

Studying cardiac arrhythmias in nematodes

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Researchers at the Goethe University have developed a simple model using the nematode *Caenorhabditis elegans* that can be used to test substances for treating genetically-mediated cardiac arrhythmias. They used the nematode feeding apparatus for this purpose, a rhythmically active muscle pump that resembles the muscle cells in the mammalian heart. This could be an important step on the road to personalised treatment.

Cardiac arrhythmias often have genetic causes. The same mutation is often detected in patients with the same type of arrhythmia. However, it is not clear from the outset whether other mutations in the same gene have the same effects. The effects of the arrhythmia could also differ depending on the type of mutation. This knowledge could definitely be significant for treatment. This is because a type of medication that works particularly well for a specific mutation could be less beneficial for other mutations. Researchers have long been searching for a simple model that can be used to create certain genetic defects and in which the efficacy of substances can be tested.

The research group, led by Alexander Gottschalk at the Institute of Biochemistry and the Buchmann Institute at the Goethe University, used the nematode *Caenorhabditis elegans* because it is easy to modify it genetically. The nematode feeding apparatus uses ion channels similar to those in [muscle cells](#) of the mammalian heart. Ion channels play an important role in regulating cardiac muscle excitation, and mutations in their genes often lead to arrhythmias.

The researchers used optogenetic techniques, since the feeding apparatus, i.e. the pharynx, does not naturally pump as regularly as required in order to recognise arrhythmias. They introduced photo-activated [ion channels](#) into the muscle cells using a genetic approach. In this way, the apparatus can be transformed into a light-activated muscle pump with highly regular action. They then introduced various ion channel mutations, which are

responsible for the so-called Timothy syndrome (LQT8) in humans. In practice, the mutated pharynx then demonstrated aberrant pump behaviour.

"We were able to improve or reverse these arrhythmic effects using a substance that is already known to be pharmacologically active, and which is administered to patients with Timothy syndrome in a modified form", explains Prof Alexander Gottschalk. The goal is to use the worm to search for new active substances for other types of arrhythmia. These could even potentially be patient-specific if the exact mutation is transferred to the worm. The ease of genetic mutability of the nematode is highly advantageous in this regard when compared to a mouse model, which would be very difficult to generate. In order to facilitate the search for new medications, the researchers also developed a new optical method with which several animals can be analysed in parallel.

More information: "Arrhythmogenic effects of mutated L-type Ca²⁺-channels on an optogenetically paced muscular pump in *Caenorhabditis elegans*." *Scientific Reports* 5: 14427.

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