The Therapeutic potential of Human Umbilical Mesenchymal Stem Cells from Whartons Jelly in the Treatment of Rat Liver Fibrosis

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摘要

Abstract

We investigated the effect of human umbilical mesenchymal stem cells (HUMSCs) from Wharton's jelly on carbon tetrachloride (CCl4)-induced liver fibrosis in rats. Rats were treated with CCl4 for 4 weeks, and this was followed by a direct injection of HUMSCs into their livers. After 4 more weeks of CCl4 treatment (8 weeks in all), rats with HUMSC transplants [CCl4 (8W)+HUMSC liver] exhibited a significant reduction in liver fibrosis, as evidenced by Sirius red staining and a collagen content assay, in comparison with rats treated with CCl4 for 8 weeks without HUMSC transplants [CCl4 (8W)]. Moreover, rats in the CCl4 (8W)+HUMSC (liver) group had significantly lower levels of serum glutamic oxaloacetic transaminase, glutamic pyruvate transaminase, alpha-smooth muscle actin, and transforming growth factor-beta1 in the liver, whereas the expression of hepatic mesenchymal epithelial transition factor-phosphorylated type (Met-P) and hepatocyte growth factor was up-regulated, in comparison with the CCl4 (8W) group. Notably, engrafted HUMSCs scattered mostly in the hepatic connective tissue but did not differentiate into hepatocytes expressing human albumin or alpha-fetoprotein. Instead, these engrafted, undifferentiated HUMSCs secreted a variety of bioactive cytokines that may restore liver function and promote regeneration. Human cytokine assay revealed that the amounts of human cutaneous T cell-attracting chemokine, leukemia inhibitory factor, and prolactin were substantially greater in the livers of the CCl4 (8W)+HUMSC (liver) group, with considerably reduced hepatic inflammation manifested by a micro positron emission tomography scan. Our findings suggest that xenogeneic transplantation of HUMSCs is a novel approach for treating liver fibrosis and may be a promising therapeutic

intervention in the future.