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Review on lysosomal enzymes

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Abstract

Cells maintain their homeostasis through continuous synthesis and degradation of their components. Impairment in the balance within such cycles can be responsible for the pathogenesis of various human diseases. One major site for intracellular degradation is the lysosome. Lysosomes are spherical, membrane bound organelles that are generated by the golgi apparatus. They contain hydrolytic enzymes, and so function as part of the recycling system of the cell. This review focuses on our present knowledge on, formation, functions, and list of hydrolases of lysosomes.

Key words: Endosomes,phagocytosis,autophagy

Introduction:

Lysosomes are spherical membranous sacs of enzymes and are degradation centers of the cell. It contains around 50 hydrolytic enzymes capable of digesting nucleic acids(**Nucleases**), carbohydrates (**Amylase**), lipids(lipases), and proteins(proteases). Lysosomes were first described by de Duve *et al.* in 1955 through tissue fractionation of rat liver, and characterized as membrane-bound vesicles containing multiple acid hydrolases(1). Originally, De Duve had termed the organelles the "suicide bags" or "suicide sacs" of the cells, for their hypothesized role in apoptosis. However, it has since been concluded that they only play a minor role in cell death.

Lysosomes contain numerous hydrolytic enzymes which remain inactive inside the lysosomes. When the pH of the interior lysosomes changed to acidic pH 4.8, enzymes become active. At pH 4.8, the interior of the lysosomes is acidic compared to the slightly alkaline cytosol (pH 7.2). The lysosome maintains this pH differential by pumping protons (H^+ ions) from the cytosol across the membrane via proton pumps and chloride ion channels. The lysosomal membrane protects the cytosol, and therefore the rest of the cell, from the degradative enzymes within the lysosome. The cell is additionally protected from any lysosomal acid hydrolases that leak into the cytosol as these enzymes are pH-sensitive and function less well in the alkaline environment of the cytosol(2).

Lysosome Formation

Lysosomes are formed from the fusion of vesicles from the Golgi complex with endosomes. Endosomes are vesicles that are formed by endocytosis as a portion of the plasma membrane pinches off and is internalized by the cell. In this process, extracellular material is taken up by the cell. As endosomes mature, they become known as late endosomes. Late endosomes fuse with transport vesicles from the Golgi complex that contain acid hydrolases. Once fused, these endosomes eventually develop into lysosomes[3]

Types of Lysosomes

There are two main types, these include:

Primary lysosomes - are formed from Golgi apparatus appearing as small vesicles. Although primary lysosomes are popular on Golgi apparatus, they also occur as granulocytes and monocytes. These lysosomes are surrounded by a single phospholipid layer and contain acid hydrolases. The pH value of the acid in these vesicles is important in that its changes activate or deactivate the enzymes. Ultimately, most of the primary granules will fuse with phagosomes, which results in the formation of secondary lysosomes.

Secondary lysosomes - are formed when primary lysosomes fuse with phagosomes/pinosome (they are also referred to a endosomes). The fusion also causes the previously inactive enzymes to be activated and capable of digesting such biomolecules as nucleic acids and lipids among others. Compared to primary lysosomes, secondary are larger in size and capable of releasing their content (enzymes) outside the cells where they degrade foreign material[4].

Functions:
Lysosomes serve two major functions[5]

1.Intracellular Digestion: To digest food, the lysosome membrane fuses with the membrane of food vacuole and squirts the enzymes inside.The digested food then diffuses through the vacuole membrane and enters the cell to be used for energy and growth.
2.Autolytic Action: Cell organelles that need to be get ridden are covered by vesicles or vacuoles by the process of autophagy to form autophagosome.The autophagosome is then destroyed by the action of lysosomal enzymes.

Lysosomes play a crucial role to overcome pathological conditions[6]:

1. Heterophagy:

Heterophagy is the lysosomal digestion of extracellular materials by the process of endocytosis(Endocytosis is a cellular mechanism by which, a cell internalizes substances).
Heterophagy are of two types: phagocytosis and pinocytosis.
i) Phagocytosis: A phagocyte, is a immune cell in the immune system that performs phagocytosis, in several steps
Step 1. In the case of immune cells, activation occurs when the cells are near bacterial cells or parts of bacterial cells. Receptors on the surface of the cells bind to these molecules and cause the cells to respond.

