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

Biological Sciences (Biological Sciences)

Title of Project： Association of immune responses with racial differences of cancer development

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Research Project Number：17H06162　Researcher Number：10444431
Research Area：　Biological Science, Oncology, Tumor biology
Keyword：　Cancer development, Cancer immunity

【Purpose and Background of the Research】

Genome instability induces high frequencies of mutations in oncogenes and tumor suppressor genes (so-called cancer driver genes), resulting in transformation of cells leading to cancer development. While Asians and Caucasians are similarly exposed to carcinogens such as UV, radiation and carcinogenic chemical substances, the frequency of cancer development depending on driver gene mutations often exhibits racial differences, indicating that host defense mechanism(s) against cancer development play critical roles for the differences.

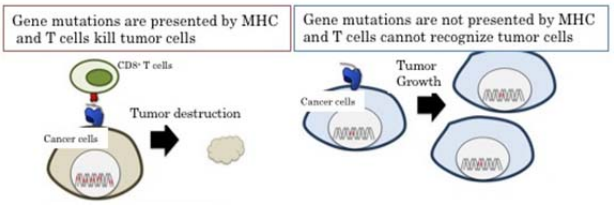
In this study, we focus on the racial differences of HLA allele because our preliminary data reveal that racial differences of cancer development can be attributed to HLA differences. The association between lung cancer development by driver genes and HLA allele is investigated. The differences of HLA allele represent the distinct antigen presentation, resulting in different immune responses against the abnormal gene products. HLA alleles resistant/sensitive to driver gene-induced cancers elicit different immune responses against mutated driver gene products that can induce tumor rejection in humans with resistant HLA allele (immune surveillance), leading to the elucidation of essential anti-tumor immune responses.

【Research Methods】

1) The association between lung cancer development by driver genes such as EGFR and KRAS and HLA allele, is investigated and HLA allele sensitive to the cancer development is elucidated.

2) Based on the data in 1), immune responses against abnormal gene products are predicted for antigen presentation and then confirmed by inducing T cells in humans with/without sensitive HLA allele. The T-cell responses are functionally and phenotypically investigated in depth.

3) Whether the immune responses are faithfully associated with cancer immune surveillance is evaluated with mouse models with HLA allele.



【Expected Research Achievements and Scientific Significance】

Clarifying racial differences of cancer development uncovers people susceptible to develop cancers associated with driver gene mutations, leading to preventive medicine.

The immune responses responsible for cancer immune surveillance are closely associated with anti-tumor immune responses inducing tumor regression, leading to the development of effective cancer immunotherapy.

【Publications Relevant to the Project】

・Saito T, Nishikawa H, et al; Two FOXP3+CD4+ T cell subpopulations distinctly control the prognosis of colorectal cancers. **Nat Med**. 22(6):679-84 2016.

・Maeda Y, Nishikawa H, et al. Detection of self-reactive CD8+ T cells with an anergic phenotype in healthy individuals. **Science**. 346(6216):1536-40 2014.

【Term of Project】 FY2017-2021

【Budget Allocation】 161,700 Thousand Yen

【Homepage Address and Other Contact Information】

https://www.med.nagoya-u.ac.jp/medical_J/laboratory/basic-med/micro-immunology/immunology/
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