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Generation of induced secretome from adipose-derived stem cells specialized for disease-specific treatment: an experimental mouse model

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Introduction: Recently, the exclusive use of mesenchymal stem cell (MSC)-secreted molecules, named as the secretome, rather than cells has been evaluated for overcoming the limitations of cell-based therapy while maintaining its advantages. The goal of this study was to improve cell-free therapy by adding disease-specificity through stimulation of MSCs using disease-causing materials.

Methods : We collected the secretory materials (named as inducers) released from AML12 hepatocytes that had been pretreated with thioacetamide (TAA) and generated the TAA-induced secretome (TAA-isecretome) after stimulating adipose-derived stem cells (ASCs) with the inducers. The TAA-isecretome was intravenously administered to mice with TAA-induced hepatic failure and those with partial hepatectomy.

Results : TAA-isecretome infusion showed higher therapeutic potential in terms of (a) restoring disorganized hepatic tissue to normal tissue, (b) inhibiting proinflammatory cytokines (interleukin-6 and tumor necrosis factor- α), and (c) reducing abnormally elevated liver enzymes (aspartate aminotransferase and alanine aminotransferase) compared to the naïve secretome infusion in mice with TAA-induced hepatic failure. However, the TAA-isecretome showed inferior therapeutic potential for restoring hepatic function in partially hepatectomized mice.

Conclusions : Our results suggest that appropriate stimulation of MSCs with disease-causing agents leads to the production of a secretome specialized for treating a specific disease. Additionally, isecretome therapy is expected to open a new way of developing various specific therapeutics based on the high plasticity and responsiveness of MSCs.

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