【Grant-in-Aid for Scientific Research (S)】

Understanding the molecular and cellular basis and controlling cellular phenomena: A New Concept for Intracellular Delivery of Antibodies

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Project Information	Project Number : 24H00051	Project Period (FY) : 2024-2028
	Keywords : antibody, delivery peptide, cell membrane, intracellular delivery, cell phenomenal control	

Purpose and Background of the Research

●Outline of the Research

Antibodies (IgG) are proteins produced when foreign substances such as bacteria and viruses invade our bodies. If antibodies can be delivered into cells, they can play a useful role in detecting the intracellular presence of proteins that have important functions in the cell and their interactions with other intracellular molecules. In addition, delivery of antibodies against disease-associated proteins may reduce the progression of disease. However, the lack of an effective means to deliver antibodies intracellularly has hindered the development of these applications.

The principal investigator previously developed the intracellular antibody delivery peptide L17E and found that when the trimer of L17E is mixed with a fluorescently labeled antibody, a droplet-like complex forms and contacts the cell, resulting in a rapid influx of antibody into the cell. With a view to utilizing this phenomenon as a general method for cell manipulation in biology, chemistry, and medicine, this study aims to 1) study peptide design and cellular responses on antibody influx and improve the delivery system, and 2) establish it as a practical method for detecting intracellular proteins in cultured cells and regulating protein-protein interactions. We aim to establish this method as a practical method for detecting intracellular proteins in cultured cells and regulating protein-protein interactions. In addition, with medical applications in mind, we will 3) investigate the feasibility of antibody delivery using this method in mouse tissues.

Understanding the molecular and cellular basis and controlling cellular phenomena:
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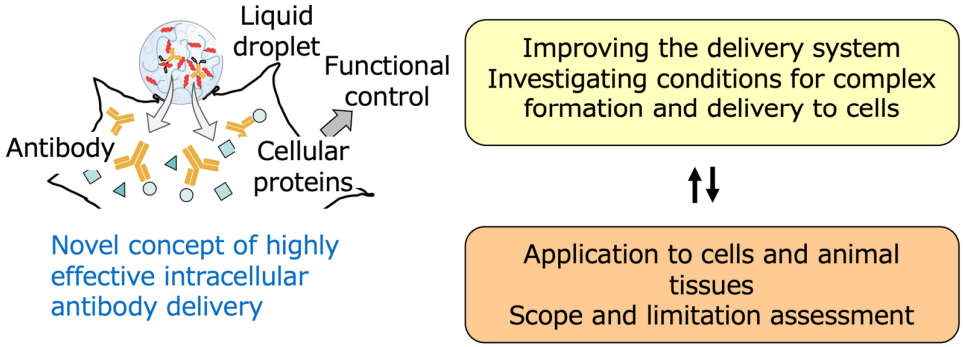

Figure 1. Outline of the research

● Aims of this study

1) To study the conditions required for peptide, carrier and antibody to improve the delivery capacity.
In this study, peptides such as L17E supported on polymeric carriers and their complexes with antibodies will be prepared. The sequence and physicochemical properties of the peptide, carrier and antibody will be investigated to improve the efficiency of antibody delivery.
2) Establishment of a practical system for the regulation of intracellular protein function
We will investigate the mode of antibody delivery from droplet-like complexes into cells to find the conditions under which antibodies transferred into cells to exert their maximum effect.
3) Integrating information for medical applications
Establish a system for delivering antibodies into mouse tissues.

Expected Research Achievements

●Investigation of conditions required for peptides, carriers and antibodies to improve delivery capacity

Reduce the antibody concentration required to improve delivery and achieve the expected intracellular effect.

● Establish a practical system for regulating intracellular protein function

Verification of intracellular effects and cellular characteristics of introduced antibodies / Verification and development of intracellular signal transduction and cancer growth suppression effects.

● Gathering information for medical treatment development

To confirm the transfer of antibodies into cancer tissue cells and their cancer shrinking activity / to study their disposition in droplet-like complexes.

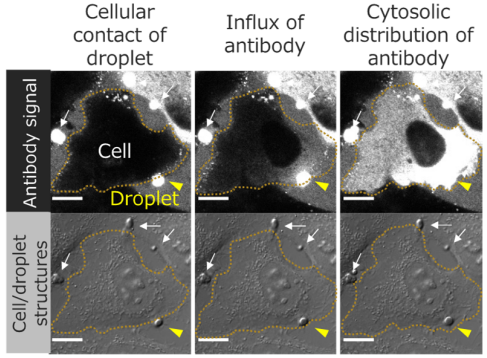

Figure 2. Steep cytosolic influx of antibody via liquid droplet after contact with the cell membrane, completed in approximately one minute.

● Expectations for this research

Efforts to improve the efficiency of the transfer system in this study will deepen our scientific understanding of the formation of droplet-like complexes, the mode of uptake of complexes into cells, the requirements for droplet/peptide formation to enable intracellular influx of antibodies, and cellular responses. This understanding is expected to lead to the creation and development of novel biomaterials and manipulation techniques.

Homepage Address, etc.	https://www.scl.kyoto-u.ac.jp/~bfdc/index.html