ERK1/2 and cardiac hypertrophy

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Technology description

Summary

Background Heart disease is the leading cause of death in the United States and is a major cause of disability. Approximately 27% of all U.S. deaths each year are caused by heart disease. Cardiac hypertrophy, which decreases the size of the heart chamber including both right and left ventricles, is the cause of high blood pressure (hypertension) and heart valve stenosis, affecting more than 60 million Americans. In the early stages cardiac hypertrophy is the heart' s response to mechanical stress such as tissue injury, but sustained hypertrophy can lead to heart failure. Biotechnology companies are in a continuous search for new protein targets in the treatment of heart disease. Like other involved proteins and discovered targets, Extracellular Signal-Related Kinase 1/2 (ERK1/2) has been identified as a player in cardiac hypertrophy, but due to the complexity of the signal pathways, the extent to which it contributes is unknown. Clarification of the mechanisms or proteins initiating the complex cardiac hypertrophic response will lead to better understanding of heart failure to improve treatment from various stimuli. Technology A research team at the University of Colorado led by Dr. Carmen Sucharov has produced results, through multiple in vivo and in vitro studies, supporting the use of a family of methods for treating cardiac hypertrophy or heart failure by administering an inhibitor of ERK1/2, which plays a crucial role in the various signal systems that effect hypertrophic signaling. ERK1/2 activity in myocytes stimulates and creates a cascade effect on signaling systems including various kinases, ultimately initiating hypertrophic signaling. The studies varied concerning which inhibitor to select from a group of ERK 1/2 molecules, as well as how it was administered (intravenously, transdermally, etc.) and if it was administered prior to another hypertrophic therapy, simultaneously, or after. Methods included treating a cell with the inhibitor, measuring one or more cardiac hypertrophy parameters, and comparing results to one or more cardiac hypertrophy parameters in a cell not treated with the inhibitor, yielding extensive results as to the difference in cardiac hypertrophy parameters among the cells in question. This method can be used to treat identified patients as well as to prevent onset in those who are identified as at risk, exhibiting longstanding uncontrolled hypertension, congenial predisposition to heart disease, or a familial history of cardiac hypertrophy. Administering the inhibitor may be performed by direct injection into the tissue, orally, or by sustained, controlled, or delayed release. This method can also be paired with a second therapy, such as a beta blocker before,

after or simultaneously. This treatment has the potential to greatly improve overall quality of life and decrease disease related mortality.

Institution

University of Colorado