ABSTRACT

Title: Targeting Fibronectin in Organ Fibrosis: Development of Antisense-Based Therapeutic Strategies

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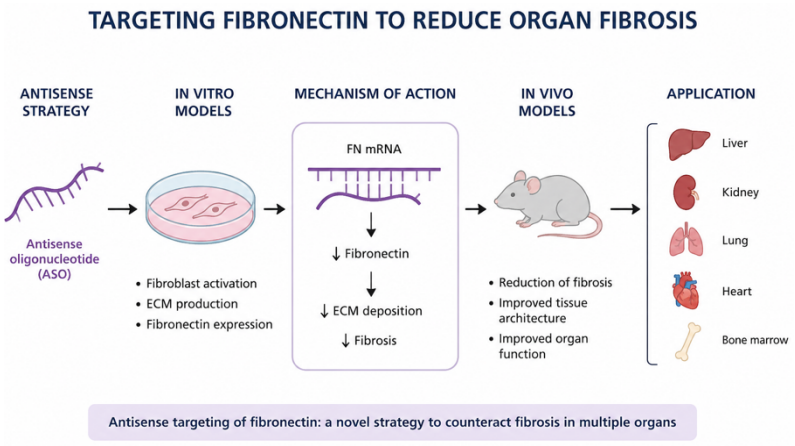
Research Theme/Topic: Tissue Regeneration and Translational Medicine

Main Abstract:

Fibrosis is a common pathological process underlying the progression of numerous chronic diseases affecting organs such as the liver, kidney, lung, heart, and bone marrow. It is characterized by excessive deposition of extracellular matrix (ECM) components, leading to tissue remodeling, loss of organ function, and ultimately organ failure. Despite significant advances in the understanding of fibrotic diseases, effective anti-fibrotic therapies remain limited. Fibronectin is a key ECM glycoprotein involved in matrix assembly, regulation of growth factor signaling, fibroblast activation, myofibroblast differentiation, and tissue remodeling. Dysregulated fibronectin expression and fibril formation are common features of several fibrotic disorders and contribute to the establishment and progression of the fibrotic microenvironment. Therefore, targeting fibronectin represents a promising therapeutic strategy to limit pathological ECM accumulation and restore tissue homeostasis. The aim of this project is to evaluate antisense oligonucleotide (ASO)-based approaches directed against fibronectin in both cellular and animal models of fibrosis. *In vitro* studies will investigate the effects of fibronectin silencing on fibroblast activation, extracellular matrix production, and pro-fibrotic signaling pathways. Efective ASO candidates will subsequently be tested in experimental animal models of organ fibrosis to assess their ability to reduce fibrotic tissue remodeling, improve tissue architecture, and restore organ function. The project combines molecular, cellular, and *in vivo* approaches to elucidate the role of fibronectin in fibrogenesis and to establish innovative RNA-based therapeutic strategies for the treatment of fibrotic diseases. Successful completion of this translational study may provide the basis for the development of novel anti-fibrotic interventions applicable across multiple organ systems.



Techniques: Cell cultures, primary cell isolation, antisense oligonucleotide delivery, gene silencing, qPCR, Western blot, ELISA, immunofluorescence, immunohistochemistry, flow cytometry, cell sorting, extracellular matrix analysis, confocal microscopy, animal models of fibrosis, RNA sequencing, histological and morphometric analyses, bioinformatic and statistical analyses.