And the beat goes on: Scientists jump-start the heart by gene transfer

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Scientists from the Universities of Michigan and Minnesota show in a research report published online in the *FASEB Journal* that gene therapy may be used to improve an ailing heart's ability to contract properly. In addition to showing gene therapy's potential for reversing the course of heart failure, it also offers a tantalizing glimpse of a day when "closed heart surgery" via gene therapy is as commonly prescribed as today's cocktail of drugs.

"We hope that our study will lead some day to the development of new genetic-based therapies for heart failure patients," said Todd J. Herron, Ph.D., one of the researchers involved in the study and research assistant professor of molecular and integrative physiology at the University of Michigan. "The advent of molecular motor-based gene transfer for the failing heart will hopefully improve cardiac function and quality of life for heart failure patients."

To make this advance, Herron and colleagues treated heart muscle cells from the failing hearts of rabbits and humans with a virus (adenovirus) modified to carry a gene which produces a protein that enables heart cells to contract normally (fast molecular motor) or a gene that becomes active in failing hearts, which is believed to be part of the body's way of coping with its perilous situation (slow molecular motor). Heart cells treated with the gene to express the fast molecular motor contracted better, while those treated with the gene to express the slow molecular motor were unaffected.

"Helping hearts heal themselves, rather than prescribing yet another drug to sustain a failing organ, would be a major advance for doctors and patients alike," said Gerald Weissmann, M.D., Editor-in-Chief of the *FASEB Journal*. "Equally important, it shows that gene therapy remains one of the most promising approaches to treating the world's most common and deadliest diseases."

According to the U.S. Centers for Disease Control and Prevention, heart failure is a condition where the heart cannot pump enough blood and oxygen to meet the needs of other body organs. Approximately 5 million people in the United States have heart failure, about 550,000 new cases are diagnosed each year, and more than 287,000 people in the United States die each year of heart failure. The most common causes of heart failure are coronary artery disease, hypertension or high blood pressure, and diabetes. Current treatments usually involve three to four medicines: ACE inhibitors, diuretics, digoxin, and beta blockers.

Current clinical agents and treatments focus on the amount of calcium available for contraction, which can provide short-term cardiac benefits, but are associated with an increased mortality in the long-term. Results from this study show that calcium-independent treatments could have implications for heart diseases associated with depressed heart function, due to the effectiveness of fast molecular motor gene transfer on the improved contractions of human heart muscle cells.

More information: Todd J. Herron, Eric Devaney, Lakshmi Mundada, Erik Arden, Sharlene Day, Guadalupe Guerrero-Serna, Immanuel Turner, Margaret Westfall, and Joseph M. Metzger. Ca2+-independent positive molecular inotropy for failing rabbit and human cardiac muscle by alpha-myosin motor gene transfer. FASEB J. doi:10.1096/fj.09-140566

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