Regulation of the collagen phenotype expression of gamma-irradiated vascular smooth muscle cells by heparan mimetics (RGTA).

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Abstract

Restenosis is characterized by vascular smooth muscle cell (VSMC) proliferation and accumulation of collagen III in a hypertrophic and disorganized extracellular matrix. Restenosis is prevented by antimitotic agents or irradiation but no significant progress has been made to control collagen expression deregulation. Previously, we have shown that a new family of biopolymers named RGTA (heparan mimetics elaborated by grafting on dextran of carboxylate, sulfate, and benzylamide units) stimulate in vivo tissue repair and reduce fibrosis in various models. Using VSMC in vitro (pig aortic VSMC irradiated with a 60Co source and labeled with [3H]Proline), we now show that gamma-irradiation reduced cell survival by 50% and collagen synthesis 6-fold with a major increase in the ratio of collagen III to collagen I biosynthesis taken as a fibrotic index. RGTA added to the cells enhanced their survival up to 80% and reduced collagen III/I ratio back to values found in normal vascular tissues. These results suggest that RGTA combined with gamma-radiation could be an efficient strategy against restenosis.