Normal metabolic pathway of lipids in the human cells

The lipids are essential components of the human organism and the most of them are hydrophobic and amphipathic. Some lipids are fatty acids, cholesterol, steroid hormones, eicosanoids, bile salts and glycerophospholipids in the human body. The synthesis of these lipids is very important in metabolism. The main catabolic pathway of the lipids is the fatty acid oxidation (β-oxidation) in which the fatty acids chains are broken down to acetyl CoA. In this essay will provide a clear explanation of the normal metabolic pathway of lipids in the human cells. After this, disorders associated with in-born errors of metabolism will be mentioned. Throughout the essay one of the disorders are analyzed giving the symptoms causes and the treatment.

Lipid metabolic pathway

The liver is the main fat storage and recovery. The lipids especially fatty acids which are entering the livers is released from adipose tissue and transported in the systemic blood plasma with albumin. Fatty acids are oxidized by a pathway called beta-oxidation (β-oxidation) and divided into two stages. The first stage is the activation of fatty acids and the second stage is the degradation as acetyl CoA. The products of the fatty acids oxidation which are NADH and ubiquinol (QH2) oxidized by the respiratory electron-transport chain and the acetyl CoA enter the citric acid cycle.

In human cells the beta-oxidation takes place in mitochondria and in the organelles peroxisomes. The first step of beta-oxidation is oxidation in which acyl-CoA dehydrogenase catalyzes the formation of a double bond and the acyl group shortened by two carbons. QH2 which is oxidized by the membrane-associated electron transport and trans-2-Enoyl CoA produced.

The second step named hydration in which added water in the trans-2-enoyl CoA and produced the enzyme 2-enoyl-CoA hydratase. In the third step a second oxidation catalyse the enzyme above and produced 3-ketoacyl CoA, and a NADH. In the final step a thiolysis cleavage reaction catalyse the 3-ketoacylm CoA to Acyl CoA by the sulfhydryl group Hs-CoA. The Acyl CoA molecule is a substrate for another round of the beta oxidation reactions until the molecule converted to acetyl-CoA.

Acetyl-CoA initiate the citric acid cycle which is a way of production ATP. The first stage of the cycle is the citrate formed to isocitrate by an isomerisation. The second stage isocitrate dehydrogenase oxidise isocitrate to a-ketoglutarate and CO2. Also NAD reduced to NADH. The third stage is a-ketoglutarate oxidised to succinyl CoA and CO2. NAD is the cofactor and reduced to NADH as well. Continuously, succinyl CoA synthase enzyme convert the previous product to succinate and CoA and ATP produced too. Further, the enzyme succinate dehydrogenase converts succinate to fumarate and FADH2. Furthermore, fumarate dehydrated to Malate by fumarase. Last but not least, Malate oxidised to Oxaloacetate by malate dehydrogenase and also produced NADH. Finally the cycle completed with the convert of oxaloacetate to citrate by citrate synthase.

The last way is the active transport of ATP, ADP and Pi across the mitochondrial membrane. For the reason that the membrane of the mitochondria is impermeable to charged substances, needed a transporter to allow entering ADP and leaving ATP. The transporter called ATP synthase.

The last metabolic pathway is the electron transport. In the inner mitochondria membranes there are electron transporter which are transport electrons from NADH and FADH2 to the oxygen. These transporters are consisting of three complexes. The first complex named as Complex I or NADH dehydrogenase that is contain FMN and the accepted electrons are produced FMNH2 and then the electrons passed to ubiquinone. . Moreover FADH2 is reoxidised to FAD by donating two electrons to succinate dehydrogenase complex and from there passed to ubiquinone as well. Ubiquinone is the coenzyme Q and transferred the electrons to cytochrome bc complex which is the complex III. This complex accepts electrons from the coenzyme Q and passes them to cytochrome c. Continuously, cytochrome c is the complex IV and transfer electrons to oxygen. The electron synthesis finished with the oxidative phosphorylation which is the ATP synthesis and is associated with the oxidation of NADH and FADH2 from ADP and Pi through the ATP synthase transporter which is uses the energy from the proton gradient. From this process three ATP molecules are synthesized per NADH oxidised and two ATP per oxidation of FADH2.

Disorders of lipids metabolism

Lipids are on the most important energy source in the human body. Lipidoses, lipids accumulation in the body, caused disorders and also some enzyme abnormalities avoid the lipid conversation into energy. The associated lipid disorders called fatty acid oxidation disorders. One major disorder is Gaucher’s disease that is an inherited disease of the lipids catabolism and is a result from glucocerebrosidase deficiency in macrophages of the reticuloendothelial system. The infants with the

Gaucher’s disease die within a year but adults and children who develop later the disease can survive. Moreover, the acyl-CoA dehydrogenase (MCAD) deficiency is one of the most common inherited disorders of metabolism. Another one inherit disease is Tay-Sachs disease in that the gangliosides accumulate in tissues and have as a result an early death. In addition to this, Refsum’s disease is a lipid storage disease in which the production of phytanic acid leads to nerve and retinal damage, and also changes in the bone and skin. Further, Niemann-Pick disease is a lysosomal storage disease in which the deficiency of a specific enzyme has a result of the accumulation of spingomyelin or cholesterol. This disorder is consisting of five groups, A, B, C, D and E. Another disorder is Wolman’s disorder that is a rare hereditary disorder in which a specific type of cholesterol produced in tissues as a result of the enlargement of liver and spleen. Infants with this disease die 6 months after their birth.