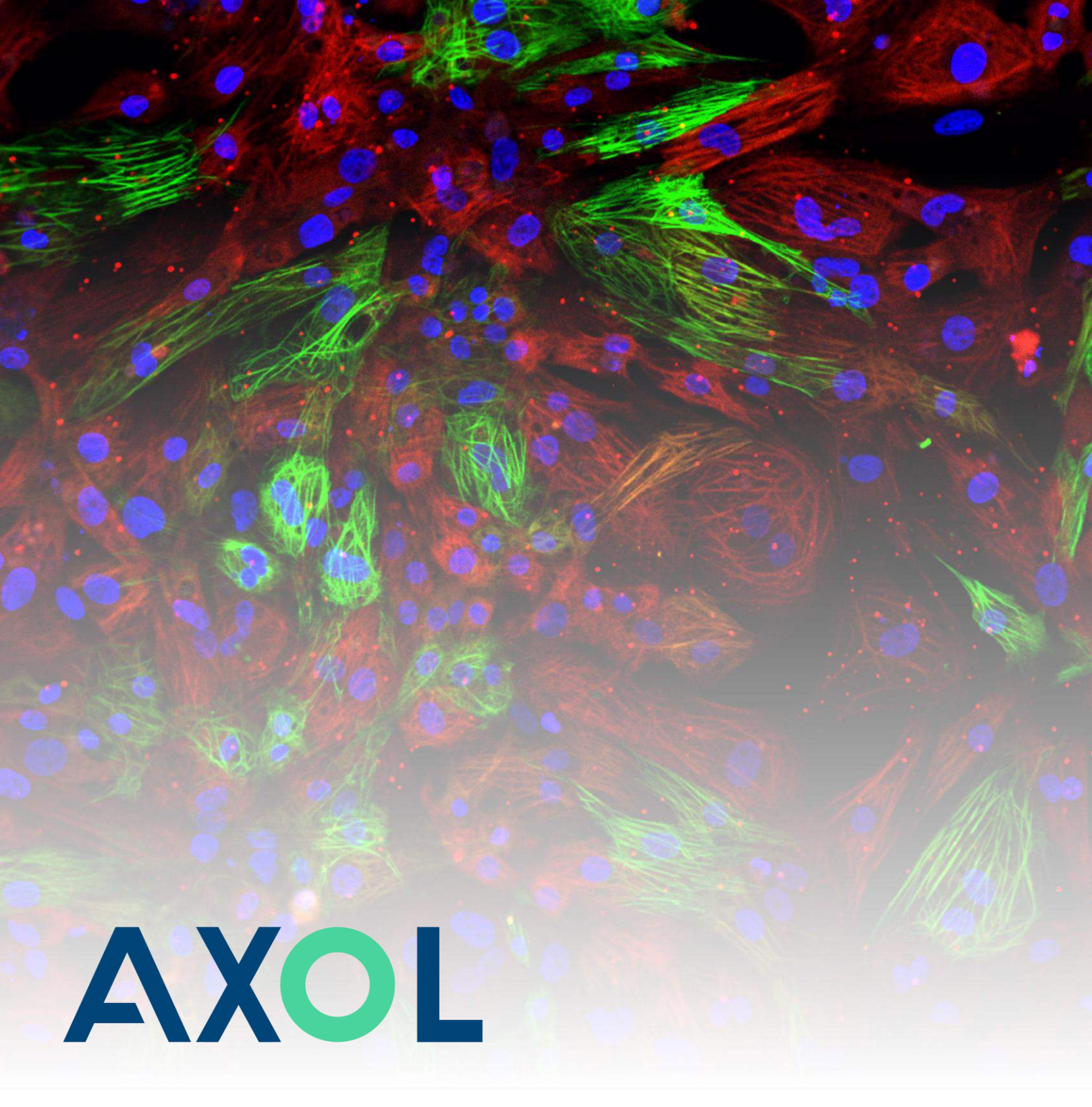


AXOL

Chamber-specific human iPSC-derived cardiomyocytes for disease modeling and safety

Featured application: improving maturation in ventricular cardiomyocytes using Myomax™

www.axolbio.com

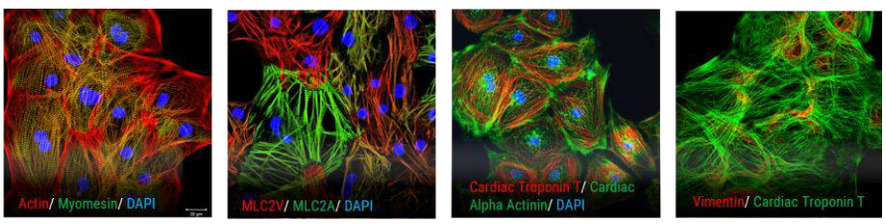
iPSC-derived cardiomyocytes for drug discovery, research and cardiotoxicity studies

Terminally differentiated cardiomyocytes derived from human iPSCs recapitulate key features of healthy human cardiac biology and function, providing a robust *in vitro* system for drug discovery, toxicity assessment, and fundamental research into cardiac health and disease. Axol offers highly validated, chamber-specific cardiomyocytes that exhibit distinct atrial or ventricular pharmacology and phenotypes, generated from both female and male donors.

