Fibrosis

Fibrosis is the formation of excess fibrous connective tissue in an organ or tissue in a reparative or reactive process.

This can be a reactive, benign, or pathological state. In response to injury, this is called scarring, and if fibrosis arises from a single cell line, this is called a fibroma. Physiologically, fibrosis acts to deposit connective tissue, which can obliterate the architecture and function of the underlying organ or tissue. Fibrosis can be used to describe the pathological state of excess deposition of fibrous tissue, as well as the process of connective tissue deposition in healing.

Myofibroblasts represent the principal cellular mediators of fibrosis, due to their extracellular matrix producing activity, and originate from different types of precursor cells, such as mesenchymal cells, epithelial cells, and fibroblasts. Profibrotic activation of myofibroblasts can be triggered by a variety of mechanisms, including the transforming growth factor-β signaling pathway, which is a major factor driving fibrosis. Interestingly, preclinical and clinical studies showed that fibrotic degeneration can stop and even reverse by using specific antifibrotic treatments. Increasing scientific evidence is being accumulated about the role of sirtuins in modulating the molecular pathways responsible for the onset and development of fibrotic diseases. Sirtuins are NAD+ -dependent protein deacetylases that play a crucial role in several molecular pathways within the cells, many of which at the crossroad between health and disease [1)].

Prolactinomas are the most common functioning pituitary neuroendocrine tumors. While dopamine agonists are a primary method of therapeutic treatment, the rate of resistance to these drugs continues to increase each year. During previous long-term clinical investigations, Hu et al., found that partial resistant prolactinomas exhibited significantly more fibrosis than did sensitive adenomas, suggesting a role of fibrosis in their drug resistance. Furthermore, resistant adenomas with extensive fibrosis mainly express type I and type III collagens. Since TGF-β1 is the key factor in the initiation and development of tissue fibrosis, including in the pituitary, in this study, they aimed to determine whether TGF-β1 mediated fibrosis in prolactinomas and whether fibrosis was related to prolactinoma drug resistance. Using immunochemistry and western blotting, they found that the TGF-β1/Smad3 signaling pathway-related proteins were elevated in resistant prolactinoma specimens with high degrees of fibrosis compared to levels in sensitive samples, suggesting that this pathway may play a role in prolactinoma fibrosis. In vitro, TGF-β1 stimulation promoted collagen expression in normal HS27 fibroblasts. Furthermore, the sensitivity of rat prolactinoma MMQ cells to bromocriptine decreased when they were co-cultured with HS27 cells treated with TGF-β1. The TGF-β1/Smad3 signaling-specific inhibitor SB431542 counteracted these effects, indicating that TGF-β1/Smad3-mediated fibrosis was involved in the drug-resistant mechanisms of prolactinomas. These results indicate that SB431542 may serve as a promising novel treatment for preventing fibrosis and further improving the drug resistance of prolactinomas [2)].

Cochlear Fibrosis

Cochlear Fibrosis.

Epidural fibrosis

see Epidural fibrosis.

1)
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2)
Hu B, Mao Z, Jiang X, He D, Wang Z, Wang X, Zhu Y, Wang H. Role of TGF-β1/Smad3-mediated fibrosis in drug resistance mechanism of prolactinoma. Brain Res. 2018 Jul 26. pii: S0006-8993(18)30408-6. doi: 10.1016/j.brainres.2018.07.024. [Epub ahead of print] PubMed PMID: 30055965.