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

Section III

Title of Project: Construction of PLAMP for determination of boundary between self and non-self in intracellular pathogens

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【Purpose of the Research Project】

The host has an immune system that responds to infection by pathogens such as viruses, bacteria, and parasites. Initially, the innate and acquired immune systems respond to these pathogens and then recognize pathogen specific patterns as the boundary between "self" and "non-self". On the other hand, in the cell-autonomous immune system, which directly attacks pathogens in cells, it is not well understood what determines "self" and "non-self". This is because most pathogens are decorated by host-derived membranes inside the cell (Figure. 1), and the 'self-derived' membrane would be recognized as 'non-self'. We hypothesized that this phenomenon is due to the recognition of a unique intracellular pattern generated by the pathogen life cycle as "non-self", and named this pattern PLAMP (Pathogen Life-cycle Associated Molecular Pattern). In this Research Project, we aim to create a new concept of self/non-self recognition mechanism through the study of PLAMP.

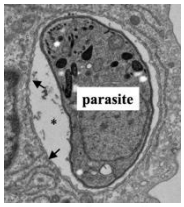

Figure. 1: Electron microscope image.
*; Toxoplasma in parasitic vacuole
Arrows; Parasitic vacuolar membrane

【Content of the Research Project】

The concept of "PLAMP" was proposed based on the idea that the "non-self" targeted by cell-autonomous immunity is originally derived from the "self". On the other hand, pathogens have various virulence factors to hide their "non-self" and create a favorable environment for their survival in the cell. Therefore, the molecular patterns that pathogens produce in the cell for their own survival can be regarded as "PLAMPs" in a broad sense. In this Research Project, we will demonstrate the PLAMPs produced by various pathogens. Dr. Arasaki of Tokyo University of Pharmacy and Life Sciences will participate in the research on PLAMPs of bacteria, and Dr. Hashiguchi of Kyoto University will participate in the research on PLAMPs of virus. The specific research topics are as follows.

(Yamamoto): We will study the recognition mechanism against *Toxoplasma* and *Plasmodium falciparum*, pathogenic parasites, by the cellular autonomic immune system during the process of non-self, then demonstrate the physiological importance of PLAMP and the cell-autonomous immune system in determining the boundary between self and non-self in intracellular parasitic pathogens.

(Arasaki): We will study the survival mechanism of *Legionella*, a pathogenic bacterium, in host cells, and clarify the molecular mechanism of PLAMP in the host by *Legionella*.

(Hashiguchi): We will study the mechanism of PLAMP generation by cell entry (self) and budding (non-self) in viral infections, then elucidate the mechanism of virulence regulation against pathogenic viruses, combining with the correlation with other biological phenomena.

【Expected Research Achievements and Scientific Significance】

This Research Project is expected to identify novel PLAMPs that exist between pathogens and hosts and elucidate novel virulence mechanisms through the study of the cellular autonomic immune system on the host side, which will greatly accelerate our understanding of host-pathogen interactions. Furthermore, by promoting multifaceted research on infectious diseases such as viruses, bacteria, and parasites, we can contribute basic research on infectious diseases worldwide, and build a system to prepare for the emergence of new infectious diseases. In addition to infectious immunology, membrane fusion and fission, which are involved in the determination of the boundary between "self" and "non-self," play an extremely important role in the maintenance and disruption of biological homeostasis from microorganisms to higher plants and organisms. The results of this research project are expected to have a ripple effect on the life sciences in general, since these phenomena cover a very large range of biological fields, including infection, fertilization, development, intra- and intercellular transport, and inter-neural communication.

【Key Words】

Cell-autonomous immune system: An immune system that actively stops the growth of pathogens and kills them in cells infected by pathogens. It is strongly induced in infected cells by interferons which are released by innate and acquired immune systems

PLAMP (Pathogen “Life-cycle” Associated Molecular Pattern): Unlike the pathogen-associated molecular patterns (PAMPs) recognized by the innate and acquired immune systems as non-self, PLAMPs are produced as host-derived non-self patterns by pathogens in infected cells.

【Term of Project】 FY2020-2022

【Budget Allocation】 122,300 Thousand Yen

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