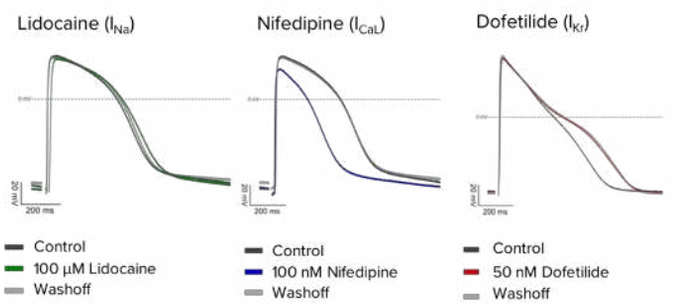
To further enhance the predictive power of iPSC-derived cardiomyocyte platforms, we continue to innovate and optimize our technologies. For applications requiring increased cellular maturity, we have developed MyoMax™, a proprietary maturation medium that specifically promotes advanced functional and structural maturation of ventricular iPSC-derived cardiomyocytes.

Comprehensive user guides and complete media kits streamline the establishment and scale up of iPSC-based cardiac models, and our scientific team are always available to help.

axoCells™ ventricular cardiomyocytes

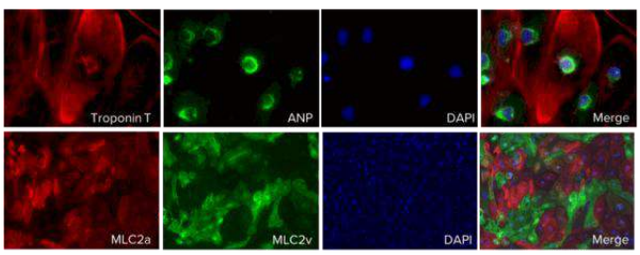


Immunocytochemistry of axoCells™ ventricular cardiomyocytes stained for key markers. Key morphological features are demonstrated including sarcomere alignment. Magnification 63x for images 1,2 and 4; 40x for image 3. Scale bar = 20 µm.



axoCells™ human iPSC-derived ventricular cardiomyocytes express the core cardiac ion channels I_{Na}, $I_{Ca,L}$ and I_{Kr}. Here we present representative patch clamp traces of evoked action potentials recorded under control conditions (grey) and in the presence of 100 µM Lidocaine (green), 100 nM Nifedipine (blue) or 50 nM Dofetilide (red), which show expected effects on action potential amplitude and duration.

axoCells™ atrial cardiomyocytes

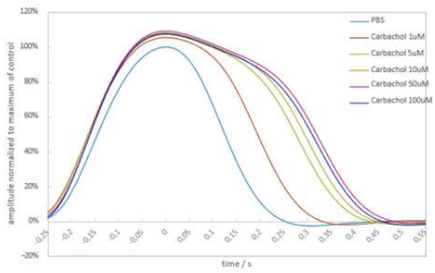


Immunocytochemistry demonstrating expression of cardiac- and atrial-specific markers troponin T, atrial myosin light chain 2 (MLC2a) and atrial natriuretic peptide (ANP). Troponin T staining (red) confirmed the presence of cardiac myocytes, ANP is specifically secreted by atrial myocytes upon atrial stretching and MLC2a facilitates cardiac contractility. The nuclear marker DAPI was used as a counterstain.

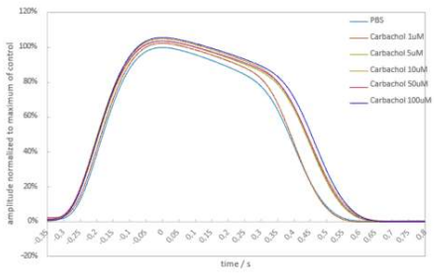
Chamber-specific pharmacological response

The effect of carbachol, an activator of I_{KAch} in atrial cardiomyocytes, on the contractility of axoCells atrial (**a**) and ventricular (**b**) cardiomyocytes, as measured on the InnoVitro FLEXcyte 96.

a)

