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# Targeting transforming growth factor- $\beta$ receptors in pulmonary hypertension

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**A review of the role of the TGF- $\beta$ -activin-nodal branch in pulmonary arterial hypertension and how this knowledge has not only provided insight into understanding its pathogenesis, but has also paved the way for possible novel therapeutic approaches** <https://bit.ly/2Pujk8O>

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**ABSTRACT** The transforming growth factor- $\beta$  (TGF- $\beta$ ) superfamily includes several groups of multifunctional proteins that form two major branches, namely the TGF- $\beta$ -activin-nodal branch and the bone morphogenetic protein (BMP)-growth differentiation factor (GDF) branch. The response to the activation of these two branches, acting through canonical (small mothers against decapentaplegic (Smad) 2/3 and Smad 1/5/8, respectively) and noncanonical signalling pathways, are diverse and vary for different environmental conditions and cell types. An extensive body of data gathered in recent years has demonstrated a central role for the cross-talk between these two branches in a number of cellular processes, which include the regulation of cell proliferation and differentiation, as well as the transduction of signalling cascades for the development and maintenance of different tissues and organs. Importantly, alterations in these pathways, which include heterozygous germline mutations and/or alterations in the expression of several constitutive members, have been identified in patients with familial/heritable pulmonary arterial hypertension (PAH) or idiopathic PAH (IPAH). Consequently, loss or dysfunction in the delicate, finely-tuned balance between the TGF- $\beta$ -activin-nodal branch and the BMP-GDF branch are currently viewed as the major molecular defect playing a critical role in PAH predisposition and disease progression. Here we review the role of the TGF- $\beta$ -activin-nodal branch in PAH and illustrate how this knowledge has not only provided insight into understanding its pathogenesis, but has also paved the way for possible novel therapeutic approaches.