【Grant-in-Aid for Transformative Research Areas（A）】

Autophagy expanded: decoding membrane interface biology

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Project Information	Project Number : 25A303　　Project Period (FY) : 2025-2029 Keywords : membrane interface, phase separation, molecular cooperation, autophagy

Purpose and Background of the Research

●Outline of the Research

About 60% of the human body is water, while most of the remainder consists of proteins and lipids. These substances collectively form cells, the fundamental units of life. Proteins, synthesized according to DNA, vary in shape and function, playing crucial roles within the body. Traditionally, research has focused on individual proteins or protein complexes; however, recent studies emphasize the dynamic assembly and collective actions of protein groups as essential for life processes. Lipids have long been recognized primarily as stable structures forming cell and organelle boundaries. Research on their dynamic collective behavior and sophisticated roles had been limited. Recently, advances in protein research have revealed that lipids also dynamically interact with proteins, demonstrating that their coordinated collective behaviors are vital to life. Thus, proteins and lipids work collaboratively, not individually, driving complex biological phenomena primarily at membrane interfaces, such as cell and organelle membranes.

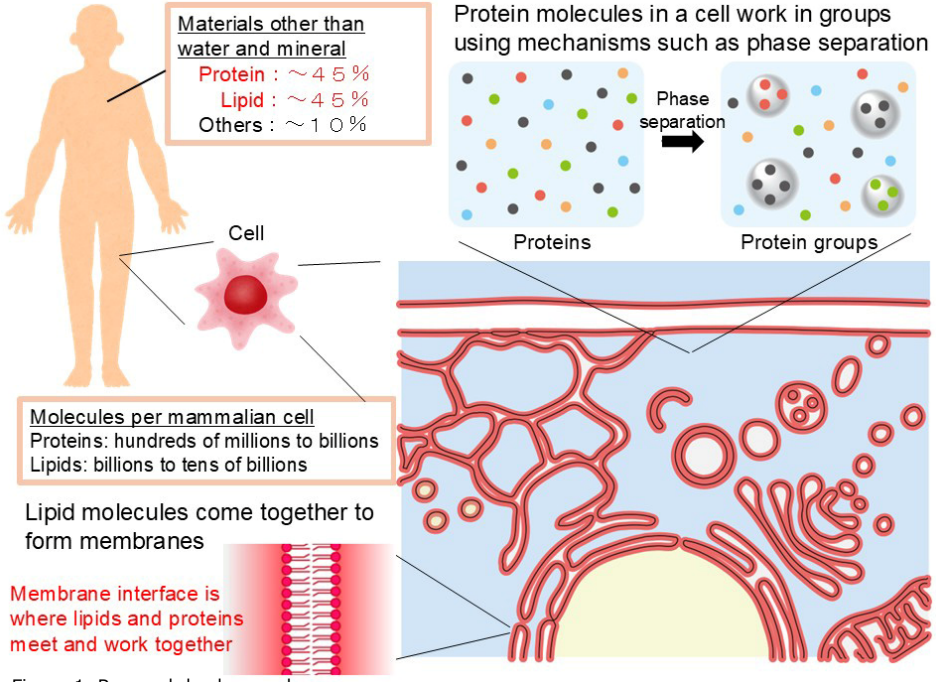

Figure 1. Research background

●Protein–lipid coordination at membrane interfaces

At membrane interfaces, proteins and lipids collaborate closely (Fig. 2). This cooperation is notably observed in autophagy, a cellular process for degrading unwanted materials. Recent studies indicate that such coordination is also crucial in various biological processes beyond autophagy. Eukaryotic cells, having extensively developed organelles, exhibit much larger membrane surface areas compared to prokaryotes, implying many intracellular events occur at these interfaces. However, the fundamental role of membrane interfaces in sustaining life remains understudied.

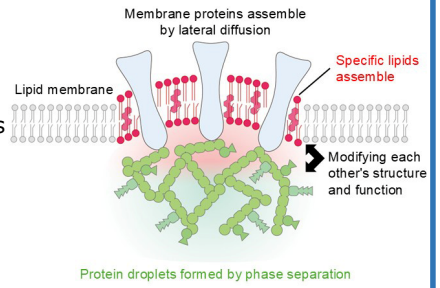

Figure 2. Protein–lipid coordination at membrane interfaces

Expected Research Achievements

●Various membrane interface phenomena in research projects A01–A03

In this research area, scientists studying membrane interfaces related to autophagy collaborate with researchers investigating membrane interfaces involved in diverse biological phenomena beyond a single cell, such as synaptic transmission, cell adhesion, and viral infection. Additionally, researchers skilled in advanced techniques, including physics, computational science, structural biology, optogenetics, and chemical biology, are contributing to this interdisciplinary effort. Through such multidisciplinary collaboration, we aim to establish a new scientific field, termed "Membrane Interface Biology," to elucidate the diverse functions and common mechanisms of molecular coordination at membrane interfaces. The establishment and advancement of membrane interface biology will provide novel directions in cell biology and enable global leadership in fundamental research. Furthermore, since membrane interface phenomena are directly implicated in numerous diseases, including cancer, epilepsy, and viral infections, the artificial manipulation methods developed in this research hold promise for applications in disease prevention and therapy.

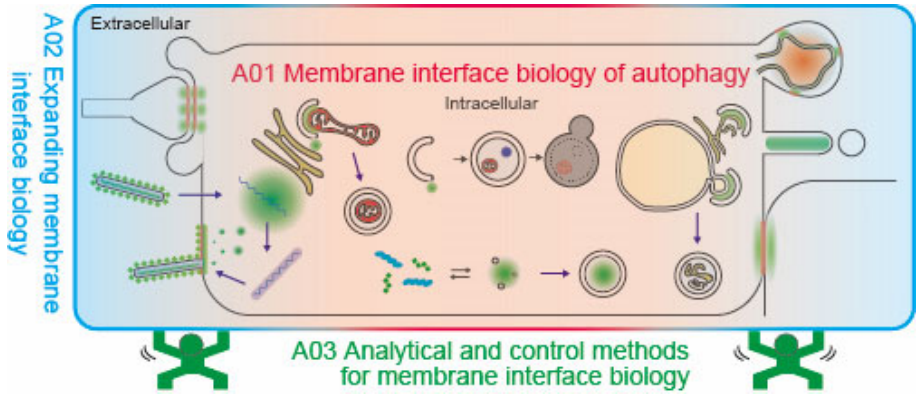

Figure 3. Various membrane interface phenomena to be addressed in research items A01-A03

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