Role of Wnt Signaling in Tissue Fibrosis, Lessons from Skeletal Muscle and Kidney

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Abstract

Several studies have provided clear evidence of the importance of Wnt signaling in the function of several tissues. Wnt signaling has been related to several cellular processes including pre-natal development, cell division, regeneration and stem cell generation. By contrast, deregulation of this pathway has been associated with several diseases such as cancer, Alzheimer's disease, diabetes and, in recent years, fibrotic diseases in tissues such as skeletal muscle and kidney. Fibrotic diseases are characterized by an increase in the production and accumulation of extracellular matrix (ECM) components leading to the loss of tissue architecture and function. In a classical view, several molecules are related to the establishment of the fibrotic condition, including angiotensin II, transforming growth factor β (TGF-β) and the connective tissue growth factor (CTGF) and a crosstalk has been suggested between these signaling molecules and the Wnt pathway. Skeletal muscle fibrosis, the most common disease, is typical of muscle dystrophies, where deregulation of the regenerative process in postnatal muscle leads to fibrotic differentiation and eventually to the failure of skeletal muscle. The fibrotic condition is also present in kidney pathologies such as polycystic kidney disease (PKD), in which fibrosis leads to a loss of tubule architecture and to a loss of function, which in almost all cases requires kidney surgery. A new actor in the pro-fibrotic effect of Wnt signaling in the kidney has been described, the primary cilium, an organelle that plays an important role in the onset of fibrosis.

The aim of this review is to discuss the pro-fibrotic effect of Wnt signaling in both skeletal muscle and kidney, and to try to understand how this pathway is associated with the TGF-β, CTGF and angiotensin II pro-fibrotic pathway.

Keywords: Fibrosis disease, kidney diseases, skeletal muscle, Wnt signaling.