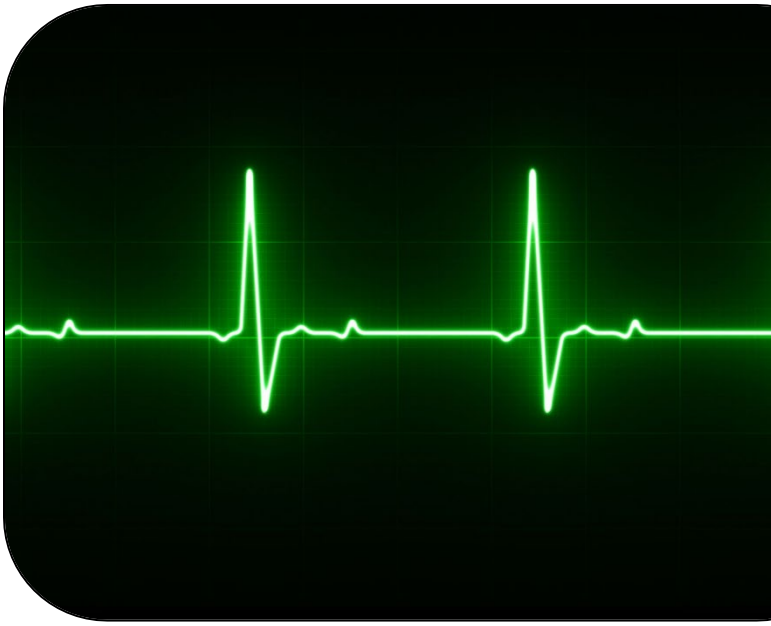
>> Cardiac Disease Modeling

Biologically relevant cardiac disease models are essential for advancing our understanding of pathological mechanisms and developing innovative therapeutic strategies. While conventional *in vivo* animal models and *in vitro* endpoint assays can increase your costs and delay your progress, Axion BioSystems' next-generation Maestro MEA platform provides sensitive functional analysis of human cardiomyocytes designed to accurately recapitulate disease phenotypes and quickly predict drug efficacy and toxicity.



Learn how the Maestro can support cardiac disease research with these selected publications:

Frameshift variants in C10orf71 cause dilated cardiomyopathy in human, mouse, and organoid models

Yang L, Ma K, et al. The Journal of Clinical Investigation. (2024)

Dilated cardiomyopathy (DCM) is widely associated with various genetic mutations. Here, researchers identify a candidate causal gene, *C10orf71*, and use hiPSC-derived cardiomyocytes and organoids to assess the effects of *C10orf71* mutation on cardiomyocyte electrophysiology and DCM.

Highlights:

- *C10orf71* frameshift mutations are associated with DCM, and *C10orf71* is specifically expressed in cardiomyocytes.
- Contractility analysis of hiPSC-derived heart organoids using the Maestro indicates impaired contractile function evident via decreased amplitude and increased excitation-contraction delay.
- Contractile protein activation via OM treatment rescues contractile dysfunction *in vivo*, suggesting therapeutic potential for DCM treatment.

Read more >>

The pseudoenzyme ADPRHL1 affects cardiac function by regulating the ROCK pathway

Tian L, Guo T, et al. Stem Cell Research & Therapy. (2023)

Evidence suggests the pseudoenzyme ADPRHL1 is involved in cardiac development, but the relationship is unclear. The team characterizes ADPRHL1-KO iPSC-derived cardiomyocytes to assess developmental mechanisms and potential pathways for therapeutic intervention in ADPRHL1-related disease.

Highlights:

- CRISPR/Cas9 was used to generate ADPRHL1-KO hESCs, which were then differentiated into cardiomyocytes.
- ADPRHL1-KO CMs exhibit decreased conduction velocity and increased field potential duration, characterized using the Maestro.
- Inhibition of the ROCK-myosin II pathway restores conduction velocity, suggesting regulation of the ROCK-myosin II pathway as a critical role of ADPRHL1 in cardiac development.

Read more >>

Genome sequencing in a genetically elusive multi-generational long QT syndrome pedigree identifies a novel LQT2-causative deeply intronic KCNH2 variant

Tobert KE, Tester DJ et al. Heart Rhythm. (2022)

Many cases of long QT syndrome (LQTS) can be attributed to specific variants of KCNQ1, KCNH2, and/or SCN5A, but a small subset have no identified genetic cause. Scientists used genome sequencing on some of these patients to identify a novel KCNH2 variant that was not identified on initial screening.

Highlights:

- Genome sequencing was performed on six family members with LQTS, and all expressed a novel deep intronic KCNH2 variant.
- Patient-derived iPSC-CMs assessed on the Maestro demonstrate significantly increased field potential duration and action potential duration (APD90, via LEAP) than isogenic controls.
- This novel KCNH2 variant, as well as other deep intronic variants of KCNH2, KCNQ1, and SCN5A may be responsible for LQTS in cases where a cause is not identified from more common variants.

Read more >>

Development of iPSC-based clinical trial selection platform for patients with ultrarare diseases

Sequiera GL, Srivastava A, et al. Science Advances. (2022)

Personalized prescreening platforms are important when considering clinical trial enrollment or other experimental treatment paradigms for patients with ultrarare diseases. The authors of this study establish an iPSC-based platform to assess efficacy of various drugs to assist with clinical decision-making.

Highlights:

- Patients with ultrarare pathogenic mutations can be difficult to treat and are often subjected to a "trial and error" approach, prompting a need for personalized screening.
- Using iPSCs from a patient with Leigh-like syndrome, researchers created a screening platform including both safety and efficacy measurements of neurons and cardiomyocytes.
- The Maestro provides functional analysis of neurons for drug efficacy, along with functional cardiomyocyte analysis for drug safety assessment.

Read more >>

Thyroid hormones regulate cardiac repolarization and QT-interval related gene expression in hiPSC cardiomyocytes

Ulivieri A, Lavra L, et al. Scientific Reports. (2022)

While some cardiac symptoms are associated with thyroid dysfunction (e.g., tachycardia, arrhythmias), the relationship between thyroid dysfunction and QT prolongation is not fully understood. Researchers use hiPSC-derived cardiomyocytes to assess the influence of thyroid hormones on ventricular repolarization.

Highlights:

- hiPSC-CMs represent a model to examine cardiotoxicity and QT interval in response to compound treatment.
- Using the Maestro, hiPSC-CMs were treated with thyroid hormones, T3 and T4, to determine effects on field potential duration and action potential duration, representing repolarization.
- Thyroid hormones at high doses induce QT prolongation, suggesting a therapeutic target for patients with thyroid disease or other conditions leading to QT prolongation.

Read more >>

Modeling secondary iron overload cardiomyopathy with human induced pluripotent stem cell-derived cardiomyocytes

Rhee JW, Yi H, et al. Cell Reports. (2020)

Iron accumulation in the heart leads to iron overload cardiomyopathy (IOC) that can result in end-stage heart failure if untreated, yet the mechanisms of iron accumulation and effects of iron on cardiomyocytes are poorly understood. Here, scientists use hiPSC-CMs to model IOC and evaluate potential therapeutics.

Highlights:

- hiPSC-CMs treated with iron demonstrate uptake and contractile dysfunction in a concentration-dependent manner.
- Maestro recordings of hiPSC-CMs exhibit increased field potential duration and action potential duration, as well as early after depolarizations when exposed to iron.
- FPD prolongation and ROS production is rescued via treatment with ebselen, a DMT1 inhibitor and antioxidant, suggesting therapeutic potential for IOC treatment.

Read more >>