

배아 줄기세포와 중간엽 줄기세포의 동종면역반응에 대한 억제 효과

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Immunosuppressive Effects of Embryonic Stem Cells and Mesenchymal Stem Cells on Alloimmune Response

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Purpose : Recently, both embryonic stem cells and adult stem cells are known to have immunosuppressive effects. To test their applicability for tolerance induction, we tried to elucidate the immunosuppressive effects of both embryonic stem cells (ESC) and mesenchymal stem cells (MSC) on alloimmune response.

Methods : We used a murine ESC line originated from C57BL/6 mice, and isolated murine MSCs by a differential culture method from Balb/C mice. Suppressive effects of stem cells were investigated by adding ESCs or MSCs to allogeneic mixed lymphocyte cultures for 72 hours. The degree of proliferation was measured by using thymidine uptake, and interferon-gamma (IFN- γ) production was measured by ELISA. IDO (indoleamine 2, 3-dioxygenase) activity of stem cells was evaluated by measuring tryptophan and kynurenine in co-culture. To investigate in vivo immunosuppressive effects of stem cells, either ESCs or MSCs were adoptively transferred, one week before allogeneic skin transplantation.

Results : The ESCs expressed alkaline phosphatase, SSEA-1, and Oct-4, murine ESC markers on immunocytochemistry. The MSCs expressed CD106, Sca-1, and CD44, but not CD34 on flow cytometry. We could induce osteogenesis and lipogenesis from these cells under differentiation media. Proliferation and IFN- γ secretion was minimal in mixed culture of responders and stem cells, indicating that immunogenicity of stem cells was very low. Both ESCs and MSCs suppressed proliferation effectively in MLR. Interestingly, their suppressive effects were strain-independent. There was no change in IDO levels by stem cells. They also suppressed IFN- γ secretion from allogeneic lymphocytes. However, they failed to prolong skin graft survival significantly, not only across major mismatch barriers, but also a minor mismatch barrier (male to female). Combination therapy of ESCs and anti-CD40L also failed to induce DBA/2 skin graft tolerance in C57BL/6 mice.

Conclusion : Either ESCs or MSCs can not suppress allograft rejection in stringent murine skin transplantation models, although both stem cells can suppress in vitro alloimmune response. However, It is still possible to use stem cells in combination with other immune modulating agents to suppress graft rejection.