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Mismatched mesenchymal stem cells as an initial trigger of ocular chronic graft-versus-host disease following allogeneic bone marrow transplantation

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Abstract

Chronic graft-versus-host disease (cGVHD) is a complication after minor antigen mismatched bone marrow transplantation (BMT) characterized by an autoimmune-type reaction in ocular surface immunity. Although mismatched mesenchymal stem cells (MSCs) play some role in immunomodulation, the precise source and roles of MSCs in the pathogenesis of cGVHD are still unknown. Here we show using a minor antigen mismatched cGVHD model that transplantation of mismatched, but not syngeneic MSCs triggered the onset of cGVHD, which was associated with tissue fibrosis, increased IL-6 secretion, decreased Foxp3+ regulatory T cells and increased Th17cells in the peripheral blood. Mismatched MSCs alone were sufficient to induce cGVHD, while removal of donor MSCs rescued mice from cGVHD. T cell deficient RAG2 knockout recipient mice did not suffer cGVHD, indicating that host T cells were involved. These results were supported by clinical data where the number of residual host T cells was significantly higher in cGVHD patients compared to non-cGVHD patients. In addition, fibroblasts expressing both HLA-DR and co-stimulatory molecules were observed in human cGVHD lacrimal gland and conjunctival mucosal membrane by attaching with activated T cells. Our results suggest that mismatched MSCs induce immune responses in residual host T cells, leading to cGVHD related inflammation and dry eye.

Biography

Yoko Ogawa has completed her Ph.D at the age of 35 years from Keio University and postdoctoral studies from Keio University School of Medicine. She is the director of Dry Eye Outpatient Clinic, and the Project Associate Professor of Department of Ophthalmology, Keio University. She has published more than 50 papers in reputed journals and serving as a Medical Advisory Board of Tear Film & Ocular Surface Society.