

## 동종피부이식모델에서 interleukin-6를 표적으로 하는 minicircle DNA투여가 미치는 영향

가톨릭대학교 서울성모병원 장기이식연구소<sup>1</sup>, 신장내과<sup>2</sup>, 면역질환융합사업단

도경찬<sup>1</sup>, 임선우<sup>1</sup>, 김룡<sup>1</sup>, 김건<sup>1</sup>, 박상국<sup>1</sup>, 정병하<sup>2</sup>, 양철우<sup>2</sup>

### Effect of Blocking with Minicircle DNA of Interleukin-6 on Skin Allograft Rejection

Kyoung Chan Doh<sup>1</sup>, Sun Woo Lim<sup>1</sup>, Jin Long<sup>1</sup>, Jin Jian<sup>1</sup>  
Shang Guo Piao<sup>1</sup>, Byung Ha Chung<sup>2</sup>, Chul Woo Yang<sup>2</sup>

Transplant Research Center<sup>1</sup>, Division of Nephrology Department of Internal Medicine<sup>2</sup>, CRCiD  
Seoul St. Mary's Hospital, The Catholic University of Korea

**본문:** Blocking of proinflammatory cytokine, interleukin-6 (IL-6) is effective in decreasing resistance to allogenic tolerance. In this study, we investigated whether anti-IL-6 receptor producing nonviral minicircle (MC)-DNA, is competent to inhibit alloresponse-induced IL-6 in highly immunogenic murine skin allograft model. We designed MC-DNA producing IL-6R antibody and verified in vitro system. One day before skin allograft modeling, systemic MC-DNA exposed via hydrodynamic delivery of MC-DNA in vivo (50 ug of DNA, tail vein, single injection). Using GFP tagging MC-DNA, we confirmed its organ distribution. At day 5, we measured the amount of IL-6 and IL-6R antibody in serum. As functional examinations, we evaluated survival rate, morphological changes of graft, immune cell infiltration, and population of T helper 17 cells (Th17, FACS marker: CD4+/RoR $\gamma$ t) and regulatory T cells (Treg, FACS marker: CD4+ Foxp3+). We compared its alloimmunity and graft survival efficiency with the cyclosporine A (CsA)-treated group (50 mg/kg, daily administration via oral gavage). Hydrodynamic delivery of MC-DNA was mainly localized in hepatocytes. Serum IL-6 and IL-6R antibody detected in anti-IL-6R MC-DNA treated mice. At day 8.5, untreated mice completely rejected the graft confirming by daily observation of loss of skin graft and erosion. However, mice received either anti-IL-6R MC-DNA or CsA presented prolonged acceptance of graft until day 15 or 15.6, respectively. Results from morphological changes and immune cell infiltration in the graft were also consistent with survival rate. FACS results showed that anti-IL-6R MC-DNA treatment markedly suppressed Th17 population compared with the untreated mice. However, there was no effect on Treg population. On the other hand, administration of CsA showed the increased Th17 and decreased Treg population compared with untreated group. We found that single injection of nonviral minicircle DNA targeting IL-6R is effective in both acute allograft acceptance and allogenic tolerance. This suggests that simple and effective gene therapy method using antibody producing minicircle DNA may represent a powerful tool for the transplantation.

**Key Words:** 동종피부이식, 인터루킨-6, 면역조절세포

Skin allograft, Interleukin-6, T helper cell, Regulatory T cell