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THE ROLE OF APOLIPOPROTEINS IN CHOLESTEROL METABOLISM, OBESITY MECHANISMS, AND SPHINGOLIPIDOSES

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Abstract: This review article comprehensively covers three important aspects of lipid metabolism: the role of apolipoproteins in cholesterol transport, adipose tissue physiology and obesity mechanisms, and the group of hereditary diseases known as sphingolipidoses. The article analyzes the molecular mechanisms, pathogenesis, and treatment methods of these processes based on modern biochemical and clinical data. Disorders of lipid metabolism represent one of the most pressing problems in contemporary medicine, playing a crucial role in the development of cardiovascular diseases, metabolic syndrome, and hereditary lysosomal storage diseases.

Keywords: apolipoproteins, lipoproteins, cholesterol transport, adipose tissue, obesity, adipokines, sphingolipidoses, lysosomes, metabolic diseases

Introduction

Lipids are biological molecules of vital importance for living organisms. They serve as the main structural component of cell membranes, energy reserves, signaling molecules, and precursors of numerous important bioactive substances. Lipid metabolism occupies a central position in ensuring the body's energetic homeostasis, intercellular signal transmission, and regulation of numerous physiological processes.

One of the important characteristics of lipids is their hydrophobic nature. This property necessitates special mechanisms for the dissolution and transport of lipids in aqueous environments. In blood plasma, lipids such as cholesterol and triglycerides are transported as part of lipoprotein particles, bound to special proteins called apolipoproteins. Disruption of this system is considered the main cause of atherosclerosis, coronary heart disease, and stroke.

For a long time, adipose tissue or adipose tissue was considered merely a passive energy reserve. However, research conducted in recent decades has shown that adipose tissue is an active endocrine organ and plays an important role in regulating the entire body's metabolism. Adipose tissue produces a number of hormones and biologically active substances that control food consumption, energy expenditure, insulin sensitivity, and many other physiological processes. Disruption of adipose tissue function leads to the development of obesity, insulin resistance, type 2 diabetes, and other metabolic diseases.

Sphingolipids are an important component of cell membranes and, in addition to providing structure, also participate in cell signaling and the organization of membrane microdomains. Hereditary defects in enzymes involved in the lysosomal catabolism of sphingolipids cause a

group of severe diseases called sphingolipidoses. These diseases are rare, but their study has significantly enriched our knowledge about lysosomal biology and sphingolipid function.

According to the World Health Organization, cardiovascular diseases rank first among causes of death and claim approximately seventeen million lives annually. The obesity pandemic is also spreading rapidly, with more than two billion people worldwide currently overweight or obese. These conditions are often associated with lipid metabolism disorders, and their prevention and treatment represent one of the priority directions of modern medicine.

In this review article, we will examine in detail three important aspects of lipid metabolism. First, we will analyze the types, structure, and role of apolipoproteins in the cholesterol transport process. Second, we will cover adipose tissue physiology, its endocrine functions, and obesity mechanisms. Third, we will examine diseases belonging to the sphingolipidosis group, their molecular pathogenesis, and modern treatment approaches.

General Structure and Classification of Lipoproteins

Lipoproteins are particles similar to plasma membranes, consisting of a hydrophobic core and an amphiphilic outer shell. The central core consists mainly of cholesterol esters and triglycerides, while the outer shell is covered with phospholipids, free cholesterol, and apolipoproteins. This structural organization allows lipids to be stored and transported in a soluble form in aqueous environments.

Lipoproteins are divided into several main classes based on density. Chylomicrons are the largest and lightest lipoproteins, synthesized in the intestine and transporting dietary lipids. Chylomicrons consist mainly of triglycerides and, after entering the bloodstream, break down triglycerides under the action of lipoprotein lipase enzyme. As a result, chylomicron remnants are formed and taken up by the liver.

Very low-density lipoproteins or VLDL are synthesized in the liver and transport endogenous triglycerides to peripheral tissues. VLDL particles also lose their triglycerides under the action of lipoprotein lipase, converting to intermediate-density lipoproteins (IDL), and then to low-density lipoproteins (LDL). The main function of LDL particles is to deliver cholesterol to tissues. Excessive increase in LDL is the main risk factor for atherosclerosis and cardiovascular diseases.

High-density lipoproteins or HDL are the densest and smallest lipoproteins. HDL is synthesized in the liver and intestine and collects excess cholesterol from peripheral tissues, returning it to the liver. This process is called reverse cholesterol transport and is viewed as a protective mechanism against atherosclerosis. High HDL levels generally reduce cardiovascular disease risk.

