Docket #: S23-405

Treatment of dilated cardiomyopathy and other disorders characterized by systolic heart failure with ATF4 gene therapy

Heart failure is a complex cardiovascular disease that affects 26 million people worldwide and is characterized by the inability of the heart to pump blood effectively, leading to a decline in its normal functions. Despite major improvements in the understanding of risk factors for the disease, this knowledge has not yet been fully translated into effective interventions for the primary prevention of heart failure, except for blood pressure lowering medications and statins. Dilated cardiomyopathy is a leading cause of heart failure and the most common cause of cardiac transplantation. Current treatment strategies are directed toward symptoms to preserve myocardial function. Given the consistently high morbidity and mortality of dilated cardiomyopathy, there is a pressing need to develop therapies that address the disease's underlying genetic basis.

The Karakikes Lab at Stanford has engineered a novel gene therapy approach that uses an AAV-biologic to target transcription factors related to heart failure and ultimately restoring cardiac metabolism. The researchers have already shown in small animal models that treatment with the invented gene therapy vector was able to restore expressions of key metabolic genes related to dilated cardiomyopathy and reverse the phenotype by stabilizing heart function. As there are currently no mechanism-based therapeutic for dilated cardiomyopathy, the invention provides a potential therapeutic that can be used to broadly target several metabolic pathways within the heart and improve overall outcomes for cardiac metabolism.

Stage of Development
Research – in vivo

Applications

- Cardiovascular diseases treatment

Advantages

- Currently, there is no cure for heart failure and no approved gene therapies.
- This approach is mutation agnostic, meaning that it can target a larger patient population independently on the etiology of the disease; this approach differs from most gene therapy strategies that target specific mutations causing DCM.
- Biologic can increase the expression of ATF4, a transcription factor, specifically in the cardiac myocytes.
- Approach does not replace a faulty or missing gene, but instead aims at triggering a cardioprotective effect by bolstering an integrative stress response in the failing heart.

Publications

- Perea-Gil, I., Seeger, T., Bruyneel, A. A., Termglinchan, V., Monte, E., Lim, E. W., ... & Karakikes, I. (2022). "Serine biosynthesis as a novel therapeutic target for dilated cardiomyopathy." European Heart Journal, 43(36), 3477-3489.

Patents

- Published Application: WO2026030234

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