presence in the armpit, posterior neck trigonum and renal hilum after birth.
- In adults, almost all the fat tissue is white and in certain regions, brown fat tissue can be seen again in chronic malnutrition.

•The UCP-1 gene encodes a specific mitochondrial protein called **uncoupling protein (UCP-1)** or **thermogenin** is essential for brown adipocytes metabolism (thermogenesis).
•Under normal conditions brown adipose tissue can expand in response to increased blood levels of **norepinephrine** (sympathetic nervous system)
•Metabolism of lipid in brown adipose tissue generates heat in process known as t*hermogenesis*.
•**Nonshivering thermogenesis**.
•UCP-1 activity has been shown to increase during cold stress

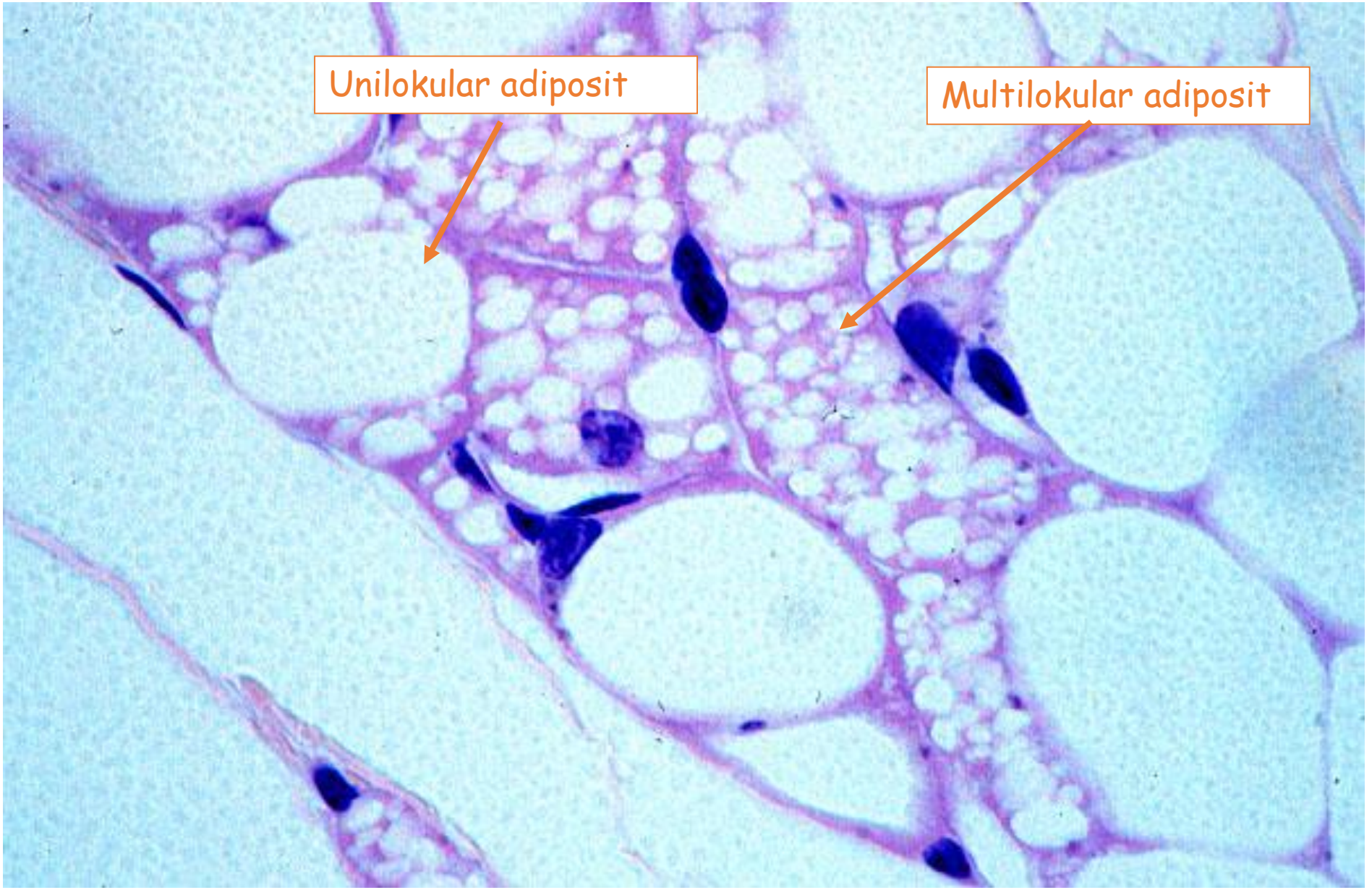
- The histological properties of this adipose tissue show significant differences from WAT
- Combined fat cells form more prominent lobules.
- Connective tissue septum between lobules is also more prominent.
- Rich blood vessels are found both inside and between the lobules.
- In terms of nerve distribution, it is richer than white adipose tissue.