Structure and Functional Characteristics of Apolipoproteins

Apolipoproteins are the protein component of lipoprotein particles and perform several important functions. First, apolipoproteins ensure the structural integrity of lipoproteins and hold lipids in a water-soluble form. Second, they serve as ligands for binding to cell surface receptors. Third, some apolipoproteins activate or inhibit lipid metabolism enzymes.

Apolipoprotein A-I or Apo A-I is the main structural protein of HDL, comprising approximately seventy percent of HDL particles. Apo A-I can transition from a linear form to an amphiphilic alpha-helical structure, enabling it to bind efficiently with lipids. The most important function of Apo A-I is to activate the LCAT enzyme and initiate the reverse cholesterol transport process. Low levels of Apo A-I increase cardiovascular disease risk.

Apolipoprotein B has two main isoforms - Apo B-100 and Apo B-48. Apo B-100 is a very large protein consisting of 4536 amino acids and is the main structural component of VLDL, IDL, and LDL. Each LDL particle contains one Apo B-100 molecule. Apo B-100 serves as a ligand for LDL receptors and ensures cholesterol entry into cells. Apo B-48 is a truncated form of Apo B-100, synthesized only in the intestine and incorporated into chylomicrons.

Apolipoprotein E or Apo E plays an important role in lipid metabolism and has high affinity for many lipoprotein receptors. Three main alleles exist for Apo E - E2, E3, and E4. Apo E3 is the most widespread variant, Apo E2 binds less efficiently to receptors, and Apo E4 has high binding capacity. The Apo E4 allele is known to increase Alzheimer's disease risk. Apo E is also synthesized in the central nervous system and participates in lipid distribution among neurons.

The apolipoprotein C family includes three members - Apo C-I, C-II, and C-III. They are small proteins that can exchange between different lipoproteins. Apo C-II is an activator of lipoprotein lipase enzyme, accelerating triglyceride hydrolysis. Hereditary deficiency of Apo C-II increases hypertriglyceridemia and pancreatitis risk. Apo C-III, conversely, inhibits lipoprotein lipase and slows triglyceride catabolism. High Apo C-III levels are associated with cardiovascular disease risk.

Reverse Cholesterol Transport Mechanism

Reverse cholesterol transport is the process of returning excess cholesterol from peripheral tissues to the liver and represents an important protective mechanism against atherogenesis. This process consists of several sequential stages and requires the coordinated work of numerous proteins and enzymes.

The first stage of the process is cholesterol efflux from the cell membrane. This process is accomplished through the ABCA1 transporter. ABCA1 uses ATP energy to transfer free cholesterol and phospholipids from the cell membrane to lipid-poor Apo A-I. As a result, disc-shaped, lipid-poor HDL particles are formed. The importance of ABCA1 is clearly seen in the example of Tangier disease associated with genetic defects of this transporter. In this disease, HDL levels drop sharply due to disrupted ABCA1 function, cholesterol accumulates in tissues, and atherosclerosis develops at an early age.

In the next stage, the LCAT enzyme converts free cholesterol to cholesterol esters on the surface of HDL particles. LCAT is a plasma enzyme activated by Apo A-I. Cholesterol esterification maintains a cholesterol concentration gradient on the HDL particle surface and continues to accept new cholesterol. The resulting cholesterol esters, being hydrophobic, move to the central core of HDL particles. This process transforms HDL from a disc-shaped to a spherical form and increases particle volume. LCAT deficiency is a rare hereditary disease in which HDL levels are low and kidney diseases may develop.

In the third stage, cholesteryl ester transfer protein or CETP transfers cholesterol esters from HDL to Apo B-containing lipoproteins, particularly LDL and VLDL. CETP is a plasma protein that enables the exchange of both cholesterol esters and triglycerides between lipoproteins. Increased CETP activity lowers HDL levels and may increase cardiovascular disease risk. Therefore, CETP inhibitors have been developed as medications, but in clinical trials their effectiveness was not as expected.

In the fourth stage, mature HDL particles interact with SR-BI receptors in the liver and other tissues. SR-BI selectively transfers cholesterol esters directly to cells without internalization of the entire HDL particle. In the liver, cholesterol undergoes metabolism in several directions. It can be used in lipoprotein synthesis, converted to bile acids, or directly excreted in bile.

