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Therapeutic vaccines using immune regulatory functions of invariant natural killer T (iNKT) cells

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Invariant natural killer T (iNKT) cells having The invariant T cell antigen receptor (TCR) α chain are a unique population to regulate the immune response between the innate and acquired immunity. iNKT cells interact with glycolipids presented via CD1d molecule on antigen-presenting cells (APCs), resulting in the activation of killing activity and the production of a variety of cytokines. KRN7000, alpha-galacosyl ceramide (α -GalCer), among glycolipids functions as the powerful ligand for not only rodent but also primate iNKT cells. As iNKT cells potentially have two bi-directional functions, one is immune activation and the other is immune suppression, it was expected that KRN7000 would be utilized as an adjuvant for various vaccines of cancer, infectious and immune diseases. However, the pharmaceutical development of KRN7000 is not successful because of the bi-directional functions of iNKT cells. In our recent studies, two functions of immune activation and suppression are dissected by the in vivo delivery system of KRN7000. Dendritic cells (DCs), the professional APCs, could be used as delivery cells of KRN7000 for immune activation. Systemic administration of KRN7000-pulsed DCs preferentially enhanced protective immunity against tumors and infection by microbes. In contrast, liposomal formulation of KRN7000 could be delivered to the marginal zone B220-positive cells in a spleen, induce regulatory T cells (Treg) and diminish immune responses in model animals of autoimmunity, allergic diseases and graft versus host diseases (GvHD).

Biography

Yasuyuki Ishii has completed Ph.D. in Tokyo Institute of Technology and postdoctoral and worked in the pharmaceutical research division of KIRIN brewery for 12 years. During the term, he has studies as research scientist in La Jolla Institute for Allergy and Immunology for about three years. After leaving the company, he joined as the principal investigator to the National institute of Advanced Industrial Science and Technology (AIST). He is now the team leader of laboratory of vaccine design in the National institute, RIKEN Research center for Allergy and immunology (RCAI).