- The cells of the brown adipose tissue form cellular clusters around the veins.
- These cells are smaller than those of WAT.
- The cytoplasm of these polygonal cells is filled with many drops of lipid in different diameters
- Another remarkable feature in cytoplasm is; high numbers of mitochondria.
- In addition to these, the nucleus becomes eccentric in these cells with the accumulation of vacuoles, but does not flatten like the nucleus in white adipose tissue.



The smooth endoplasmic reticulum participates in lipid synthesis


Unilokular adiposit
Multilokular adiposit

The regulation of Adipose Tissue

- An interconnected hormonal and neural signals emanating from the adipose tissue, alimentary tract, and central nervous system form the **brain–gut–adipose axis** that regulates appetite, hunger, satiety, and energy homeostasis
- Short-term weight regulation (controls appetite and metabolism on a daily basis)
  - Ghrelin: (GH Relsing Inducer) Secreted from GIS and induces appetite
  - Peptit YY: inhibits appetite
- Long-term weight regulation (controls on a continual basis - over months and years)
  - Leptin
  - Insulin
  - Tyroid hormones
  - Glucocorticoids

Ghrelin

- Small, 28 a.a. polypeptide
- Secreted from gastric epithelium
- Induces appetite and GH release from the anterir hypophisis
- Its receptor is in hypotalamus, creates hunger feeling

- Prader-Willi Syndrome is caused by a genetic mutation on chromosome 15 and there is an overproduction of ghrelin.
- Patients display morbid obesity and obsessive eating behavior beginning from early ages
- With the obesity complications patients are lost in the 30s

Peptide YY

- 36 aa small gastrointestinal hormone.
- Immediately after meals, secreted from small intestine to provide the feeling of fullness
- Its receptor is in hypotalamus, stops desire for eating

ELSEVIER

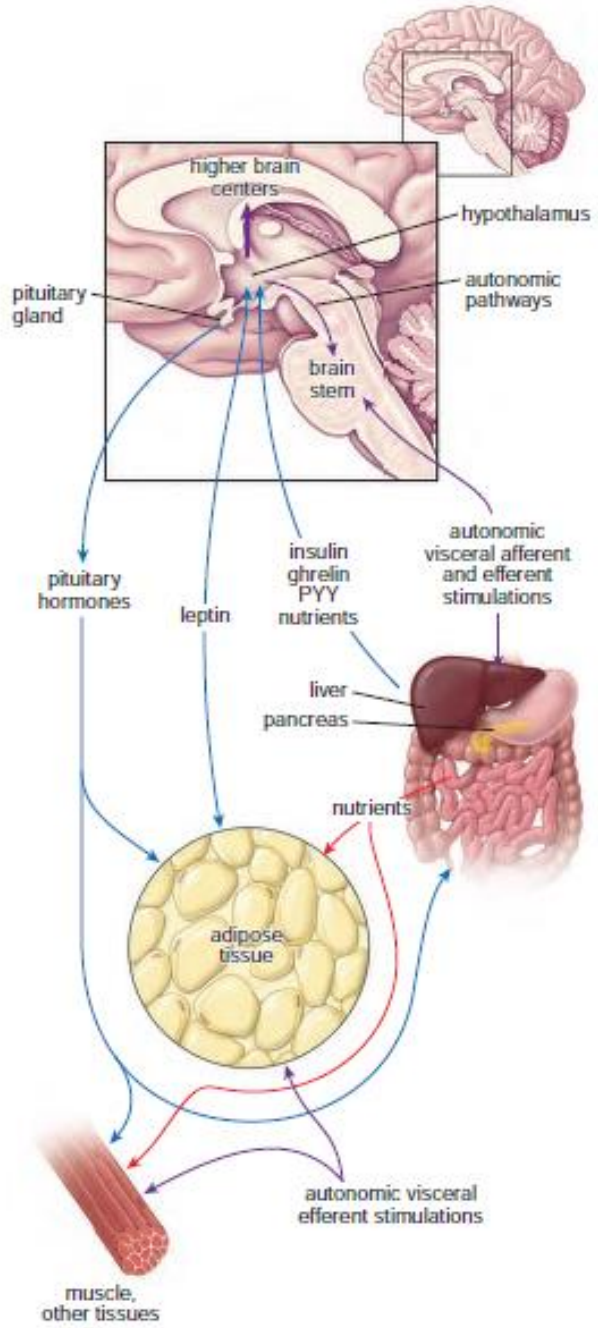
Bioorganic & Medicinal Chemistry Letters

