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Popular Article

Exploring Ultrastructural Changes in Cell Membranes

Avantika Srivastav[1], Ithrineni Karthik[2], Ankit Jaiswal[3]
Ph.D. Scholar[1,2], Division of Pathology, ICAR-Indian Veterinary Research Institute, Izatnagar, Bareilly, U.P, 243122
Ph.D. Scholar[3], Department of livestock production management ANDUAT, Kumarganj, Ayodhya, U.P, 224229
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Abstract

The given content delves into the composition of cell membranes, emphasizing the roles of phospholipids, glycolipids, cholesterols, and proteins. It explores ultrastructural changes in response to injuries, such as apoptosis and glycosphingolipids' multifaceted functions. The detection and localization of cholesterol using filipin are discussed. The role of phospholipases, both intramembrane and exogenous, in modulating membrane integrity is highlighted, along with examples like snake venom phospholipase A2. Microbial lysins and bacterial phospholipases contribute to membrane damage. The article also covers endocytosis, exocytosis, cytoplasmic blebs formation, and acute cellular swelling, providing insights into cellular membrane dynamics

Introduction

The cell membrane's ultrastructure, vital for functionality, involves phospholipids like phosphatidylcholine and sphingomyelin in the outer leaflet, and phosphatidylethanolamine and phosphatidylserine in the inner leaflet, crucial for membrane integrity. Additionally, glycolipids, cholesterols, and proteins contribute to membrane structure. These components play roles in membrane stability, with integral proteins (channel proteins, carrier proteins, enzymes, and linker proteins) embedded within the membrane, participating in diverse cellular functions. Investigating ultrastructural changes provides insights into cellular alterations and their implications in physiological and pathological conditions.

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Ultrastructural Changes in cell membrane in response to Injuries

There are various extrinsic and intrinsic causes that may lead to cell injury. During apoptosis there is externalization of phosphatidylserine (PS) (phospholipid component of cell membrane) to the outer leaflet of the plasma membrane. This externalization of PS serves as a signal for phagocytic cells, such as macrophages, which engulf and remove apoptotic cells from the tissue.

Glycolipids, specifically glycosphingolipids, constitute a significant class of lipids characterized by a ceramide backbone linked to complex glycans through a β-glycosidic bond. These molecules play diverse roles in cellular processes. Notably, they function as differentiation antigens, contributing to the recognition and classification of cells within the immune system. Additionally, glycosphingolipids serve as tumor antigens, influencing immune responses to cancerous cells. Moreover, they are involved in the expression of blood group antigens, contributing to blood type determination. Furthermore, glycosphingolipids act as receptors for microbes, participating in host-microbe interactions. The multifaceted functions of glycolipids underscore their importance in various physiological processes and immune responses, making them essential components of cellular membranes with implications for health and disease.

Cholesterol Detection and Localization

Cholesterol within membranes has been successfully detected through the application of filipin, a naturally fluorescent polyene antibiotic known for its specific affinity to cholesterol. The process involves labeling cholesterol with filipin, resulting in the formation of filipin-cholesterol complexes. Remarkably, these complexes manifest as distinct protuberances on the cell membrane when observed under electron microscopic analysis. The unique fluorescence properties of filipin facilitate the visualization and precise localization of cholesterol, contributing to a deeper understanding of the intricate interactions and distribution of this lipid within cellular membranes.

Prolonged exposure to ethanol has been identified as a factor that may induce notable ultrastructural changes in the membrane architecture of synaptosomes. These ultrastructural changes may involve modifications in membrane composition, organization, or other cellular components that play a role in synaptic transmission.

Role of Phospholipases in Membrane Dynamics

Phospholipases, both intramembrane and exogenous, play pivotal roles in inducing changes in the cell membrane. Intramembrane phospholipases are the integral components of the normal plasma membrane, are activated nonspecifically during plasma membrane stimulation and injury. In acute cellular swelling, their activation is triggered by elevated levels of intracellular calcium ions (Ca^{++}).

