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Evaluation of an appropriate therapeutic strategy with mesenchymal stromal cells in a pre-clinical mouse model of autoimmune disease

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In vitro, the effect of mesenchymal stromal cell (MSC) on immune suppression has been well studied. However, *in vivo*, questions regarding MSC optimal therapeutic strategy, homing, survival, and timing for immune suppression are still elusive. To address these questions for systemic lupus erythematosus (SLE), autoimmune lymphoproliferative syndrome (ALPS) and Sjogren's syndrome, a MLR/MpJ-Fas^{lpr}/J (Fas^{lpr}) mice model was employed. Multipotency of bone marrow derived MSC (BM-MSC) was determined by phenotypic analysis and multipotential differentiation assay. Four- to six-month-old Fas^{lpr} mice showed onset of autoimmune disease with lymphoproliferation. Optimal infusion dose was determined by serial dilution. Homing and survival of MSC were monitored by fluorescent microscopy. Infusion frequency was deduced from immunomodulatory kinetics study. BM-MSC with passage number less than 10 could properly maintain multi-lineage differentiation capacity and stem cell phenotypes. Eight rounds administration of 10×10^6 cells/kg BM-MSC improved mouse survival from 62.5% to 92.9% and reversed lymphoproliferation to normal levels at day-21 post-transplantation (PT) (p=0.189). BM-MSC mainly and eventually homed to immune organs at four months PT. Immunomodulatory kinetics showed that the optimal infusion frequency was deduced as 21 days. In conclusion, an appropriate therapeutic strategy in a pre-clinical autoimmune disease mouse model was established with a defined MSC source as well as optimal infusion dose, frequency, and administration number. It will help to standardize cell preparation, characterization and administration protocol, and minimize the outcome discrepancies between different centers worldwide.

Biography

Xiubo Fan has completed her PhD from Dalian University of Technology in 2008 and worked as Research Scientist in Singapore General Hospital, Singapore since then. She has published 14 papers in international peer reviewed journals and has been serving as an Editorial Board Member of *Autoimmune Diseases and Therapeutic Approaches.*

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