XII. ORGANELLES INVOLVED IN CELLULAR DETOXIFICATION - PEROXISOMES (MICROBODIES)

Peroxisomes are found in all eukaryotic cells, except for the red blood cells. Peroxisomes are so called because they usually contain one or more enzymes that use molecular oxygen to remove hydrogen atoms from specific organic substrates (designated here as R) in an oxidative reaction that produces ***hydrogen peroxide ($H_2 O_2$)***.

$$R H_2 + O_2 \rightarrow R + H_2 O_2$$

XII.1. ULTRASTRUCTURE

Peroxisomes are spherical or oblong structures of about 0.3-1.5 μm in diameter, which are surrounded by a lipoprotein bilayer unit membrane that is 6-8 nm thick (somewhat thinner than the plasma membrane).

They have a moderately electron-dense **inner-matrix**, which may appear amorphous, granular or crystalline. In the matrix, peroxisomes contain oxidative enzymes, such as **catalase** and **urate oxidase**, at such high concentrations that in some cells peroxisomes stand out in electron micrographs because of the presence of a crystalloid core, largely composed of **urate oxidase**.

Peroxisomes are numerous in liver and kidney cells but are found in most cells. The number of peroxisomes present in a cell increases in response to diet, drugs, and hormonal stimulation.

XII.2. FUNCTIONS

1. In addition to urate oxidase and catalase, peroxisomes contain D-amino acid oxidase, beta-oxidation enzymes, and nearly 20 other enzymes. Virtually all these produce hydrogen peroxide (H_2O_2) as a product of the oxidation reaction. Hydrogen peroxide is a toxic substance. The catalase universally present in peroxisomes carefully regulates the hydrogen peroxide content in cells, thus protecting the cell. Catalase utilizes the H_2O_2 generated by other enzymes in the organelle to oxidize a variety of other substrates- including phenols, formic acid, formaldehyde, and alcohol-by the "peroxidative" reaction:

$$H_2O_2 + R'H_2 \rightarrow R' + 2H_2O.$$

This type of oxidative reaction is particularly important in liver and kidney cells, whose peroxisomes detoxify various toxic molecules that enter the bloodstream. About a quarter of the ethanol we drink is oxidized to acetaldehyde in this way. In addition, when excess H_2O_2 accumulates in the cell, catalase converts it to H_2O ($2H_2O_2 \rightarrow 2H_2O + O_2$).

2. A major function of the oxidative reactions carried out in peroxisomes is the breakdown of fatty acid molecules. In a process called β oxidation, the alkyl chains of fatty acids are shortened sequentially by blocks of two carbon atoms at a time that are converted to acetyl CoA and exported from the peroxisomes to the cytosol for reuse in biosynthetic reactions. β oxidation in mammalian cells occurs both in mitochondria and peroxisomes.

XII.3. ALL THE COMPONENTS OF PEROXISOMES

ARE IMPORTED FROM THE CYTOSOL

Peroxisomes contain no DNA or ribosomes, they have to import all of their proteins from the cytosol. A specific sequence of three amino acids located near the carboxyl terminus of many peroxisomal proteins functions as an import signal; if this sequence is experimentally attached to a cytosolic protein, the protein is imported into peroxisomes. The importance of this import process and of peroxisomes is dramatically demonstrated by the inherited human disease **Zellweger syndrome**, in which a defect in importing proteins into peroxisomes leads to a severe peroxisomal deficiency. These individuals, whose cells contain "empty" peroxisomes, have severe abnormalities in their brain, liver, and kidneys; and they die soon after birth. One form of this disease has been shown to be due to a mutation in the gene encoding a peroxisomal integral membrane protein called peroxisome assembly factor-1.

Peroxisomes presumably have at least one unique protein exposed on their cytosolic surface to act as a receptor that recognizes the signal on the proteins to be imported. At one time it was thought that the membrane of the peroxisome forms by budding from the ER, while the content is imported from the cytosol. There is now evidence, suggesting that new peroxisomes arise only from preexisting ones, by organelle growth and fission. Presumably, the lipids required to make new peroxisome membrane are also imported.