Molecular mechanisms for the detection of microbes and cancer cells in innate immunity

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【Outline of survey】

Infctious disease is still a formidable issue, to which it could provide a key to find how we control microbial infection. We will address this issue by focusing particularly on "microbial sensing", the first line of host defense in triggering innate immune responses. Recent rapid progress in studies on innate immunity has facilitated the identification of various sensors, such as TLRs (Toll-like receptors), that detect microbe-specific components, and has elucidated their critical roles in the activation of dendritic cells. Recently, we have identified a candidate cytosolic DNA sensor called DAI (DNA-dependent activator of IRFs, previously known as DLM-1 or ZBP1). In addition, evidence has been provided regarding the existence of additional DNA sensor(s). In this study, our aim is to find a novel DNA sensing molecule(s), to determine which microbes can be recognized by them, and to elucidate a mechanism for the activation of these sensors and the related signaling pathways, leading to the induction of cytokine/chemokine genes in innate immune responses. In addition, we try to investigate the mechanism for the activation of innate immunity in the eradication of cancer cells, particularly in terms of a possible involvement of "DNA sensing" in this process.

【Expected results】

This study will contribute to further understanding of the microbial sensing mechanism for the activation of innate immune responses. In addition, it will be expected that this project may also provide a new insight into the mechanism for the pathogenesis of DNA-related diseases including autoimmune diseases and inflammatory diseases, and offer some therapeutic basis to those intractable diseases. Our research will further clarify a mechanism underlying the activity of DNA as a potent immunostimulant particularly for vaccination. The analyses for the recognition of cancer cells could provide a novel concept to the activation process of innate immunity against cancer.

【References by the principal investigator】

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【Term of project】 FY2008− 2012	【Budget allocation】 **77,200,000 yen** (direct cost)

【Homepage address】 http://www.igm.hokudai.ac.jp/sci/