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Overexpression of the growth arrest-specific homeobox gene *Gax* inhibits proliferation, migration, cell cycle progression, and apoptosis in serum-induced vascular smooth muscle cells

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ABSTRACT. The *Gax* gene has been implicated in a variety of cell-developmental and biological processes, and aberrant *Gax* expression is linked to many diseases. In this study, to provide important insights for *Gax*-based gene therapy in vein graft restenosis and its anti-restenotic mechanism, we used rabbit vascular smooth muscle cells (VSMCs) to investigate the effects of *Gax* overexpression on proliferation, migration, cell cycle, and apoptosis in a serum-stimulated culture. Rabbit VSMC lines that stably overexpressed *Gax* were established by transfection with recombinant adenoviral vector Ad5-Gax. The effect of Gax overexpression on *in vitro* serum-induced VSMCs proliferation, migration, cell cycle, and apoptosis was assessed by MTT, wound healing, and flow cytometry assays, respectively. To investigate the effect of Gax overexpression on PCNA and MMP-2 in serum-induced VSMCs, immunocytochemistry, RT-PCR, and gelatin zymography

were performed. The results clearly showed that Gax overexpression decreases PCNA expression in serum-induced VSMCs. Gax overexpression also significantly inhibited cell proliferation by blocking entry into the S-phase of the cell cycle, promoted cell apoptosis, and reduced cell migration activity by downregulating MMP-2 release and activity. These findings indicate that Gax would be an optimal target gene for gene therapy to treat vein graft restenosis.

Key words: Apoptosis; Cell cycle; Gax; Migration; VSMCs; Proliferation