The final stage of reverse cholesterol transport is the excretion of cholesterol from the liver through bile ducts to the intestine and then outside. The ABCG5 and ABCG8 transporters play an important role in this process, ensuring cholesterol excretion in bile. Additionally, cholesterol is converted to bile acids and excreted from the body in this form. Bile acid synthesis is an important mechanism for regulating cholesterol homeostasis.

Clinical Significance of Lipoprotein Metabolism

Disruption of lipoprotein metabolism is a major risk factor for cardiovascular diseases. High levels of LDL cholesterol lead to endothelial dysfunction, atherosclerotic plaque formation, and ultimately myocardial infarction and stroke. Infiltration of LDL particles into the vessel wall, their oxidation, and uptake by macrophages initiate an inflammatory process. Oxidized LDL has a toxic effect on macrophages and leads to the formation of "foam cells," which are the main component of atherosclerotic plaques.

Familial hypercholesterolemia develops as a result of mutations in the LDL receptor gene. This is an autosomal dominant disease with a frequency of approximately one in five hundred for heterozygotes. In the homozygous form, LDL levels are very high, and myocardial infarction may develop in childhood. Modern treatment methods, including statins, ezetimibe, and PCSK9 inhibitors, can significantly reduce LDL levels and decrease cardiovascular event risk.

Low HDL levels are also considered an independent risk factor. HDL provides protective effects not only through reverse cholesterol transport but also has antioxidant, anti-inflammatory, and vasodilatory properties. HDL particles contain antioxidant enzymes such as paraoxonase-1, which prevent LDL oxidation. HDL also improves endothelial function and increases nitric oxide production.

Lipoprotein(a) or Lp(a) is a special lipoprotein particle structurally similar to LDL but with apolipoprotein(a) additionally attached via disulfide bond. High Lp(a) levels are considered an independent genetic risk factor for cardiovascular diseases. Lp(a) levels are mainly determined by genetic factors and are little influenced by lifestyle or standard lipid-lowering drugs. New medications, such as antisense oligonucleotides, can reduce Lp(a) levels and are currently undergoing clinical trials.

Statins are the main medications in dyslipidemia treatment. Statins inhibit the HMG-CoA reductase enzyme, which reduces cholesterol synthesis and increases LDL receptor expression in

the liver. As a result, plasma LDL levels decrease. Clinical studies have shown that statins significantly reduce cardiovascular events and mortality risk. Ezetimibe blocks cholesterol absorption in the intestine and is often used in combination with statins. PCSK9 inhibitors are a new class of drugs that prevent LDL receptor degradation and powerfully reduce LDL levels.

Adipose Tissue Structure and Differentiation

Adipose tissue or adipose tissue is a special type of connective tissue that mainly performs lipid storage and energy homeostasis regulation functions. Adipose tissue consists of two main components - adipocytes or fat cells and the stromal-vascular fraction. The stromal-vascular fraction includes preadipocytes, fibroblasts, vascular endothelial cells, pericytes, macrophages, and other immune cells.

In mammals, two main types of adipose tissue are distinguished - white and brown adipose tissue. White adipose tissue or WAT is the main type of adipose tissue for adults, consisting of adipocytes with one large lipid droplet. In these cells, the nucleus and cytoplasm are pushed to the tissue periphery. White adipose tissue is located in various parts of the body, and its distribution depends on sex, age, and genetic factors. The main fat depots are located subcutaneously, around internal organs, in the orbit, bone marrow, and other places.

Brown adipose tissue or BAT has a brown color due to numerous iron-containing mitochondria. BAT adipocytes are rich in numerous small lipid droplets and mitochondria. Brown adipose tissue is most abundant in newborns, located in the central part of the body. In adults, BAT quantity decreases significantly, but recent studies have shown that adults also have active BAT located in the neck, supraclavicular, and paraspinal regions.

The main function of brown adipose tissue is non-shivering thermogenesis. BAT contains UCP1 or thermogenin protein, which is located in the inner membrane of mitochondria. UCP1 returns protons to the mitochondrial matrix without synthesizing ATP, and as a result, energy is dissipated as heat. This mechanism plays an important role in adaptation to cold environments and increasing overall energy expenditure. Activation of brown fat is considered a promising direction in treating obesity and metabolic diseases.

Recently, a third type of adipocytes - beige fat cells - has been identified. These cells can appear in white adipose tissue under certain stimuli and, like brown fat, express UCP1 and have thermogenic capacity. Induction of beige fat may improve metabolic health, and active research is being conducted in this area.