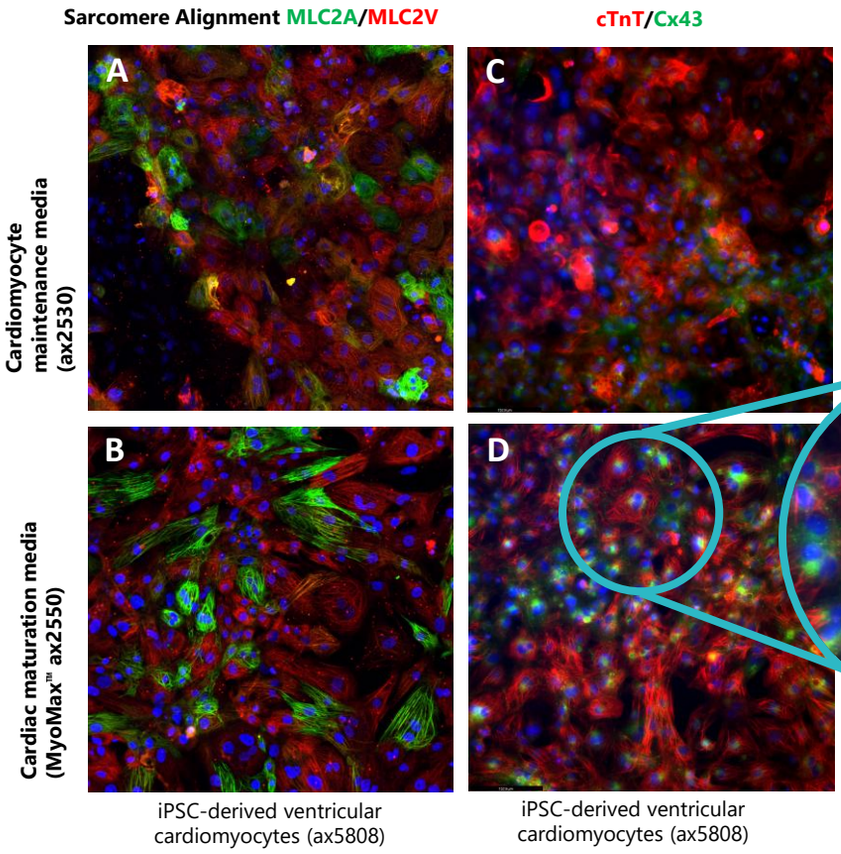


b)



Enhanced metabolic maturation of human iPSC-derived ventricular cardiomyocytes

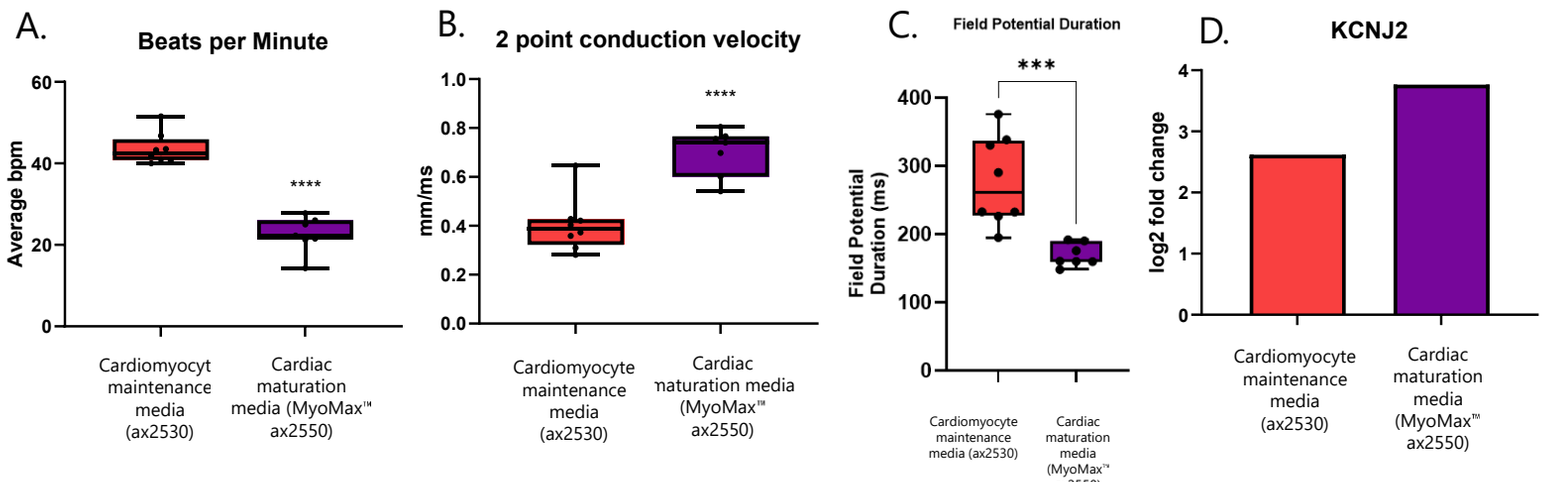
MyoMax™ metabolic maturation media supports generation of more mature ventricular cardiomyocyte populations for cardiotoxicity screening and drug development applications.



iPSC-derived ventricular cardiomyocytes (ax5808) maintained for 8 days in either (A, C) cardiomyocyte maintenance media (ax2530) or (B, D) MyoMax™ cardiac maturation media (ax2550).

iPSC-cardiomyocytes cultured in MyoMax™ cardiac maturation media showed improved sarcomere alignment (A & B) and increased expression of the cardiac maturity markers cTnT and Cx43 (B & D).

