Immunomodulatory Properties of Urine-Derived Stem Cells

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Introduction and Objectives: Human mesenchymal stem cells (MSC) play an important role in induction of peripheral tolerance, inhibition of proinflammatory immune responses, and decreased immune reactions. We recently showed that a subpopulation of human urine-derived cells (USC) have stem cell characteristics with self-renewal and multipotent capacity. The aim of this study was to investigate whether USCs can impart profound immunomodulatory effects.

Methods: USC were obtained from six urine samples of three healthy individuals. Cultured USCs at p4 (1x10⁴ cells/well) were treated with 5 µg/ml mitomycin C to reduce proliferation. Bone marrow MSC (BMSC) were treated with the same way as control. To observe immunomodulatory effect of USCs, allogeneic peripheral blood mononuclear cells (PBMNC, 1x10⁵ cells/well, from two healthy donors) were added into USC and BMSC on each well and continued cultured, respectively. Cells morphology was observed every 3 days during the incubation period with a inverted microscope until the BrdU label solution was added into each well at the 5th day. BrdU colorimetric ELISA was performed at the 6th day. After mixing culture with the mononuclear cells, the reaction product was quantified by the absorbance at the respective wavelength using a scanning multiwall spectrophotometer. In addition, USC and BMSC were collected to detect the co-stimulatory molecular CD80 and CD86 expression with flow cytometry.

Results: Peripheral blood mononuclear cells proliferated when mixed with other cells due to immune response. PBMNC concentrations in USC wells were much lower than in MSC culture wells. BrdU colorimetric ELISA showed less BrdU labeled in the USC PBMNC mixed culture wells compared to BMSC culture wells. Flow cytometry showed that 3.35% of BMSCs were positive for CD80 compared to 1.05% of USCs; 1.30% of BMSC were positive for CD86 versus 0.55% of USC. Concentrations of the immunoregulatory cytokines interleukin (IL)-6 and IL-8 were elevated after stimulation by PBMNC in USC supernatant compared to the BMSC supernatant.

Conclusions: USC possess immunomodulatory properties to inhibit proliferation of allogeneic lymphocytes. IL-6 and IL-8 might be the main immunomodulatory cytokines in this response, which is of potential use in preventing and treating tissue or organ transplantation rejection or other immune system disorder diseases.