CD137-CD137L interactions regulate B-cell autoimmunity during alloimmune responses

Jong Soo Lee, Kyung Sun Park, Jong-ha Park, Hyunchul Chung
Department of Internal Medicine-Nephrology, Ulsan University Hospital, Korea, Republic of

**Objectives:** CD137L/CD137 costimulatory pathway seems to participate in immune regulation. In this study we address the immune regulatory role of CD137L signaling on alloimmune challenge.

**Methods:** We used mice bone marrow transplantation model. Transfer of H2-Ab^{bmi2} splenocyte to CD57BL/6 mice breaks B-cell autoimmunity which results in chronic graft-versus-host disease (GVHD) with a SLE-like phenotype.

**Results:** In this chronic GVHD model, CD137^{−/−} recipients were shown to be severely impaired in autoantibody production but instead had an acute type of GVHD, indicating that Th1 responses were activated in CD137^{+/+} mice. Analysis of CD137^{−/−} spleens demonstrated that there was an increase in IL-12-producing CD8α^{+} DCs, which was caused by the absence of CD137L signaling in pre-DCs. Accordingly, IFN-γ-producing donor Th1 cells were preferentially differentiated in CD137^{−/−} spleens, providing an explanation for why chronic GVHD was converted toward acute GVHD in CD137^{−/−} recipients. Interestingly, differentiation of follicular helper T cells was severely impaired in CD137^{−/−} spleens and so was that of germinal center B cells and plasma cells.

**Conclusions:** Taken together, our results suggest that CD137-CD137L interactions regulate many aspects of immune cell differentiation during alloimmune responses.