# Basic study for determine the structure and function of CD26 for development of molecular target therapy for autoimmune disorders and immune deficiency syndrome

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**【Outline of survey】**

CD26 is a T cell costimulatory molecule with DPPIV enzyme activity in its extracellular region. In a recent study we showed that caveolin-1 is a binding protein of CD26 and CD26-caveolin-1 interaction plays a role in the up-regulation of CD86 on TT-loaded monocytes. In our proposal study, we plan to further determime the structure and function of CD26 in T cell function and activation and to establish molecular target therapy for autoimmune disorders and immune deficiency syndrome. Following are our aims:

1. To determine the molecular basis of CD86 up-regulation on monocytes by soluble CD26 and determine the active domain of CD26.
2. To identify the costimulatory ligand for CD26 and determine the precise CD26 mediated signaling and function.
3. To define the clinical relevances of CD26 and its related molecules and develop the clinical utilization of CD26 and its concept for the therapy of immune mediated disorders.

**【Expected results】**

Patients with autoimmune diseases such Grave ' s disease and rheumatoid arthritis have increased level of CD26+ T cells in their inflamed tissues such as thyroid and synovial membrane and fluids. In addition, enhancement of CD26 expression in these autoimmune diseases may correlate with disease severity. Moreover, we have shown that T cells migrating through endothelial cell monolayers in vitro express high levels of CD26, while the fact that chemokines play a key role in T cell migration supports the notion that CD26/DPPIV may interact with these biological factors. These findings imply that CD26+ T cells play a role in the inflammation process and subsequent tissue damage in autoimmune diseases. Our results may thus provide a new approach to the treatment of autoimmune diseases or other immune-mediated disorders by directly interfering with activated T cell and APC interaction. Moreover, targeting the interaction of the pocket structure of CD26 and the scaffolding domain of caveolin-1 may lead to novel therapeutic approaches utilizing agonists or antagonists regulating antigen-specific immune response in not only immune-mediated disorders, but also cancer immunotherapy and viral vaccination as strategies to enhance immune response.

**【References by the principal researcher】**

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【Homepage address】 none