Innovations
UNIVERSITY OF COLORADO
ANSCHUTZ MEDICAL CAMPUS

Treatment For Filamin C-Related Cardiomyopathies

Product

Crenolanib

Indication

FLNC Mutant Dilated Cardiomyopathy

Value Propositions

- Improve cardiac contractility and reduce arrythmias
- Prevent or delay need for cardiac transplant

Market

- $300 million—Global DCM therapeutic market

Intellectual Property

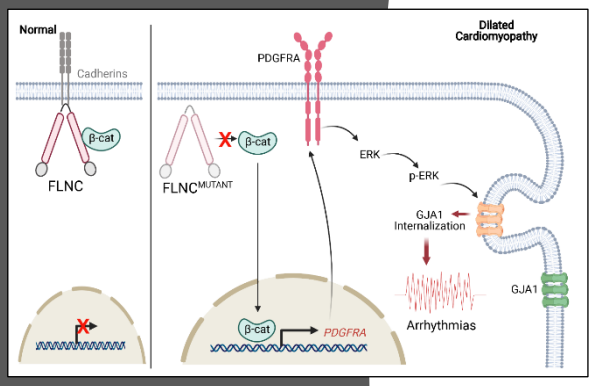
- Patent pending*
- Available for licensing

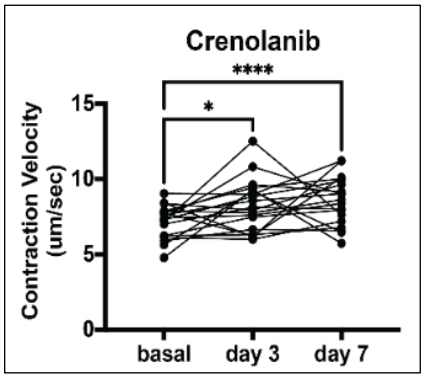
Background on CU5815H

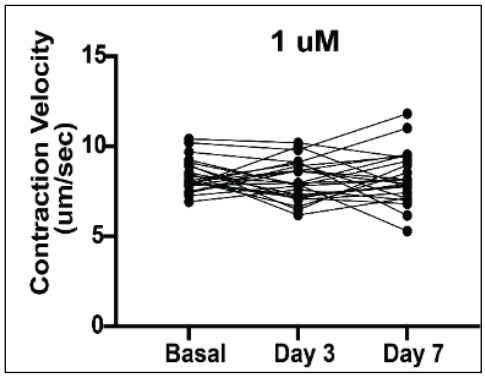
Dilated cardiomyopathy (DCM) is a common cause of heart failure (HF) and is the most common diagnosis in patients who undergo cardiac transplantation. DCM is characterized by dilatation and systolic dysfunction of one or both ventricles. Family-based studies of first-degree relatives of patients with idiopathic DCM have established that a genetic cause of cardiomyopathy can be identified in 20 to 35 percent of patients. Filamin C (FLNC) mutations have been identified as a genetic cause of DCM. These patients have an arrhythmogenic phenotype and are at risk for ventricular arrhythmias and sudden cardiac death. Many of these patients also develop heart failure, requiring heart transplant. There are currently no specific treatments for DCM due to FLNC mutations.

Technical Innovation

A team led by Dr. Suet Nee Chen has discovered that platelet-derived growth factor receptor-alpha (PDGFRA) is a potential preventive and therapeutic target in FLNC-related cardiomyopathies. This is because the activation of PDGFRA by FLNC truncating mutations causes pro-arrhythmic downstream signaling (see figure below). Therefore, the team is pursuing PDGFRA inhibition with Crenolanib in order to improve contractile function and decrease arrhythmogenic potential in patients with FLNC mutant DCM. *In vitro* studies suggest that PDGFRA inhibition with Crenolanib improves contractile function and reduces arrythmias in patient iPSC cardiomyocytes. The team will pursue *in vivo* studies for further validation of clinical benefit. A therapeutic for the treatment of FLNC mutant DCM may improve life for thousands of affected individuals in the U.S. through a reduction in fatal arrythmias and preventing or delaying cardiac transplant.







Figures: Normal FLNC phenotype and mutant FLNC signaling leading to arrhythmogenic phenotype in FLNC related DCM (left figure). Treatment with crenolanib (middle figure) significantly improved contractility and reduced arrhythmias in iPSC-CMs derived from FLNC patients, but not healthy control individuals (right figure).

***Provisional patent pending:** 63/292,377—"Treatment to rescue arrhythmias in FLNC related cardiomyopathies"—Filed December 21, 2021.*

***Link to manuscript:** https://www.science.org/doi/10.1126/sciadv.abk0052*

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