Extracellular matrix stiffness and Wnt/?-catenin signaling in physiology and disease

Astudillo P.

The Wnt/?-catenin signaling pathway plays fundamental roles during development, stem cell differentiation, and homeostasis, and its abnormal activation can lead to diseases. In recent years, it has become clear that this pathway integrates signals not only from Wnt ligands but also from other proteins and signaling routes. For instance, Wnt/?-catenin signaling involves YAP and TAZ, which are transcription factors with crucial roles in mechanotransduction. On the other hand, Wnt/?-catenin signaling is also modulated by integrins. Therefore, mechanical signals might similarly modulate the Wnt/?-catenin pathway. However, and despite the relevance that mechanosensitive Wnt/?-catenin signaling might have during physiology and diseases such as cancer, the role of mechanical cues on Wnt/?-catenin signaling has received less attention. This review aims to summarize recent evidence regarding the modulation of the Wnt/?-catenin signaling by a specific type of mechanical signal, the stiffness of the extracellular matrix. The review shows that mechanical stiffness can indeed modulate this pathway in several cell types, through differential expression of Wnt ligands, receptors and inhibitors, as well as by modulating ?-catenin levels. However, the specific mechanisms are yet to be fully elucidated.

integrins

mechanosensing

stiffness

Wnt

Wnt/?-catenin pathway

?-catenin