

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

Broad Section I



Title of Project : Investigation on pathological implications of guidance molecules in neuro-immune-metabolism

Atsushi Kumanogoh
(Osaka University, Graduate School of Medicine, Professor)

Research Project Number : 18H05282 Researcher Number : 10294125

Keyword : Immunometabolism, axon guidance molecule, chronic inflammation

【Purpose and Background of the Research】

The immune, nervous, and metabolic systems are indispensable for body homeostasis. Previous studies showed that these systems interact closely with each other. However, the mechanisms underlying these interactions remain unknown. We have unveiled the existence of the semaphorins, a group of molecules that works in both the nervous and immune systems. In addition, we have obtained insights suggesting that the expression of semaphorins and their related molecules is regulated by metabolic signaling, and that breakdown in the regulatory system can result in development of lesions of chronic inflammatory diseases, including angiitis, multiple sclerosis, metabolic diseases and malignancies. By establishing the novel concept of “Neuro-Immune-Metabolism,” this research aims to elucidate the mechanism underlying the interactions among the immune, nervous, and metabolic systems (Fig. 1).

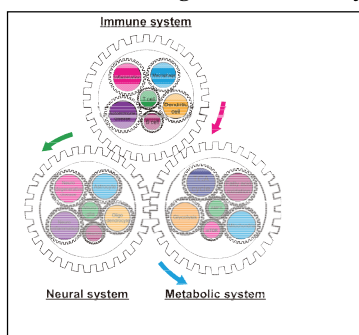


Figure 1

【Research Methods】

Towards elucidation of Neuro-Immune-Metabolism regulatory mechanism and control of the mechanism, this study employs the following viewpoints to achieve the study objective:

- 1) Elucidation of the mechanism by which immune and inflammatory cells are activated or differentiated by molecules that regulate Neuro-Immune-Metabolism
- 2) Elucidation of the involvement of abnormal expression of semaphorin-related molecules in disease pathology and the control of semaphorin expression

Additionally, this study proactively integrates basic and clinical approaches (“Bench to Bed” and “Bed to Bench”) to pursue the study objectives.

【Expected Research Achievements and Scientific Significance】

Studies that focus on the pairwise relationships between the immune, nervous, and metabolic systems have started to receive a great deal of attention. However, studies that examine the relationships among these three systems from a single perspective have just begun. This research uses the “window” of semaphorins and their related molecules to investigate the relationships among these three systems, with the aim of elucidating the mechanisms underlying their interactions. Based on the novel concept of Neuro-Immune-Metabolism, the resultant knowledge should contribute to development of diagnostic and therapeutic mechanisms for diseases that are caused by any breakdown of the control system (Fig. 2).

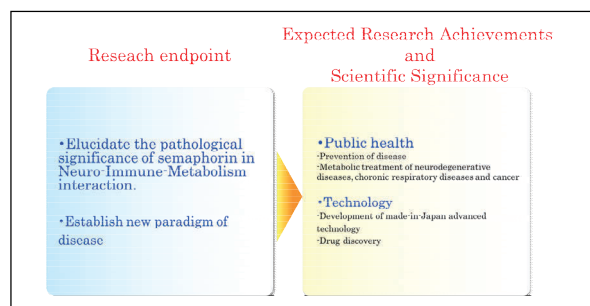


Figure 2

【Publications Relevant to the Project】

- Kang S, Nakanishi Y, Kumanogoh A et al. (2018) Semaphorin 6D reverse signaling controls macrophage lipid metabolism and anti-inflammatory polarization. *Nature Immunology*, 19, 561-570.
- Hosen N, Kumanogoh A et al. (2017) The activated conformation of integrin β_7 is a novel multiple myeloma-specific target for CAR T cell therapy. *Nature Medicine*, 12, 1436-1443.

【Term of Project】 FY2018-2022

【Budget Allocation】 147,800 Thousand Yen

【Homepage Address and Other Contact Information】

<http://www.imed3.med.osaka-u.ac.jp/>