Adipocyte differentiation or adipogenesis is a complex process involving the formation of mature adipocytes from mesenchymal stem cells. This process is regulated by a series of transcription factors. The main regulators are PPARγ (peroxisome proliferator-activated receptor gamma) and members of the C/EBP (CCAAT/enhancer-binding protein) family. PPARγ is the main regulator of adipogenesis, and without its activation, fat cell development is nearly impossible. C/EBPα, C/EBPβ, and C/EBPδ also play important roles at different stages of adipogenesis.

Endocrine Functions of Adipose Tissue

For a long time, adipose tissue was considered only a passive energy reserve. However, the discovery of leptin in 1994 fundamentally changed the view of adipose tissue. Leptin is a hormone produced by adipocytes that regulates energy balance and appetite. Since then, adipose tissue has been identified as an important endocrine organ producing hundreds of biologically active substances - adipokines.

Leptin is synthesized proportionally to adipose tissue mass and signals the hypothalamus to reduce food consumption and increase energy expenditure. Leptin activates POMC (proopiomelanocortin) neurons in the hypothalamus and inhibits NPY/AgRP (neuropeptide Y/agouti-related peptide) neurons. Genetic deficiency of leptin or mutations in its receptors lead to severe obesity and hyperphagia. However, in most obese patients, leptin levels are high, indicating the development of leptin resistance. The mechanisms of leptin resistance are not fully clear, but inflammation, endoplasmic reticulum stress, and disruption of signaling pathways may play important roles.

Adiponectin is another important adipokine produced by adipose tissue. Unlike leptin, adiponectin levels decrease in obesity. Adiponectin increases insulin sensitivity, has anti-inflammatory effects, and inhibits atherosclerosis development. Adiponectin increases fatty acid oxidation in the liver and reduces gluconeogenesis. Additionally, it increases glucose uptake and fatty acid oxidation in skeletal muscles. Low adiponectin levels are associated with insulin resistance, type 2 diabetes, and cardiovascular diseases.

Resistin is a cytokine produced by adipocytes and immune cells that confers resistance to insulin action. The significance of resistin in humans is not yet fully clear, but its high levels are associated with inflammation and insulin resistance. Resistin increases gluconeogenesis in the liver and reduces glucose uptake in skeletal muscles.

Adipose tissue also produces a number of inflammatory cytokines, including TNF-alpha, IL-6, IL-1β, and MCP-1. In obesity, macrophages and other immune cells infiltrate adipose tissue and are the main source of these cytokines. Inflammatory cytokines disrupt insulin signaling and lead to insulin resistance development. TNF-alpha increases serine phosphorylation of insulin receptor substrate-1 (IRS-1), which weakens insulin signaling. IL-6 increases synthesis of high-sensitivity C-reactive protein (CRP) in the liver, which is a general marker of inflammation.

Obesity Mechanisms and Pathogenesis

Obesity develops as a result of excessive adipose tissue accumulation and is characterized by a body mass index exceeding thirty kg/m². The main cause of obesity development is a long-term positive energy balance, meaning consumed energy exceeds expended energy. However, the pathogenesis of obesity is much more complex, involving genetic, epigenetic, physiological, psychological, and environmental factors.

Adipose tissue growth can occur through two main mechanisms. The first is hypertrophy - increasing the volume of existing adipocytes. The second is hyperplasia - formation of new adipocytes and increase in their number. Healthy adipose tissue expansion occurs mainly through hyperplasia, in which case new, small adipocytes are formed. These adipocytes are metabolically healthy and respond well to insulin. However, when adipose tissue loses its expansion capacity,

existing adipocytes become excessively enlarged. Hypertrophic adipocytes undergo hypoxia, their function is disrupted, and they begin to produce more inflammatory mediators.

Adipocyte hypoxia occurs as a result of inadequate vascular network development during adipose tissue expansion. Hypoxia activates the HIF-1α (hypoxia-inducible factor-1alpha) transcription factor, which increases expression of inflammatory genes. Hypoxic adipose tissue attracts macrophages, particularly M1-type pro-inflammatory macrophages. These macrophages form ring-like structures - "crown-like structures" - surrounding dying adipocytes.

Adipose tissue fibrosis is also an important pathological change. In obesity, extracellular matrix components, particularly collagen, accumulate in adipose tissue. Fibrosis reduces adipose tissue elasticity and hinders its further expansion. This intensifies adipocyte stress and increases metabolic dysfunction.

