

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



**Title of Project :** Investigation of Differential Immune Status among Cancer Patients and Development of Personalized Cancer Therapy by Combining Immunomodulation

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Research Area : Biological Sciences, Oncology, Tumor therapeutics

Keyword : Cancer therapy, Personalized medicine, Immunotherapy, Immunomodulation

**【Purpose and Background of the Research】**

Immune status varies among cancer patients, and was reported to correlate with patients' prognosis and response to cancer therapy. However, it has not been established. The investigation of its mechanism and role in cancer treatment may lead to the understanding of cancer immunopathology and the development of new cancer therapy by combining immunomodulation.

Based on our previous researches, we are proposing the hypothesis that differential immune status is defined by balance of the anti-tumor immune induction pathway which is regulated by status of endogenous tumor antigens and immune-reactivity of patients, and the immunosuppression pathway which is regulated by oncogene and signal alterations in cancer cells.

In this study, we will attempt to develop new cancer treatment strategy by modulation of immune-status through researches on immunopathology using system biological and immunological analyses of clinical samples and *in vivo* experiments using various murine models.

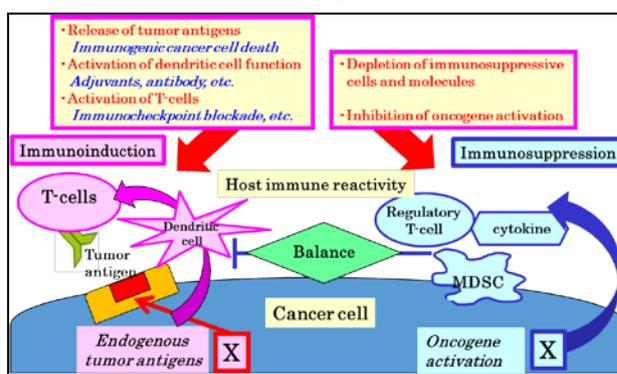
**【Research Methods】**

1. Investigation of the anti-tumor T-cell induction pathway and the development of its enhancing methods: Confirmation of the recognition of endogenous tumor antigens (e.g. mutated peptides) by tumor infiltrating T-cells. Investigation of the differential expression of immune molecules and cells, and their modulating strategies in the T-cell induction pathway.

2. Investigation of the cancer induced immunosuppression pathway and the development of its improving methods: Analyses of immunosuppressive conditions regulated by immune cells, stromal cells, and cancer cell subsets by using system biological and immunological analyses of clinical samples and *in vivo* experiments using various murine models. Development of their modulating strategies.

3. Investigation of enhancement of anti-tumor effects of various cancer therapies by immunomodulation: Evaluation of the identified immunomodulators on the augmentation of

anti-tumor effects of various cancer therapies. Proposal of clinical trials after confirmation of the role of the identified immune-targets by correlation analyses between target expression and various clinicopathological factors.



**Figure, Differential immune status and augmentation of cancer therapy by immunomodulation**

**【Expected Research Achievements and Scientific Significance】**

This study's unique goal is development of personalized cancer therapy by targeting immunopathology of cancer. This study will lead to not only advance of cancer biology but also development of new diagnostic and therapeutic strategies, and will contribute to the society.

**【Publications Relevant to the Project】**

1. Kawakami Y, et al. Roles of signaling pathways in cancer cells and immune cells in generation of immunosuppressive tumor associated microenvironments. in "The Tumor Immuno-environment", Springer Science p307-323, 2013
2. Galon J, Kawakami Y, et al. Towards the introduction of the Immunoscore in the classification of malignant tumors. J Pathol. 232: 199-209, 2014

**【Term of Project】** FY2014-2018

**【Budget Allocation】** 150,100 Thousand Yen

**【Homepage Address and Other Contact Information】**

<http://keiocancer.com/>