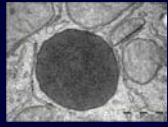
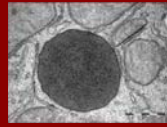


LYSOSOME PEROXISOME

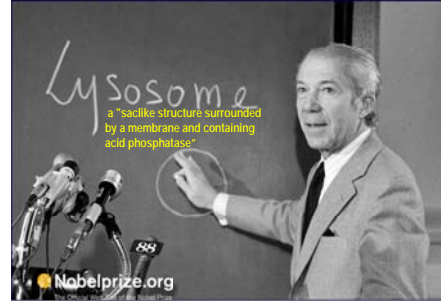


LYSOSOME

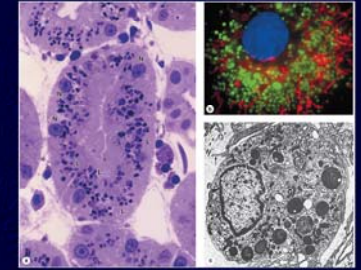
LYSO- (*lysis*, meaning 'to loosen' 'breaking down')
-SOME (*soma*, meaning 'body')
'body that lyses' or 'lytic body'.



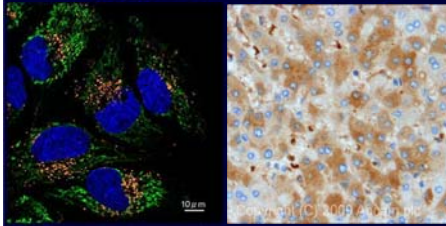
The Nobel Prize in Physiology or Medicine, 1974
Albert Claude, Christian de Duve, George E. Palade



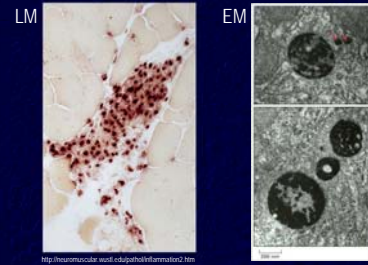
LYSOSOMES LIGHT AND ELECTRON MICROSCOPY



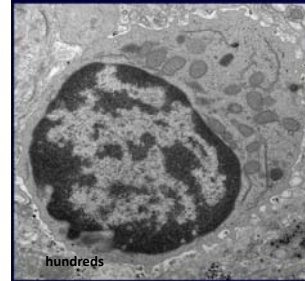
LYSOSOME IN LIGHT MICROSCOPY MARKER ENZYMES – ACID HYDROLASES



LYSOSOME IN MICROSCOPY STANDARD MARKER ENZYME, ACID PHOSPHATASE



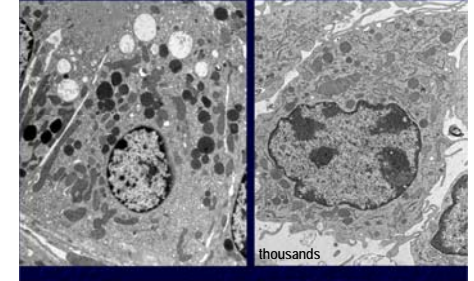
LYSOSOME IN ELECTRON MICROSCOPY



Vesicular/vacuolar organelle, round or unregulated shape, heterogeneous diameter, heterogeneous morphology, heterogeneous opacity of the lumen

hundreds

LYSOSOME IN ELECTRON MICROSCOPY



thousands

Lysosome ultrastructure

Ultrastructural elements of lysosome

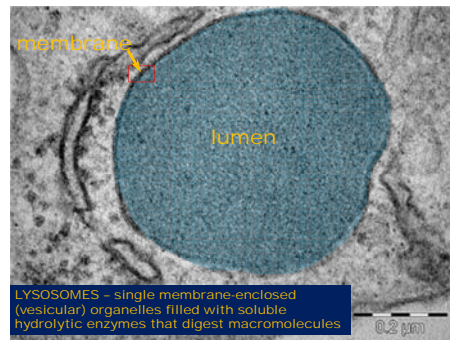
- membrane (single lipid bilayer)
- lumen (electron dense, heterogeneous)

Lysosome classification – functional evolution

- primary lysosomes (homogenous content)
- secondary lysosomes (heterogeneous content)
- tertiary lysosomes (residual bodies, lamellar content)