Ectopic fat accumulation is considered an important mechanism of obesity-related metabolic complications. Ectopic fat is the accumulation of lipids in organs outside adipose tissue, particularly in the liver, skeletal muscles, heart, and pancreas. Ectopic fat accumulation directly disrupts insulin signaling. Fat accumulation in liver cells is called non-alcoholic fatty liver disease (NAFLD), a condition that increases risk of type 2 diabetes and cardiovascular diseases. In extreme cases, NAFLD can progress to non-alcoholic steatohepatitis (NASH), leading to cirrhosis and liver failure.

Differences Between Visceral and Subcutaneous Fat

The anatomical distribution of fat is important for metabolic health. Subcutaneous fat is located under the skin and comprises approximately eighty percent of total body fat. Visceral fat is located in the abdominal cavity, around internal organs. Although visceral fat is relatively small, it is particularly important for metabolic disease risk.

Visceral adipocytes differ from subcutaneous adipocytes in several characteristics. Visceral adipocytes are more metabolically active, more sensitive to lipolysis, and release more free fatty acids into the blood. Because venous blood flow from visceral fat is directed directly to the liver through the portal vein, free fatty acids and adipokines released from visceral adipose tissue directly affect the liver. This leads to hepatic insulin resistance, increased gluconeogenesis, and increased VLDL synthesis.

Visceral fat produces more inflammatory cytokines and has higher macrophage infiltration. In visceral fat, low adiponectin levels and high resistin and TNF-alpha levels are observed. Additionally, visceral adipose tissue is richer in glucocorticoid receptors and 11β-hydroxysteroid dehydrogenase type 1 enzyme, which increases local cortisol production and contributes to metabolic dysfunction.

Men and women have different fat distribution patterns. Men typically accumulate more visceral fat, called an "apple shape." In women, fat accumulates more in subcutaneous depots, particularly in the thigh and buttock regions, called a "pear shape." Sex hormones play an important role in this difference. Estrogen encourages subcutaneous fat accumulation and limits visceral fat accumulation. During menopause, decreased estrogen levels lead to increased visceral fat accumulation in women and increases metabolic disease risk.

Epidemiological studies show that waist circumference is an independent predictor of cardiovascular diseases and mortality. Waist circumference is a simple and practical indicator reflecting visceral fat amount. Even with normal body mass index, it is possible to have excess visceral fat, a condition called "metabolically obese normal weight" and associated with high risk levels.

Obesity-Related Complications

Obesity is associated with numerous serious health problems. Type 2 diabetes is one of the most common complications, with development risk in obese patients nearly eighty times higher. Insulin resistance is the main mechanism linking obesity and diabetes. Free fatty acids and inflammatory cytokines released from adipose tissue disrupt insulin signaling and weaken pancreatic beta-cell function.

Cardiovascular diseases are another important complication associated with obesity. Obesity increases risk of arterial hypertension, dyslipidemia, atherosclerosis, and coronary heart disease. In obesity, cardiac load increases, left ventricular hypertrophy develops, and heart failure risk increases. Additionally, obesity increases arrhythmia risk, particularly atrial fibrillation.

Non-alcoholic fatty liver disease is almost constantly associated with obesity, with frequency in obese patients comprising seventy to ninety percent. NAFLD development can lead to cirrhosis and hepatocellular carcinoma. NAFLD is viewed as a hepatic manifestation of metabolic syndrome and independently increases cardiovascular disease risk.

Sleep apnea is widespread in obese patients and is characterized by intermittent cessation of breathing during sleep. Sleep apnea leads to intermittent hypoxia, sleep fragmentation, and sympathetic activation. This increases risk of arterial hypertension, cardiovascular diseases, and cognitive impairments.

Some cancer types, particularly esophageal, pancreatic, liver, kidney, breast, and colorectal cancers, are associated with obesity. Excess adipose tissue produces hormones, particularly estrogen and insulin-like growth factor-1, which increase cell proliferation. Additionally, inflammation and oxidative stress contribute to cancer development.

Reproductive system disorders are also associated with obesity. In women, polycystic ovary syndrome (PCOS), menstrual cycle disruption, and infertility may develop. In men, testosterone levels decrease and erectile dysfunction risk increases. During pregnancy, obesity increases risk of gestational diabetes, preeclampsia, and birth complications.

Psychological and social problems are also widespread with obesity. Obese individuals often face discrimination and stigmatization. Depression, anxiety, and low self-esteem are common in obese patients. These psychological factors complicate obesity treatment and can lead to vicious cycles.