Volume 27, Issue 16, 15 August 2017, Pages 3829-3832

Potent antiobesity effect of a short-length peptide YY-analogue continuously administered in mice

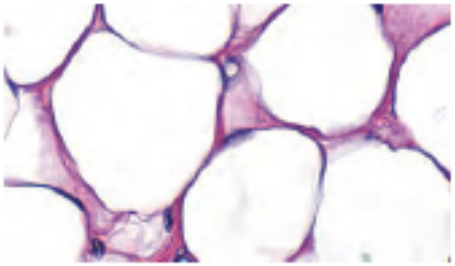
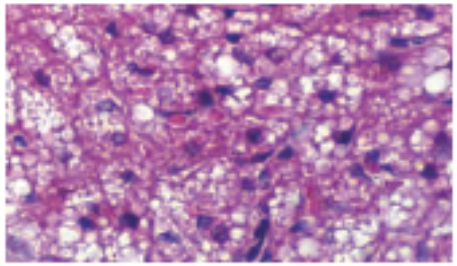
Naoki Nishizawa, Ayumu Niida, Yusuke Adachi, Yasushi Masuda, Satoshi Kumano, Kotaro Yokoyama, Tomoko Asakawa, Hideki Hirabayashi, Nobuyuki Amano, Shiro Takekawa, Tetsuya Ohtaki, Taiji Asami

PMID: 28684122



One of the major metabolic functions of adipose tissue involves the **uptake of fatty acids** from the blood and their **conversion to triglyceride** within the adipocyte (**insülin)**

When adipose tissue is stimulated by neural or hormonal mechanisms (**thyroid hormones**, and **adrenal steroids, glucagon, GH**), triglycerides are broken down into glycerol and fatty acids, a process called **mobilization**. The fatty acids pass through the adipocyte cell membrane to enter a capillary. Here they are bound to the carrier protein **albumin** and transported to other cells, which use fatty acids as metabolic fuel.

Features	White Adipose Tissue	Brown Adipose Tissue
		
Location	Subcutaneous layer, mammary gland, greater omentum, mesenteries, retroperitoneal space, visceral pericardium, orbits (eye sockets), bone marrow cavity	Large amounts in newborn Remnants in adults at the retroperitoneal space, deep cervical and supraclavicular regions of the neck, interscapular, paravertebral regions of the back, mediastinum
Function	Metabolic energy storage, insulation, cushioning, hormone production, source of metabolic water	Heat production (thermogenesis)
Adipocyte morphology	Unilocular, spherical, flatten nucleus, rim of cytoplasm Large diameter (15–150 μm)	Multilocular, spherical, round eccentric nucleus Smaller diameter (10–25 μm)
Transcription factors "master switch" in differentiation	PPAR-γ/RXR	PRDM16/PGC-1
UCP-1 genes expression	No	Yes (unique to brown fat)
Mitochondria	Few, poorly developed	Many, well developed
Innervation	Few sympathetic nerve fibers	High density of sympathetic nerve fibers
Vascularization	Few blood vessels	Highly vascularized tissue
Response to environmental stress (cold exposure)	Decreased lipogenesis Increased lipoprotein lipase activity	Increased lipogenesis Decreased lipoprotein lipase activity
Growth and differentiation	Throughout entire life from stromal-vascular cells	Only during fetal period Decreases in adult life (exception: individuals with pheochromocytoma and hibernoma)