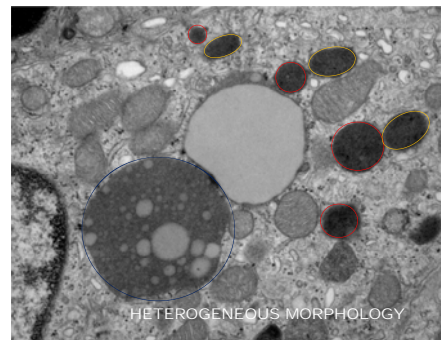
Lysosome classification – active site

- conventional lysosomes (inside the cells)
- secretory lysosomes (lysosomal enzymes secreted outside the cells)

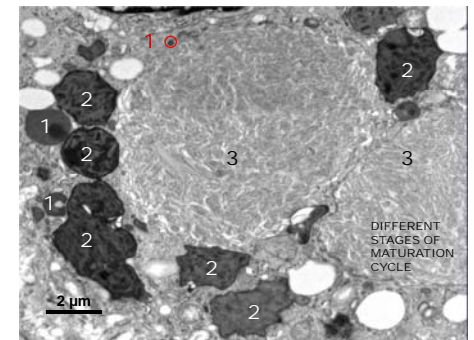


LYSOSOMES – single membrane-enclosed (vesicular) organelles filled with soluble hydrolytic enzymes that digest macromolecules

0.2 μm

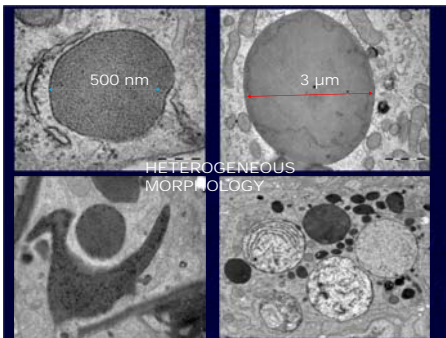


HETEROGENEOUS MORPHOLOGY



DIFFERENT STAGES OF MATURATION CYCLE

2 μm

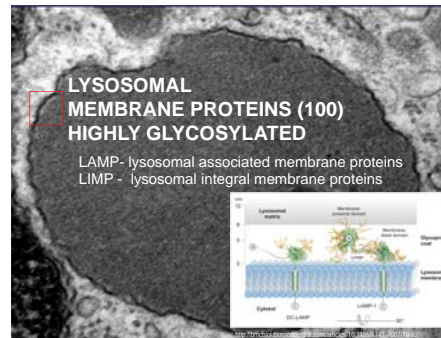
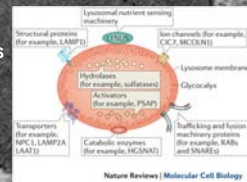


HETEROGENEOUS MORPHOLOGY

LYSOSOMAL MEMBRANE

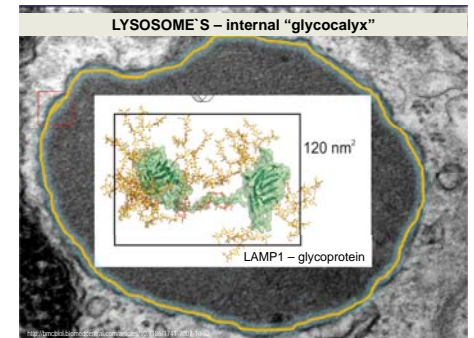
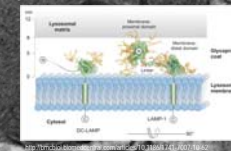
single-lipid bilayer + integral and peripheral proteins

