Biochemical Interactions of siRNA-Based Gene Silencing To Augment Elastogenesis in Abdominal Aortic Aneurysms

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Abdominal aortic aneurysms (AAAs) are expansions of the aorta characterized by enzymatic breakdown of wall elastic fiber structures, causing weakening & fatal rupture. Current management involves periodic image-based growth monitoring with no established drug-based therapies. Reversing disease pathophysiology is difficult as cells are unable to regenerate new elastic fibers. siRNA interferes with gene expression by degrading mRNA after transcription and can be used to stimulate elastic matrix assembly and inhibit proteolytic enzymes (MMPs). The objective was to determine if gene silencing of EGFR is essential in aneurysmal smooth muscle cells to stimulate regeneration of elastic matrix and inhibit proteolytic enzymes. It was hypothesized that siRNA sequences that inhibit the EGFR gene, can therapeutically reverse elastic matrix aberrations associated with AAAs to regenerate & restore healthy elastic matrix to slow or reverse AAA growth. siRNA effects on MMP expression levels & elastic fiber assembly were studied in In vitro cultures of aortic smooth muscle cells (EaRASMC) from simulated rat models. Four strengths of siRNA were analyzed to identify an optimal concentration that is most effective in inhibiting the EGFR gene. Relative gene expression of EGFR and secondary elastogenesis genes were determined with polymerase chain reaction. This resulted in improved elastic matrix regeneration through decreases in proteolytic enzyme activity & increases in elastic matrix production and shows the implementation of siRNA-based gene silencing to augment elastogenesis can be used as a treatment alternative for AAAs. The study provides an effective, non-invasive, cost-efficient reparative solution that can both slow, and reverse elastic matrix aberrations.

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