Exogenous phospholipases are found in chemical solvents, venoms, bacterial lysins, and other biological toxins, can exert enzymatic attacks on phospholipids within the plasma membrane, representing a major cause of lethal cellular injury. This hydrolytic action leads to membrane leakage and cellular lysis. For example, all snake venoms contain a phospholipase A2, which specifically targets membrane phospholipids, resulting in the release of unsaturated fatty acids and lysophosphatides. The actions of both intramembrane and exogenous phospholipases underscore their significant roles in modulating cell membrane integrity and function, influencing critical cellular responses to various stimuli and injuries.

Microbial lysins, such as the potent α-toxin produced by *Clostridium perfringens*, exhibit highly lethal effects through their interaction with cell membranes. Specifically, the α-toxin targets membrane lecithin moieties, converting them into phosphorylcholine and a diglyceride. When these toxins released into the muscle tissue it causes rapid and indiscriminate lysis of the cells that leads to the destruction of various cell types including myocytes, endothelial cells and erythrocytes.

The enzymatic activity of bacterial phospholipases leads to the hydrolysis of phospholipid molecules, resulting in alterations to the lipid composition and organization of the membrane. This, in turn, gives rise to a spectrum of membrane lesions, ranging from minute disruptions in the form of small holes to more substantial damage in the form of large cavities and pits.

Changes in cell membrane during endocytosis and exocytosis

Endocytosis is a cellular process involving the uptake of fluids, macromolecules, and particulate matter through the inward invagination of the plasma membrane, forming pits. Upon receiving the appropriate signal, membrane proteins relocate to the point of contact, causing changes in membrane viscosity. Subsequently, a vesicle forms and penetrates the cytosol, encapsulating the cargo. Animal tissues utilize various endocytic pathways, including pinocytosis, caveolar endocytosis, clathrin-mediated endocytosis, and phagocytosis.

In pinocytosis membrane bound vesicle is formed from the cell surface that traps the fluid and solutes from the extracellular environment and these incoming pinocytic vesicles fuse with lysosomes. Caveolae are invaginated vesicles of uniform diameter that plays a prominent role in

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endothelial cells, smooth muscle cells, and fibroblasts, participating in endocytosis, cell signaling, and lipid recycling. Clathrin-coated pits and vesicles, characterized by an exterior surface coat of fibrillar clathrin, form in response to ligand-receptor interactions. Phagocytosis involves the massive deformation of the cell surface to envelop particulate cargo, with specific domains in the plasma membrane playing a crucial role.

Exocytosis is the release of cellular materials through membrane-bound vesicles that includes exosomes and small vesicles originating from multivesicular bodies or by surface budding. These mainly presenting the antigens and transferring nucleic acids to other cells.

The other type of membranous changes includes cytoplasmic blebs formation. These are released by cells through shedding when bullae form at the surface. The exogenous proteins forming complexes called porins are also involved in the membrane damage. Perforin induced cell death is very common and mediated by cytotoxic T cells and natural killer cells, leads to the formation of ring-shaped structures causing ion leakage from the cytosol.

The Acute cellular swelling results in irregular plasma membrane and significant changes in cell architecture. This also leads to the changes in the distribution of integrins, receptors, and adhesion molecules, leading to cellular segregation and bulging from epithelial limits. Scanning electron microscopy reveals waves and pits in swollen epithelial cells.

Conclusion

Ultrastructural changes in cell membranes includes the alterations in the fine details of the membrane's structure at the microscopic level. These changes can occur in response to various stimuli, including injuries, physiological processes, or pathological conditions. Ultrastructural analysis allows researchers to observe and understand modifications in the composition, organization, and morphology of cell membranes. Key factors influencing ultrastructural changes include apoptosis-induced externalization of phospholipids like phosphatidylserine, glycosphingolipids' multifaceted functions, cholesterol localization using filipin, and the impact of phospholipases on membrane integrity. These changes contribute to a deeper understanding of cellular dynamics and their implications in health and disease.

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