

Organ-on-a-Chip Mimics Heart's Biomechanical Properties



Scientists at Vanderbilt University have created a 3D organ-on-a-chip that can mimic the heart's biomechanical properties. The device ("I-Wire Heart-on-a-Chip") and the results of initial experiments demonstrating that it faithfully reproduces the response of cardiac cells to two different drugs that affect heart function in humans are described in report published in the journal Acta Biomaterialia.

The I-Wire device consists of a thin thread of human cardiac cells 0.014 inches thick (about the size of 20-pound monofilament fishing line) stretched between two perpendicular wire anchors. The amount of tension on the fibre can be varied by moving the anchors in and out, and the tension is measured with a flexible probe that pushes against the side of the fibre.

The fibre is supported by wires and a frame in an optically clear well that is filled with liquid medium like that which surrounds cardiac cells in the body. The apparatus is mounted on the stage of a powerful optical microscope that records the fibre's physical changes. The microscope also acts as a spectroscope that can provide information about the chemical changes taking place in the fibre. A floating microelectrode also measures the cells' electrical activity.

I-Wire's ability to control the mechanical force applied to cardiac cells allows the researchers to reproduce the mechanical conditions of the living heart. "Heart tissue, along with muscle, skeletal and vascular tissue, represents a special class of mechanically active biomaterials," explained Gordon A. Cain University Professor John Wikswo, who heads up the project. "Mechanical activity is an intrinsic property of these tissues so you can't fully understand how they function and how they fail without taking this factor into account."

The I-Wire system can be used to characterise how cardiac cells respond to electrical stimulation and mechanical loads and can be implemented at low cost, small size and low fluid volumes, which make it suitable for screening drugs and toxins. "We believe it could prove invaluable in studying cardiac diseases, drug screening and drug development, and, in the future, in personalised medicine by identifying the cells taken from patients that can be used to patch damaged hearts effectively," Wikswo noted. Because of its potential applications, Vanderbilt University has patented the device.

To demonstrate the I-Wire's value in determining the effects that different drugs have on the heart, the researchers tested its response with two drugs known to affect heart function in humans: isoproterenol and blebbistatin. Isoproterenol is a medication used to treat bradycardia (slow heart rate) and heart block (obstruction of the heart's natural pacemaker). Blebbistatin inhibits contractions in all types of muscle tissue, including the heart.

According to Veniamin Sidorov, the research assistant professor at the Vanderbilt Institute for Integrative Biosystems Research and Education (VIIBRE) who led its development, the device faithfully reproduces the response of cardiac cells in a living heart. "This confirms that our hearton-a-chip model provides us with a new way to study the elastic response of cardiac muscle, which is extremely complicated and is implicated in heart failure, hypertension, cardiac hypertrophy and cardiomyopathy," Sidorov added.

Source: Vanderbilt University Image Credit: VIIBRE/Vanderbilt

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