STRUCTURAL PROTEINS
TRANSPORTERS
CATABOLIC ENZYMES
TRAFFICKING PROTEINS
ION CHANNELS



LYSOSOMAL MEMBRANE PROTEINS (100) HIGHLY GLYCOSYLATED

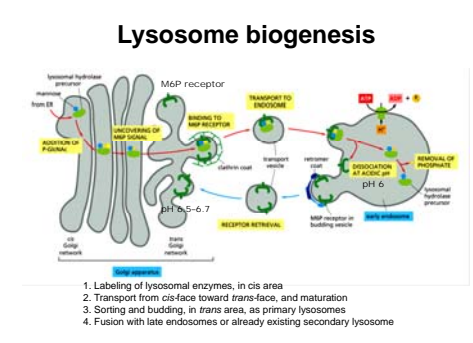
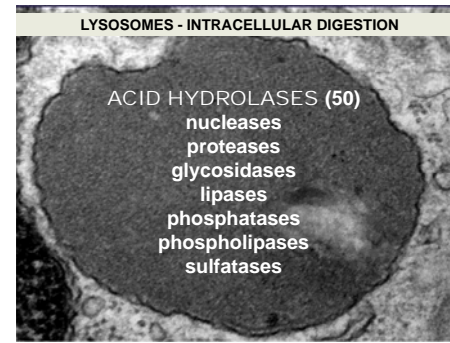
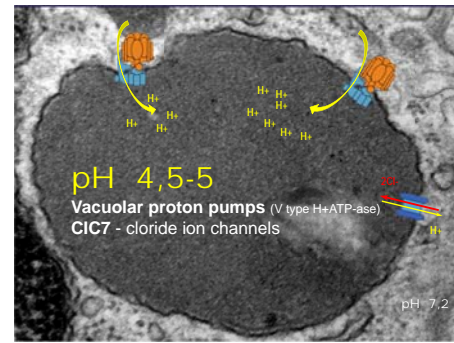
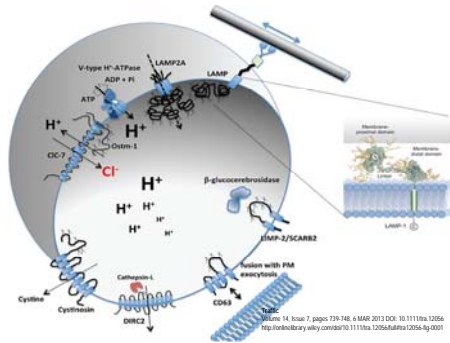
LAMP - lysosomal associated membrane proteins
LIMP - lysosomal integral membrane proteins



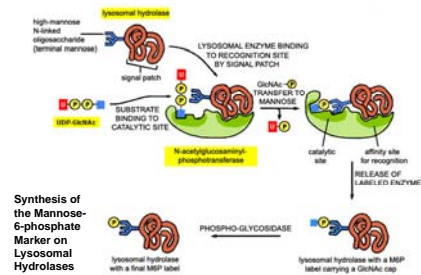
LYSOSOME'S – internal "glycocalyx"

120 nm²

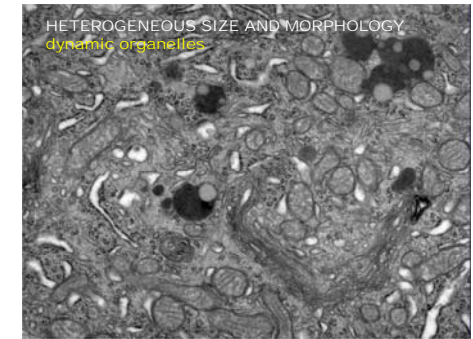
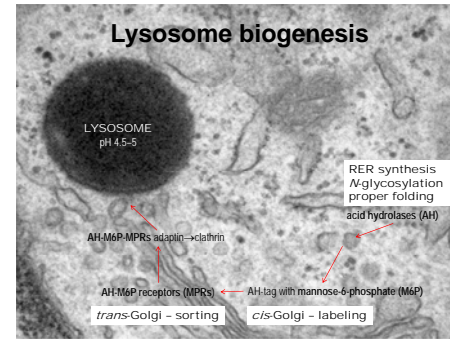
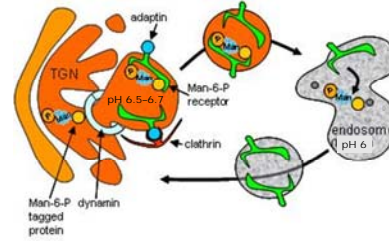
LAMP1 – glycoprotein



Lysosome enzyme labeling

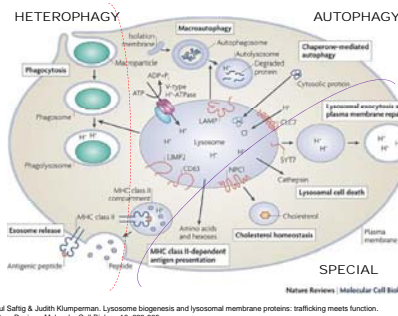
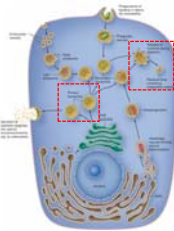


