【Grant-in-Aid for Scientific Research(S)】
Biological Sciences (Medicine, dentistry, and pharmacy I)

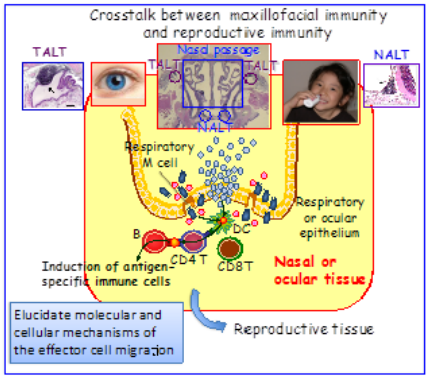
Title of Project：Crosstalk between maxillofacial immunity and reproductive immunity

Hiroshi Kiyono
(The University of Tokyo, Institute of Medical Science, Professor)

Research Area：Medical Science
Keyword：Mucosal immunology

【Purpose and Background of the Research】

It is well known that a mucosal sensitization at one site results in the induction of antigen-specific immune responses at another distant mucosa. While the gut imprinting molecules associated with the migration of antigen-specific immune cells from Peyer's patches to distant intestinal mucosa have been recently identified, the molecular mechanisms how antigen-specific immune cells induced by intranasal or ocular immunization migrate into the distant reproductive mucosa have been still unknown. In this project, our specific aim is to elucidate how antigen-specific effector memory $CD4^+/CD8^+$ T cells and IgA^+ B cells are generated in nasopharinx associated lymphoid tissue (NALT), tear duct associated lymphoid tissue (TALT) and other mucosal immune inductive site forming the facial immune system and how the effector cells are acquiring the ability to migrate into the reproductive tissues by identifying reproductive imprinting molecules. Our goal is thus to establish the immunological foundation for the development of novel mucosal vaccine against sexual transmitted diseases (STDs).



【Research Methods】

We are going to investigate the molecular and cellular mechanisms for the induction of reproductive imprinting molecules for antigen-specific effector memory $CD4^+/CD8^+$ T cells and IgA^+ B cells induced by the immunization with antigens through nasal or ocular mucosa. The specific experiments include 1) analyzing the fate of nasally or ocularly administered antigens by macro-fluorescent imaging system 2) identifying the migration-imprinting molecules expressing on the effector cells 3) identifying the inductive/regulatory factors for the reproductive imprinting molecules expressed on dendritic cells directing the effector cell migration and 4) examining and comparing of NALT or TALT dependent and independent pathways of antigen uptake for the induction of reproductive imprinting molecules.

【Expected Research Achievements and Scientific Significance】

The vaccine against human papilloma virus causing cervical carcinoma has been established; however, the vaccine preventing other STDs caused by HIV, HSV, or Chlamydia has not yet been developed. In this study, we are going to investigate the molecular and cellular mechanisms how intranasal and ocular immunizations induce both humoral and cellular immune responses specific for the viral or bacterial antigens in the distant reproductive mucosa. Especially, elucidation of reproductive imprinting molecules will lead to the basic foundation for the development of STD vaccine. Our project will thus contribute scientifically for our understanding of the reproductive imprinting system, which leads to the development of effective vaccine against STDs for the improvement of public health.

【Publications Relevant to the Project】

Fukuyama S, *et al.* Initiation of NALT organogenesis is independent of the IL-7R, LTβR, and NIK signaling pathways but requires the Id2 gene and $CD3^-CD4^+CD45^+$ cells. Immunity. 17:31-40. 2002

Nagatake T, *et al.* Id2-, RORγt-, and LTβR-independent initiation of lymphoid organogenesis in ocular immunity. J Exp Med.206:2351-64. 2009.

【Term of Project】 FY2011-2015
【Budget Allocation】 165,200 Thousands Yen
【Homepage Address and Other Contact Information】
www.ims.u-tokyo.ac.jp/EnMen/index_j.html