

Mitochondrial Calcium Uptake Enhancers for the Treatment of Cardiac Disease

Substances that enhance mitochondrial calcium uptake in cardiomyocytes and normalize aberrant cardiomyocyte calcium handling

Reference: Calcium Uptake Enhancers



Header image is illustrative. Source: pixabay.com/vectors/electrocardiogram-ecg-heartbeat-36732/, Pixabay Licence

IP Status

Patent application submitted

Seeking

Development partner

About **LMU Munich**

Ludwig-Maximilians-Universität München is the University in the heart of Munich. LMU is recognized as one of Europe's premier academic and research institutions. The LMU Munich community is engaged in generating new knowledge for the benefit of society at large.

Background

Though cardiovascular diseases remain the number one cause of death and hospitalization worldwide, current pharmacotherapies are still limited. Especially diseases affecting the myocardium, like arrhythmias and heart failure remain difficult to treat while prevalences for these diseases continue to raise. Both, antiarrhythmics and positive inotropes are prone to severe side effects and it remains a central goal of cardiovascular pharmacology research to develop safer therapies. Since diseases of the myocardium are often associated with disturbances in cardiomyocyte calcium handling, regulators of intracellular calcium represent promising target structures.

Tech Overview

Researchers at LMU Munich have recently identified a new class of substances which enhance mitochondrial calcium in cardiomyocytes (MiCUps). They demonstrate that enhanced mitochondrial calcium uptake prevents propagation of arrhythmogenic calcium signals in cardiomyocytes and thus arrhythmogenesis. Furthermore, they demonstrate efficacy of MiCUps to prevent arrhythmia in a translational mouse model for catecholaminergic polymorphic ventricular tachycardia (CPVT) and in iPSC-derived cardiomyocytes from a CPVT patient. This data thus excels MiCUps as a new class of compounds for the treatment of arrhythmias associated with disturbed intracellular calcium homeostasis, which include also some of the most prevalent arrhythmias like atrial fibrillation.

Arrhythmias are furthermore the most prevalent cause of death in heart failure patients. The clinical definition of heart failure is insufficient cardiac output mostly due to reduced contractility of the myocardium. During heart failure cardiomyocytes undergo a remodelling process in which a disarrangement of the tight interaction between mitochondria and the main calcium store of the cell, the SR, takes place, leading to reduced ATP production, reduced contractility, and arrhythmia. MiCUps represent a promising novel candidate therapeutics combining a positive inotropic effect with a protective effect against arrhythmia. In preliminary experiments we observed bigger systolic calcium signals in healthy and failing cardiomyocytes after treatment with MiCUps.

Further Details

- Wilting F, Kopp R, Schedel A, Dupper NJ, Kwon O, Nicke A, Gudermann T, and Schredelseker J. (2020) The antiarrhythmic compound efsevin directly modulates voltage-dependent anion channel 2 by binding to its inner wall and enhancing mitochondrial Ca²⁺ uptake. *Br J Pharmacol*, 177(13): 2947-2958
- Schweitzer MK, Wilting F, Sedej S, Dreizehnter L, Dupper NJ, Tian Q, Moretti A, My I, Kwon O, Priori SG, Laugwitz KL, Storch U, Lipp P, Breit A, Mederos y Schnitzler M, Gudermann T, and Schredelseker J (2017) Suppression of Arrhythmia by Enhancing Mitochondrial Ca²⁺ Uptake in Catecholaminergic Ventricular Tachycardia Models. *JACC Basic Transl Sci*, 2(6): 737-747
- Shimizu H*, Schredelseker J*, Huang J*, Lu K*, Naghdi S, Lu F., Franklin S, Fiji HDG, Wang K, Zhu H, Tian C, Lin B, Nakano H, Ehrlich A, Nakai J, Stieg AZ, Gimzewski JK, Nakano A, Goldhaber JL, Vondriska TM,

Hajnóczky G, Kwon O, and Chen JN (*shared first authorship) (2015) Mitochondrial Ca²⁺ uptake by the voltage-dependent anion channel 2 regulates cardiac rhythmicity. *Elife*, 4

Stage of Development

We have provided a proof-of-principle in translational CPVT models and are currently investigating positive inotropic effects in heart tissue.

Benefits

A new pharmacotherapy for arrhythmia and heart failure with fewer side effects compared to cardiac glycosides or antiarrhythmics of class I and III.

Applications

Treatment of patients with cardiac arrhythmia and/or heart failure.

Opportunity

We are currently seeking partners to test MiCUs in translational models for prevalent arrhythmias and heart failure and to identify novel MiCUs.

Patents

- Patent application submitted. Contact TTO for further information.

For further information, please contact us.

Ludwig-Maximilians-Universität München (LMU Munich)

Office for Research and Technology Transfer

- Corporate Partnerships -



Dr. Barbara Blaurock

+49(0)89 2180-722 13



Dr. Laura Gerwin

+49(0)89 2180-722 12

corporatepartnerships@lmu.de

www.lmu.de/researchservices/corporatepartnerships/