MANNOSE 6-PHOSPHATE RECEPTOR SORTS LYSOSOMAL HYDROLASES IN THE TRANS GOLGI NETWORK



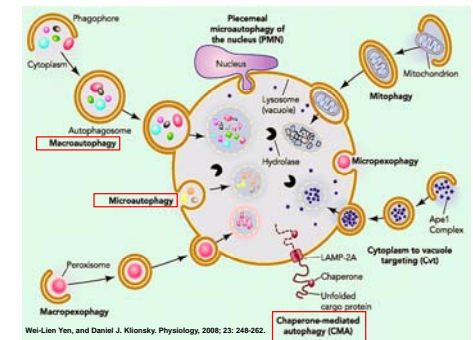
Lysosome functions

- PROTEOSTASIS
- DEGRADATION AND RECYCLING of
 - intracellular substrates
 - autophagy
 - chaperone-mediated autophagy
 - micro-autophagy
 - macro-autophagy
 - extracellular substrates
 - endocytosis
 - pinocytosis
 - receptor mediated endocytosis
 - phagocytosis
 - CHOLESTEROL HOMEOSTASIS
 - PLASMA MEMBRANE REPAIR
 - APOPTOSIS - CELL DEATH
 - SECRETION (cells with secretory Ly)

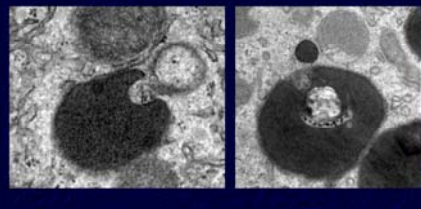


(conventional) Lysosome functions

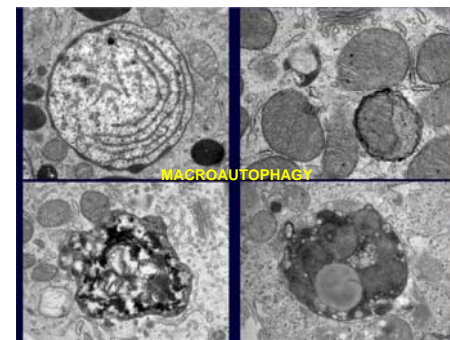
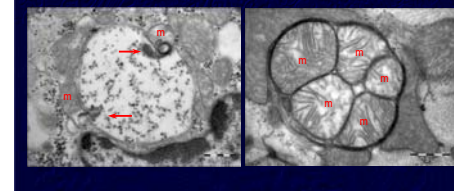
- phagein* - 'to eat'
- DIGESTING FOOD
- DIGESTING ORGANELLES
- DIGESTING CELLS
- AUTOPHAGY** - disassembles unnecessary or dysfunctional components of the cells (micro-macro-autophagy).
- CRINOPHAGY** - digestion of excess secretory vesicles.
- HETEROPHAGY** - digestion of material ingested via phagocytosis (engulfment of a solid particle to form an internal compartment known as a phagosome), endocytosis or pinocytosis (internalization of extracellular liquids).



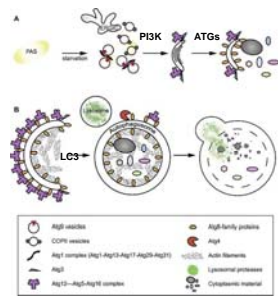
MICROAUTOPHAGY - type of autophagic pathway, mediated by direct lysosomal engulfment of the cytoplasmic cargo (cytoplasmic material is trapped by lysosomal membrane invagination).



MACROAUTOPHAGY - type of autophagic pathway in which targeted cytoplasmic constituents are isolated from the rest of the cell within a double-membraned vesicle - autophagosome. The autophagosome fuses with lysosomes to degrade and recycle intracellular materials.



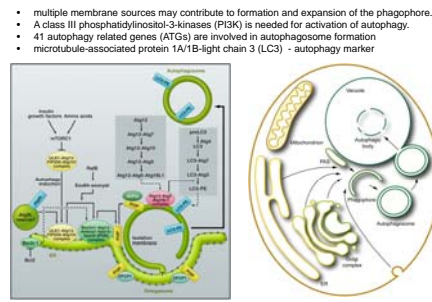
AUTOPHAGOSOME BIOGENESIS



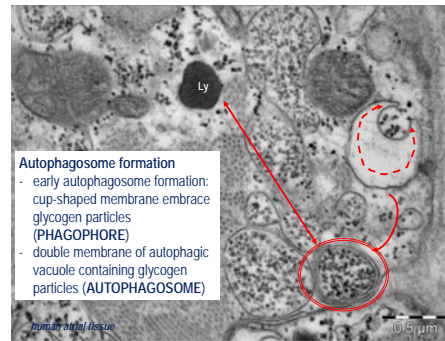
- multiple membrane sources may contribute to formation and expansion of the phagophore (ERGIC),
- a class III phosphatidylinositol-3-kinases (PI3K) is needed for activation of autophagy,
- 41 autophagy related genes (ATGs) are involved in autophagosome formation
- microtubule-associated protein 1A/1B-light chain 3 (LC3) - autophagy marker

