

# Treating congenital megacolon by transplanting GDNF and GFR $\alpha$ -1 double genetically modified rat bone marrow mesenchymal stem cells

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**ABSTRACT.** We studied the survival and gene expression of glial cell line-derived neurotrophic factor (GDNF) and GDNF receptor  $\alpha$ -1 (GFR $\alpha$ -1) double-genetically modified rat bone marrow mesenchymal stem cells (BMSCs) transplanted into the intestinal walls of the rat models with congenital megacolon and determine the feasibility of treatment by transplantation of double-genetically modified rat BMSCs. The rat colorectal intestinal wall nerve plexus was treated with the cationic surface active agent benzalkonium chloride to establish an experimental megacolon model. The rat target genes GDNF and GFR $\alpha$ -1 were extracted and ligated into pEGFP-N1. Eukaryotic fluorescent expression vectors carrying the GDNF and GFR $\alpha$ -1 genes were transfected into BMSCs by *in vitro* culture. We treated congenital megacolon by transplanting double-genetically modified rat bone marrow mesenchymal stem cells. The pEGFP-EGFP-GDNF-GFR $\alpha$ -1 double-gene co-expressing the eukaryotic expression plasmid vector was successfully established. Protein gene protein 9.5 and vasoactive intestinal peptide-positive ganglion cells showed no positive expression

in the phosphate-buffered saline transplantation group based on an immunofluorescence test at 1, 2, and 4 weeks after transplantation of BMSCs. Additionally, compared with the phosphate-buffered saline transplantation group, the expression of rearranged during transfection, GDNF, and GFR $\alpha$ -1 mRNA in the stem cell transplantation group increased gradually. The double-genetically modified BMSCs colonized and survived in the intestinal wall of the experimental megacolon rat model and expressed related genes, partially recovering the colonic neuromuscular regulatory functions and thus providing an experimental basis for treating congenital megacolon by cellular transplantation.

**Key words:** Bone marrow mesenchymal stem cells; Transplantation; Congenital megacolon; Glial cell-derived neurotrophic factor