Detail showing improved sarcomere structure.



MyoMax™ maturation media, significantly improves electrophysiological characteristics of axoCells human iPSC-derived cardiomyocytes measured on the Axion Maestro Pro MEA system after 14 days. (A) Loss of spontaneous beating is a feature of adult cardiomyocytes. Reduction in beat rate from 43.56 bpm to 22.57 bpm. Data presented as mean ±SD (n = 8 wells). Unpaired t-test with Welch's correction **** $p < 0.0001$. (B) Adult cardiomyocyte conduction velocity is between 0.3 – 1 mm/ms. Improvement in 2-point conduction velocity from 0.403 mm/ms to 0.701 mm/ms. Data presented as mean ±SD (n = 8 wells). Unpaired t-test with Welch's correction **** $p < 0.0001$. (C) Adult cardiomyocyte action potential duration ranges from 100 – 500 ms. Reduction in field potential duration from 490 ms to 312 ms. Data presented as mean ±SD (n = 8 wells). Unpaired t-test with Welch's correction *** $p = 0.0009$ (D) MyoMax™ maturation media increases transcript levels of KCNJ2, the gene encoding the Kir2.1 channel. Fold change (Log2) in the expression profile of KCNJ2 increases from 2.619 to 3.765 in human iPSC-derived cardiomyocytes cultured in metabolic maturation media.

Download the poster for more information

Comprehensive range of healthy iPSC-derived cardiomyocytes and complete media

Product name	Cells (kit)	
axoCells™ human iPSC-derived atrial cardiomyocytes, male donor, ≥1 million cells.	ax2518 (ax2510)	
axoCells™ Human iPSC-derived ventricular cardiomyocytes, male donor, ≥1 million cells. *CiPA-validated.	ax2508 (ax2500)	
axoCells™ human iPSC-derived ventricular cardiomyocytes, female donor, aged 45, ≥1 million cells	ax5808	Early Access axoCells™
axoCells™ human iPSC-derived atrial cardiomyocytes, female donor, aged 45, ≥1 million cells	ax5818	Early Access axoCells™
axoCells™ MyoMax™ Maturation Media (125 ml)	ax2550	

*axoCells™ iPSC-derived ventricular cardiomyocytes (ax2508) have been validated using the Comprehensive *in vitro* Proarrhythmia Assay (CiPA) compound panel, demonstrating their value in cardiotoxicity models.

The FDA Modernization Act 3.0 and other government and industry support is accelerating adoption of iPSC technology and new approach methodologies (NAMs). We are working with the Health and Environmental Sciences Institute (HESI) and the HESI Atrial Fibrillation Working Group to develop and validate models for atrial-specific cardiotoxicity and disease modelling.

We believe iPSC-derived models are transformative for cardiotoxicity and research, so we will continue to drive better quality standards, chamber-specific models and increase donor diversity to support the successful adoption in the sector.

At Axol Bioscience, we've been working with iPSCs in a quality-focused environment for over a decade and have developed a deep understanding of the challenges of this space. Our ISSCR-compliant quality management system drives consistency and quality in iPSC products manufactured at our ISO 9001:2015 certified production facility.

Publications featuring axoCells™ ventricular and atrial cardiomyocytes

1. Ray, S., Roth, R. & Keyel, P.A. (2022) Membrane repair triggered by cholesterol-dependent cytolysins is activated by mixed lineage kinases and MEK. Science Advances, 8(11), eabl6367. https://doi.org/10.1126/sciadv.abl6367
2. Bohannon, B.M., de la Cruz, A., Wu, X., Jowais, J.J., Perez, M.E., Dykxhoorn, D.M., Liin, S.I. & Larsson, H.P. (2020) Polyunsaturated fatty acid analogues differentially affect cardiac NaV, CaV, and KV channels through unique mechanisms. eLife, 9, e51453. https://doi.org/10.7554/eLife.51453
3. Iachetta, G., Colistra, N., Melle, G., Deleye, L., Tantussi, F., De Angelis, F. & Dipalo, M. (2021) Improving reliability and reducing costs of cardiotoxicity assessments using laser-induced cell poration on microelectrode arrays. Toxicology and Applied Pharmacology, 418, 115480. https://doi.org/10.1016/j.taap.2021.115480

If you would like to discuss the adoption of iPSC-derived cardiomyocytes into your workflow, or our specialist services provision, please contact us at operations@axolbio.com

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