

An emergent Wnt5a/YAP/TAZ regulatory circuit and its possible role in cancer

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Abstract

Wnt5a is a ligand that plays several roles in development, homeostasis, and disease. A growing body of evidence indicates that Wnt5a is involved in cancer progression. Despite extensive research in this field, our knowledge about how Wnt5a is precisely involved in cancer is still incomplete. It is usually thought that certain combinations of Frizzled receptors and co-receptors might explain the observed effects of Wnt5a either as a tumor suppressor or by promoting migration and invasion. While accepting this 'receptor context' model, this review proposes that Wnt5a is integrated within a larger regulatory circuit involving β -catenin, YAP/TAZ, and LATS1/2. Remarkably, WNT5A and YAP1 are transcriptionally regulated by the Hippo and Wnt pathways, respectively, and might form a regulatory circuit acting through LATS kinases and secreted Wnt/ β -catenin inhibitors, including Wnt5a itself. Therefore, understanding the precise role of Wnt5a and YAP in cancer requires a systems biology perspective. © 2021 Elsevier Ltd

Author keywords

Cancer; EMT; Regulatory networks; TAZ; Wnt5a; YAP; β -catenin