Step 2:Chemotaxis may occur, is the movement of phagocytes toward a concentration of molecules. Immune cells pick up chemical signals and migrate toward invading bacteria or damaged cells.
Step 3.Formation of phagosome .The cell ingests the particle, and the particle is enclosed in a vesicle (a sphere of cell membrane with fluid in it) called a phagosome. The phagosome transports the particle into the cell
Step 4.Formation of phagolysosome. A lysosome fuses with the phagosome and the particle is digested. Lysosomes are vesicles that contain hydrolytic enzymes that break down molecules. A phagosome fused with a lysosome is called a phagolysosome.
Step 5.Lysis: Lysosomes contain digestive enzymes which can destroy the internalised material. A cell ingests a particle, breaks it down with the enzymes in lysosomes, and expels waste products through exocytosis.

II. Pinocytosis is a type of endocytosis in which small particles suspended in the extracellular fluid are moved into the cell through pores formed on the cell membrane.The term pinocytosis is formed of two words "pino" and cytosis" where 'pino' means "to drink" while 'cytosis' means relating to the cell.It is a continuous process in most cells and is a non-specific way for internalizing fluid and dissolved nutrients.

2.Autophagy: The term 'autophagy', derived from the Greek meaning 'eating of self', was first coined by Christian de Duve over 40 years ago. There are three defined types of autophagy: macro-autophagy, micro-autophagy, and chaperone-mediated autophagy, all of which promote proteolytic degradation of cytosolic components at the lysosome.

Macro-autophagy delivers cytoplasmic cargo to the lysosome through the intermediary of a double membrane-bound vesicle, referred to as an autophagosome, that fuses with the lysosome to form an autolysosome.

In micro-autophagy, by contrast, cytosolic components are directly taken up by the lysosome itself through invagination of the lysosomal membrane. Both macro-and micro-autophagy are able to engulf large structures through both selective and non-selective mechanisms.

In chaperone-mediated autophagy (CMA), targeted proteins are translocated across the lysosomal membrane in a complex with chaperone proteins (such as Hsc-70) that are recognized by the lysosomal membrane receptor lysosomal-associated membrane protein 2A (LAMP-2A), resulting in their unfolding and degradation[(7)] .

3. Autolysis: Autolysis refers to the digestion of own cells by the lysosomes. Auto means self and lysis means digestion. It is self digestion. It is also otherwise known as programmed cell death or apoptopic lysis. In autolysis, the lysosome digests its own cell. Hence autolysis is also called as cellular autophagy. In this process, the lysosome ruptures inside its cell and the released enzymes digest and degrade the cell. As lysosome kills its own cell, it is called as sucidal bag.

4. Extracellular digestion: Digestion of materials outside the cell is called extracellular digestion. In certain occasions lysosomes release enzymes outside the cell by exocytosis and bring out digestion. Extracellular digestion takes place during bone erosion process. Osteoclast cell of bone contain more number of lysosomes. These cells when release their lysosomal

content on the surface of the bone, lysosomal enzymes bring about the extracellular digestion of bone and it result in bone desorption.

5. Fertilization: During fertilization process, acrosome (giant lysosome) of sperm head ruptures and releases enzymes on the surface of the egg. These enzymes digest the egg membrane and provide way for the entry of sperm nucleus into the egg. This action also activates the egg for the developmental processes.

6. Chromosomal damage: Due to the presence of DNase enzyme, lysosome had an ability to attacks chromosome and cause chromosomal breakages. These breakages can leads to diseases like cancer etc[8].

List of enzymes lysosomal hydrolases[9&10]

1.Phosphates

A. Acid phosphatases

B- Acid phosphodiesterase

2. Nucleases

A. Acid ribonuclease

B. Acid deoxy ribonuclease

2. Polysaccharides/ mucopolysaccharides hydrolyzing enzymes

A- beta Galactosidase

B- alfa Glucosidase

C- alfa Mannosidase

D- beta Glucoronidase

E- Lysozymes

F- Hyaluronidase

H- Arylsulphatase

3.Proteases

A- Cathepsin(s)

B- Collagenase

C- Peptidase

4.Lipid degrading enzymes

A- Esterase

B- Phospolipase

Conclusion: In 1955 when de Duve first proposed the name of the organelle as a lysosome. This is an area of increased research interest moving forward, Lysosomes thus represent morphologically diverse organelles defined by the common function of degrading intracellular material

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