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Enhanced survival of mice infused with bone marrow-derived as compared with adipose-derived mesenchymal stem cells

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Abstract

© 2015 John Wiley & Sons, Ltd. Aim: Less invasive therapies using mesenchymal stem cells (MSC) are being developed to treat patients with severe liver cirrhosis. MSC constitute a promising cell source for regenerative therapy and are frequently isolated from bone marrow (BMSC) or adipose tissue (ASC). Therefore, this study assessed the characteristics of these two cell types and their safety for cell infusion. Methods: In vitro, exhaustive genetic analysis was performed using human (h)BMSC and hASC. Subsequently, the expression of mRNA and protein was evaluated. In vivo, mouse (m)BMSC or mASC was infused into serial mice via the peripheral vein, and 24-h survival rate, prothrombin time and cause of death were analyzed. Results: On polymerase chain reaction, western blotting, enzyme-linked immunoassay and fluorescence-activated cell sorting, tissue factor was found to be expressed at higher levels in hASC than in hBMSC. Prothrombin time in mice infused with mASC (>120s) was markedly longer than that of untreated mice (6.5±1.7s) and that of mice infused with BMSC (6.7±0.8s) ($P<0.001$), indicating that pro-coagulation activity was potently enhanced after ASC infusion. The 24-h survival rates in the mASC- and mBMSC-infused groups were 46.4% (13/28) and 95.5% (21/22), respectively; in the former, the rate decreased with increasing number of infused mASC. This cell number-dependent effect was not observed with mBMSC. A histopathological analysis of mice that died immediately following mASC infusion revealed multiple thrombi in the blood vessels of the lungs. Conclusion: These results indicate that BMSC are a superior and safer cell source for regenerative therapy.

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Keywords

Matrix metalloproteinase, Mesenchymal stem cell, Pro-coagulation, Tissue factor