Esquivos-Torres, Soledad; Martinez, Insights into autophagosome biogenesis from in vitro reconstitutions. *Journal of Structural Biology*. 2016, 196(1):22-36. <http://dx.doi.org/10.1016/j.jsb.2016.04.005>

AUTOPHAGOSOME BIOGENESIS

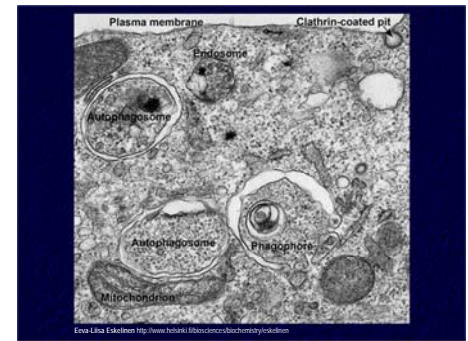


Fulvio Reggiori and Daniel J. Klionsky. *Genetics*. 2013; 194:341-361.

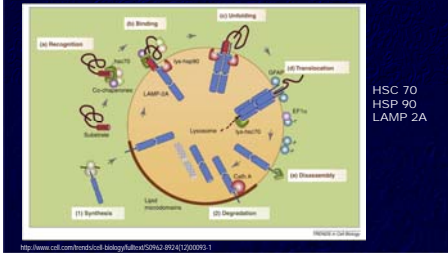


Autophagosome formation

- early autophagosome formation: cup-shaped membrane embrace glycogen particles (PHAGOPHORE)
- double membrane of autophagic vacuole containing glycogen particles (AUTOPHAGOSOME)

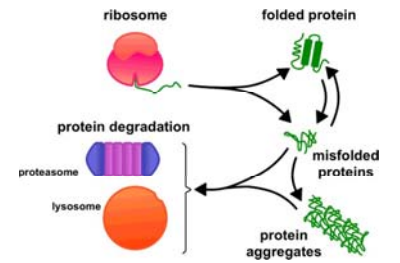


CHAPERONE-MEDIATED AUTOPHAGY – chaperone-dependent selection of soluble cytosolic proteins (selective), then targeted to lysosomes and directly translocated across the lysosome membrane for degradation.



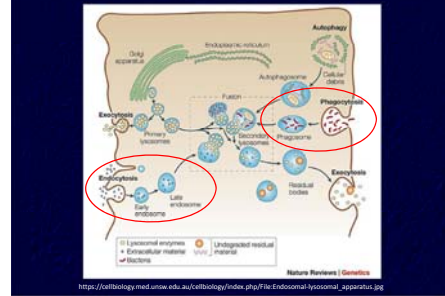
<http://www.csl.com/horselife/biology/autophagy/2016/02/09/1200093-1>

Cellular pathways of protein degradation – misfolded proteins removal –



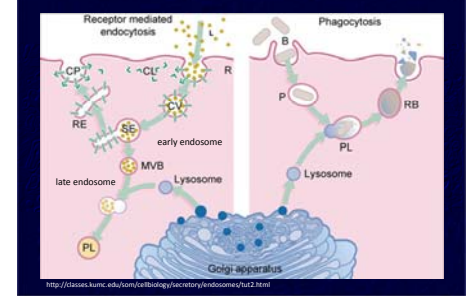
Matthew P. Jackson, Eric W. Howell. *Cellular proteostasis: degradation of misfolded proteins by lysosomes*. *Essays Biochem*. 2016; 60(2): 173-181.

