Journal of Cardiac Failure
Volume ١٤, Issue ٨, October ٢٠٠٨, Pages ٧٠٣-٧٠٩

Activin-A, Transforming Growth Factor-β, and Myostatin Signaling Pathway in Experimental Dilated Cardiomyopathy

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View references (٣٣)

Abstract

Background: The pathogenic mechanisms of dilated cardiomyopathy are still uncertain. A number of cytokines and growth factors participate in the remodeling process of the disease. Methods: We investigated the cardiac myostatin, transforming growth factor (TGF)β, and activin-A/Smad growth inhibitory signaling pathway in experimental dilated cardiomyopathy. Transvenous endomyocardial biopsies of the interventricular septum were taken weekly in ١٥ beagle dogs during the development of heart failure (HF) induced by rapid pacing over a period of ٧ weeks. Genes involved in the myostatin-TGFβ-activin-A/Smad signaling pathway and the cardiac hypertrophic process were quantified by real-time quantitative polymerase chain reaction. Left ventricular volume, function, and mass were evaluated by echocardiography. Results: Overpacing was associated with increased left ventricular volumes and decreased ejection fraction, whereas the left ventricular mass remained unchanged. TGFβ was increased in moderate HF. Activin-A mRNA expression was ٤-fold higher in overt congestive HF than at baseline. A ٢-fold decrease of activin type II receptors and activin receptor interacting protein ٢ gene expressions were observed, as well as a transient decrease of follistatin. Activin type I receptors, activin receptor interacting protein ١, follistatin-related gene, and myostatin remained unchanged. The inhibitory Smad ٧, a negative feedback loop regulator of the Smad pathway, was overexpressed in severe HF. Gene expression of the cyclin-dependent kinase inhibitor p٢١, a direct target gene of the Smad pathway, was ٨-fold up-regulated in HF, whereas cyclin D١ was down-regulated. Conclusion: We conclude that tachycardia-induced dilated cardiomyopathy is characterized by gene overexpression of the TGFβ-activin-A/Smad signaling pathway and their target gene p٢١ and by the absence of ventricular hypertrophy.

Reaxys Database Information

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Author keywords

Cell cycle; cytokine; heart failure; hypertrophy; p٢١; TGFβ

Indexed Keywords

EMTREE drug terms: activin A; activin receptor ١; cyclin dependent kinase inhibitor ١A; follistatin; messenger RNA; myostatin; Smad٧ protein; transforming growth factor beta

EMTREE medical terms: animal experiment; animal model; article; congestive cardiomyopathy; congestive heart failure; controlled study; echocardiography; gene overexpression; heart left ventricle function; heart left ventricle mass; heart left ventricle volume; heart muscle biopsy; heart ventricle hypertrophy; heart ventricle septum; male; nonhuman; priority journal; real time polymerase chain reaction; tachycardia

MeSH: Activins; Animals; Cardiomyopathy, Dilated; Cyclin D١; Cyclin-Dependent Kinase Inhibitor p٢١; Cytokines; Disease Progression; Dogs; Gene Expression; Intercellular Signaling Peptides and Proteins; Models, Animal; Myostatin; Signal Transduction
Medline is the source for the MeSH terms of this document.