

Heart-on-a-Chip Technology Directly Measures In-Vivo Cardiac Performance



At the AHA Scientific Sessions in Philadelphia, data from a study of investigational candidate, MYK-491, showed that a human iPSC-derived organ-on-a-chip technology can directly measure in vivo cardiac performance. MYK-491 increases the contractility of the heart (systolic function) with minimal or no effect on myocardial relaxation and compliance (diastolic function) by acting directly on the proteins in the heart muscle responsible for contraction.

Michael P. Graziano, PhD, chief scientific officer of TARA Biosystems said, "Replicating complex physiology in systems that up to now could only be seen in animals positions our technology as a faster, cheaper, and more human-relevant alternative to animal testing."

In the presented study, the effects of MYK-491 were evaluated in instrumented canine models and the human cardiac organoid model. The results indicate agreement between the two models, both showing improvements in systolic elastance (force production) with negligible effects on diastolic function. Both systolic and diastolic tension are dysregulated in patients with heart failure and, given their load dependency, systolic and diastolic mechanics have been difficult to measure in an in vitro setting, typically requiring studies in large animals with advanced instrumentation to capture such complex, integrated functional effects preclinically. The organ-on-a-chip platform may offer an in vitro alternative to collect such measurements in a human setting.

"In the study reported today at AHA, the human heart-on-a-chip technology provided confirmatory preclinical evidence of what we have seen in our other preclinical and clinical studies: MYK-491 appears to increase systolic contractility without impacting diastolic relaxation," said Robert McDowell, PhD, chief scientific officer of MyoKardia. "This platform may serve as a valuable human translational model for cardiovascular drug discovery with its ability to capture the nuances of human heart contraction and relaxation mechanics."

The uses of human induced pluripotent stem cells (iPSCs) holds great promise as a foundation to bridge the human translation gap. However, experimental models, which rely on iPSCs alone lack relevant physiological hallmarks and drug responses seen in human heart muscle. The research also showed how the platform could be used to model different heart diseases by using iPSCs from patients. Additionally, findings published recently in the *Journal of Toxicological Sciences*, show that the 3D-cardiac tissue platform predicts responses to a wide range of drugs known to affect cardiac function in humans, something that has been a challenge in pre-clinical models until now.

Source: AHA Scientific Sessions 2019/CG Life
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