HETEROPHAGY



https://cellbiology.med.unsw.edu.au/cellbiology/index.php/File:Endosomal-lysosomal_apparatus.jpg

HETEROPHAGY

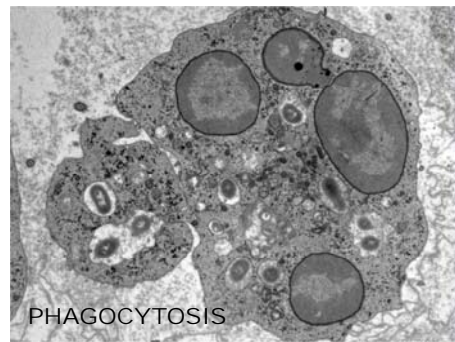


<http://classes.humc.edu/son/cellbiology/secretory/endosome/tut2.html>

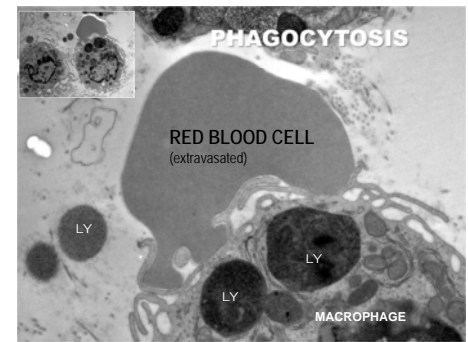
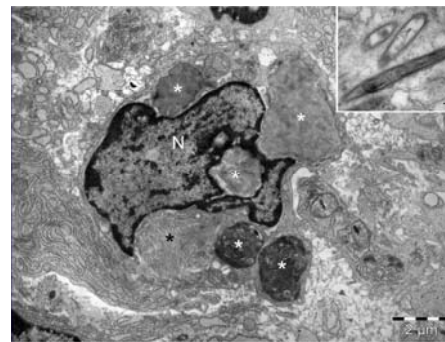
...THE FIRST LIVE-CELL MOVIE



This video is taken from a 16-mm movie made in the 1950s by David Rogers at Vanderbilt University



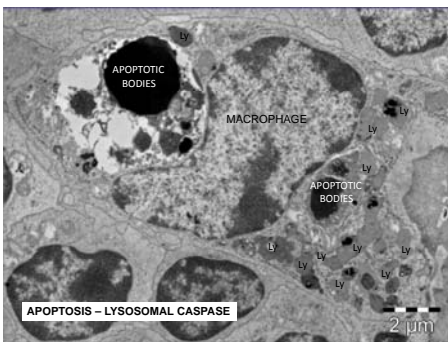
PHAGOCYTOSIS



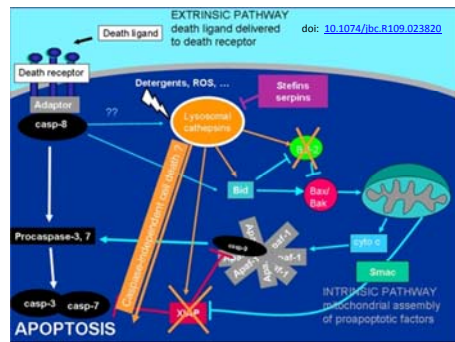
PHAGOCYTOSIS

RED BLOOD CELL (extravasated)

