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研究課題名	The study of immunological activation mechanism of umbilical cord-derived mesenchymal stromal cells
研究代表者	Haiping He（The Affiliated Hospital of Kunming University of Science and Technology・Associate professor）
研究組織 受入教員 研究分担者	 Tokiko Nagamura-Inou （IMSUT・Associate professor） Kazuaki Yokoyama （IMSUT・Assistant professor）

研究報告書

Background: Mesenchymal stromal cells (MSCs) are known to have immunosuppressive ability and have been used in clinical treatment of acute graft-versus-host disease (GVHD), which often appears as a severe complication of the hematopoietic stem cells transplantation (HSCT). However, MSCs are activated to suppress the immune system only after encountering an inflammatory stimulation. Thus, it will be ideal if MSCs are primed to be activated and ready to suppress the immune reaction before being administered. Triptolide (TPL) is a diterpene triepoxide purified from a Chinese herb, Tripterygium wilfordii Hook.f. (TWHF) and has been shown to possess anti-inflammatory and immunosuppressive properties in vitro. In this study, we aimed to use TPL to prime umbilical cord-derived MSCs (TPL-primed UC-MSCs) to enter a stronger immunosuppressive status.

Method: UC-MSCs were primed for 24 hours, TPL was washed out thoroughly, and the TPL-primed UC-MSCs were resuspended in fresh medium. To mimic the GVHD treated with UC-MSCs in vitro, we preformed mixed lymphocyte reaction (MLR) consisted of mononuclear cells (MNCs) stained with CFSE and irradiated allogenic dendritic cell lines with TPL-primed UC-MSCs.

Results: Proliferation of UC-MSCs was inhibited by TPL. However, a very low dose of TPL at 0.01 μM was tolerable and could be used for the purpose of this study. The expression pattern of the TPL-primed UC-MSCs surface markers was identical to that of non-primed UC-MSCs. TPL-primed UC-MSCs exhibited stronger anti-proliferative effect for activated CD4+ and CD8+ T cells in the allogeneic MLR assay than the non-primed UC-MSCs. TPL-primed UC-MSCs promoted the expression of IDO-1 in the presence of IFN-γ, but TPL alone was not sufficient. Furthermore, TPL-primed UC-MSCs showed increased expression of PD-L1. Conclusively, up-regulation of IDO-1 in the presence of IFN-γ and induction of PD-L1 enhances the immunosuppressive potency of TPL-primed UC-MSCs on the proliferation of activated T cells. Thus, TPL-primed MSCs may provide a novel immunosuppressive cell therapy.