Dysfunctional TGF-beta signaling contributes to Loeys-Dietz syndrome-associated aortic aneurysm

December 20 2013

Patients with the connective tissue disorder Loeys-Dietz syndrome (LDS) are at high risk for aortic aneurysm. LDS results in the presence of missense mutations within either of the genes encoding receptors for TGF-β. LDS-associated mutations are predicted to reduce TGF-β signaling; however, aortic tissue samples from LDS patients indicate that TGF-β signaling may be enhanced.

In this issue of the *Journal of Clinical Investigation*, Harry Dietz and colleagues at Johns Hopkins School of Medicine developed a mouse model of LDS, in which transgenic animals expressing *Tgfbr1* or *Tgfbr2* with LDS-associated mutations recapitulated human phenotypes. Using this model, the authors determined that even though the mutated TGF-β receptors were functionally defective, there was evidence of increased TGF-β signaling as indicated by elevated Smad2 phosphorylation. Furthermore, development of aortic aneurysms in these mice was ameliorated by treatment with an Angiotensin II type 1 (AT1) receptor antagonist.

In a companion commentary, Alan Daughtery and colleagues at the University of Kentucky discuss the therapeutic implications of this study on the use of AT1 receptor agonists to treat LDS-associated aneurism.

More information: Angiotensin II–dependent TGF-β signaling contributes to Loeys-Dietz syndrome vascular pathogenesis, *J Clin Invest.*

DOI: 10.1172/JCI69666
Aortic aneurysms in Loeys-Dietz syndrome—a tale of two pathways? *J Clin Invest.* 2014;124(1):79–81. DOI: 10.1172/JCI73906