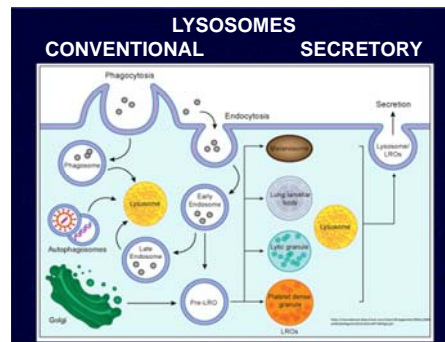
MACROPHAGE



APOPTOSIS – LYSOSOMAL CASPASE



APOPTOSIS



LYSOSOMES
CONVENTIONAL SECRETORY

SECRETORY LYSOSOMES LYSOSOME-RELATED ORGANELS

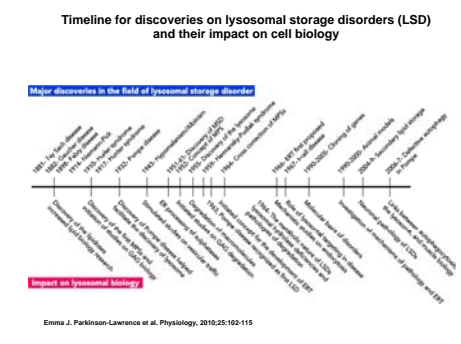
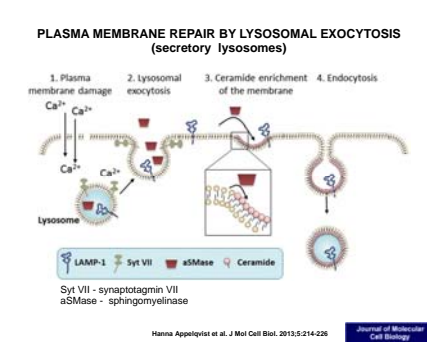
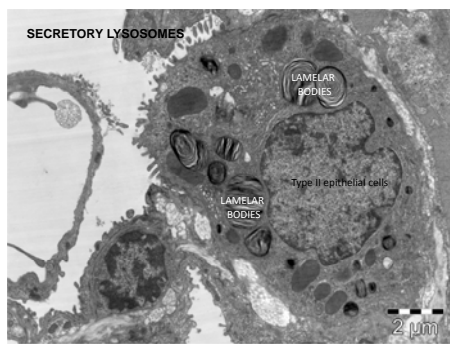
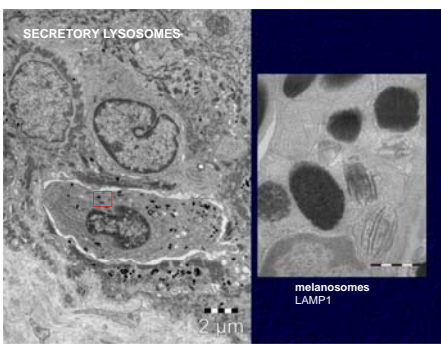
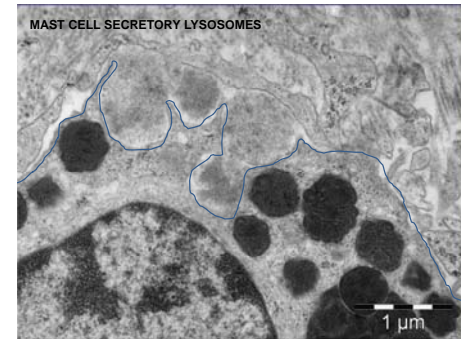
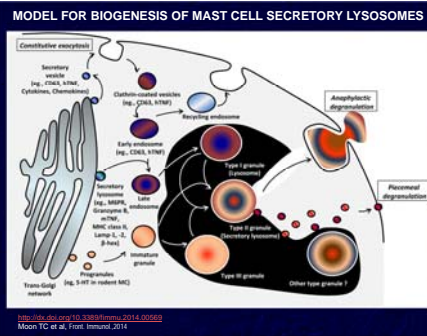
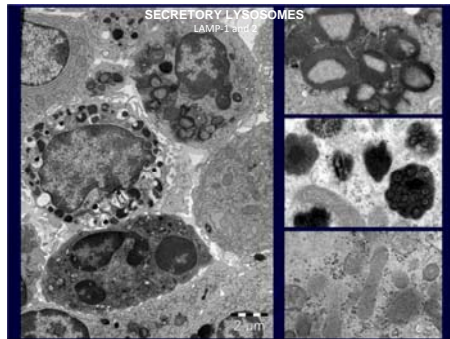
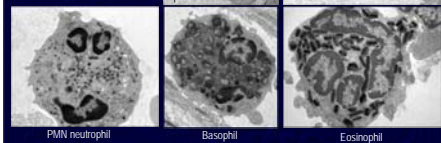
Cell type	Function	Soluble content	Specific membrane proteins	Stimulus for secretory lysosomes	Cell-specific secretory lysosomes
T cells	Target cell killing	Perforin granules	Fcγ receptor, CTLA-4	Toxic receptor	Lytic granules
Macrophages	Parasite defense	Major basic protein, Helicase	MHC class II	Fcγ receptor	Basophilic cell granules
Neutrophils	Inflammation (phagocytosis)	Chemotactic factors	CD45 ligand	Fcγ receptor and collagen	Alveolar granules
Platelets	Clotting	Clotting factors	CD45 ligand	Fcγ receptor and collagen	Platelet dense granules
Macrophages	Phagocytosis	Antigen presentation	MHC class II		
Dendritic cells	Antigen presentation		MHC class II		
B cells	Antigen presentation		MHC class II		
Macrophages	Secretion of matrix	Matrix			
Chondrocytes	Bone resorption	Lysosomal hydrolases			
Specialized cells	Various functions				

Secretory lysosomes are generally found in cells that are derived from the hematopoietic lineage. Examples of both soluble and membrane-associated proteins are shown. The stimulus to release secretory granules can vary, and is determined by the secretory lysosome and also other factors. MHC, major histocompatibility complex; CTLA-4, cytotoxic T-lymphocyte antigen 4.