Structure and Biological Significance of Sphingolipids

Sphingolipids are a family of complex lipids based on sphingosine or another amino alcohol. Sphingolipids are an important component of cell membranes, found in large quantities

particularly in nervous system cell membranes. They play important roles not only in structural function but also in cell signaling and membrane microdomain organization.

The simplest representative of sphingolipids is ceramide. Ceramide consists of the union of sphingosine and fatty acid through an amide bond. Ceramide in turn serves as a precursor of complex sphingolipids. Various sphingolipids are formed as a result of adding various polar groups to ceramide. For example, adding phosphorylcholine results in sphingomyelin, adding glucose results in glucocerebroside, and adding galactose results in galactocerebroside.

Gangliosides are the most complex sphingolipids, having an oligosaccharide chain attached to ceramide containing one or more sialic acid residues. Gangliosides are particularly abundant in the nervous system, located in the outer layer of neuronal membranes and playing important roles in neuronal function, synaptic transmission, and cell-cell interactions. Various gangliosides exist and are named GM1, GM2, GM3, GD1a, GD1b, etc., according to their oligosaccharide chain.

Sphingolipids form special microdomains in cell membranes - lipid rafts. Lipid rafts are regions rich in cholesterol and sphingolipids that exist as dynamic, ordered structures in the membrane. Many signaling molecules and receptors concentrate in lipid rafts, enabling efficient signal transmission. Additionally, lipid rafts participate in sorting proteins and lipids from membranes, cell polarization, and membrane transport.

Sphingolipids themselves also function as signaling molecules. Ceramide can induce apoptosis, cell growth arrest, and differentiation. Sphingosine-1-phosphate (S1P) regulates cell growth, migration, angiogenesis, and immune responses. The balance between ceramide and S1P is important for cell fate - ceramide encourages cell death, while S1P ensures survival.

Lysosomal Catabolism of Sphingolipids

Sphingolipid degradation occurs mainly inside lysosomes. Lysosomes are cell organelles with acidic pH filled with various hydrolases for breaking down macromolecules. Sphingolipid catabolism is a sequential process where specific enzymes remove terminal portions at each stage.

Complex sphingolipid degradation begins from their outer layer and continues toward the center. For example, to degrade GM1 ganglioside, β-galactosidase first removes the galactose residue, forming GM2. Then, to break down GM2, β-hexosaminidase A enzyme and its cofactor GM2 activator protein are needed. This enzyme removes the N-acetylgalactosamine residue and forms GM3. In subsequent stages from GM3, other enzymes participate and finally ceramide is formed. Ceramide is then broken down by ceramidase into sphingosine and fatty acid.

Sphingomyelin degradation is accomplished by sphingomyelinase enzyme. This enzyme removes the phosphorylcholine group from sphingomyelin and forms ceramide. For cerebroside degradation, glucocerebrosidase or galactocerebrosidase enzymes are needed, which remove glucose or galactose respectively.

For degradation of some sphingolipids, not only enzymes but also cofactor proteins are necessary. For example, for GM2 ganglioside degradation, in addition to β-hexosaminidase A,

GM2 activator protein is also needed. This protein presents GM2 in the correct conformation for the enzyme. A group of proteins called saposins also function as cofactors in the degradation of many sphingolipids. They bring substrates into more favorable positions for enzymes or stabilize enzyme-substrate complexes.

Molecular Basis of Sphingolipidoses

Sphingolipidoses are hereditary diseases that develop as a result of genetic defects in enzymes or cofactor proteins involved in lysosomal catabolism of sphingolipids. These diseases belong to the large group of lysosomal storage diseases (LSD).

CONCLUSION

Apolipoproteins play a crucial role in cholesterol metabolism. ApoA1 ensures reverse cholesterol transport and prevents atherosclerosis development, while ApoB delivers cholesterol to peripheral tissues. These proteins also directly affect obesity processes by regulating lipid metabolism.

In the pathogenesis of obesity, disruption of the balance between lipogenesis and lipolysis, insulin resistance, and inflammatory processes in adipose tissue occupy a central position. Sphingolipidoses develop as a result of deficiency in enzymes involved in sphingolipid degradation, leading to accumulation of toxic lipids in cells and particularly causing damage to the nervous system.

Thus, apolipoproteins, obesity, and sphingolipidoses are interconnected components of lipid metabolism, and research in this field serves to create new methods for treating cardiovascular diseases, obesity, and hereditary lipid pathologies.

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