Ernst J. Beil and Gillian M. Griffin. *Secretory lysosomes*. *Nature Reviews Molecular Cell Biology*. 2002; 3: 122-131

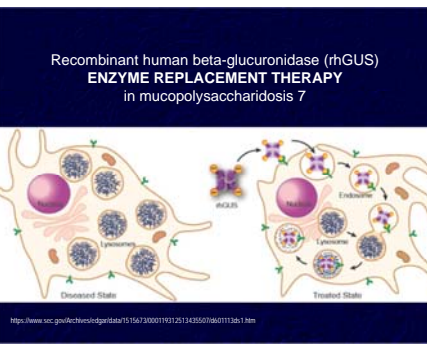
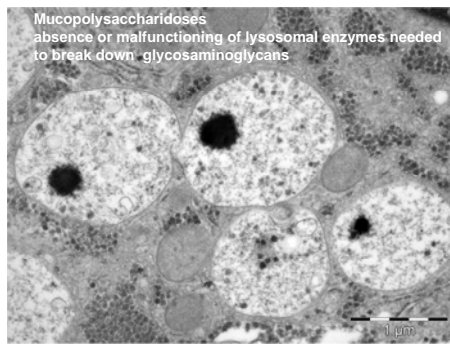
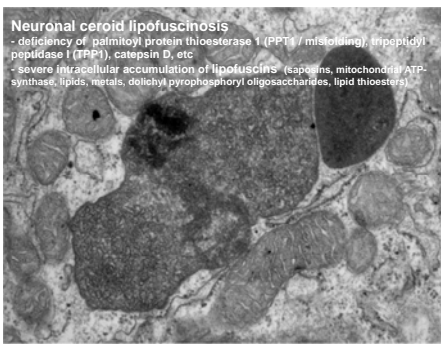
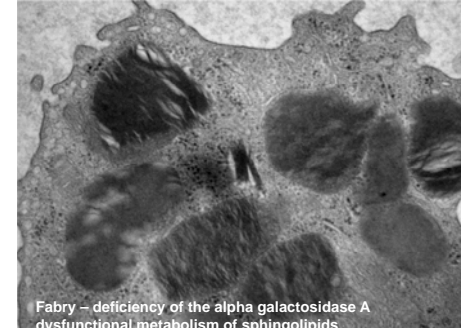
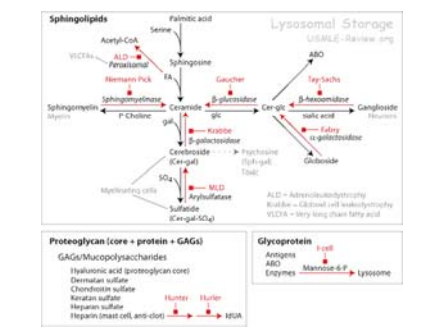
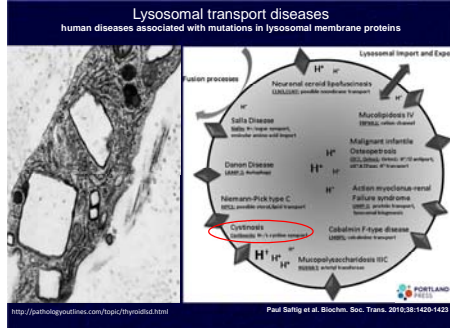
SECRETORY LYOSOMES

cells of the immune system derived from haematopoietic lineage



Lysosomal diseases

- Lysosomal storage diseases (genetic diseases)**
- about 50 different disease
 - defects in lysosomal biogenesis, membrane proteins or lysosomal enzymes
 - first described Tay-Sachs disease (1881)
 - difficult to classify
- (glycogen storage disease type II, mucopolysaccharidoses, mucopolidoses, oligosaccharidoses, lipidoses, sphingolipidoses, lysosomal transport diseases, ...)
-



- ## Lysosomes Summary
- Lysosome is a digestive organelle, feeding the cell
 - Lysosome biogenesis involve ER, Golgi and a highly controlled membrane traffic
 - There are three pathways to degradation in lysosome: endocytosis, phagocytosis and autophagy
 - Lysosome function need a significant diversity of acid hydrolases, and a pH of 5
 - Secretory lysosomes key role in immunity
-