Researchers use light to control human heart cells and expedite development of new drugs

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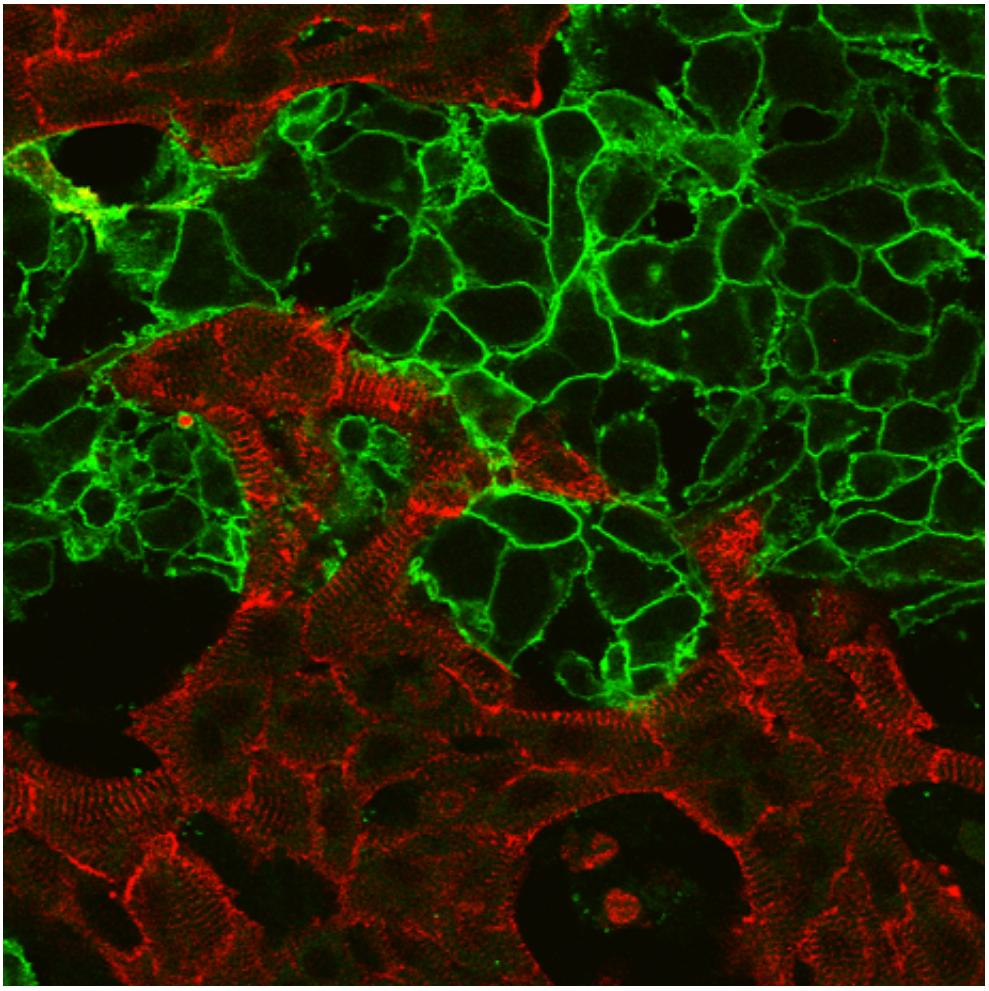

Using light, "spark" cells (green) and automation, Entcheva's lab speeds up the process of drug screening in heart cells (red) to help bring safer drugs to market. Credit: Dr. Christina M. Ambrosi

A team of researchers at the George Washington University has developed a faster method to predict whether potential new drugs will cause heart arrhythmias using optogenetics, a technique that uses light to control cells. While optogenetics has been used in neuroscience for a decade, this technique is relatively new in cardiac research.

In the newly developed system, the research team used light to both make the cardiac cells beat and to optically measure their response. This allowed them to automate the drug-testing process, offering a fast, new way to rule out potentially dangerous drugs. The technique streamlines a primarily manual process that researchers carry out to comply with FDA testing requirements and ensure the safety of the drugs. The team's current system can test 30,000 light-responsive cells in fewer than 10 minutes - a far shorter timeline than the standard practice, which can take hours or even years.

The research is outlined in a paper, "OptoDyCE as an Automated System for High-Throughput All-Optical Dynamic Cardiac Electrophysiology," which published in *Nature Communications* on Tuesday.

"This new method has the potential to vastly improve the speed at which we get safe and essential drugs to seriously ill patients," said Emilia Entcheva, professor of biomedical engineering at GW and senior author of the paper. "Importantly, we demonstrate this can be done using a patient's own blood cells by combining stem-cell techniques with our new method. One of the biggest challenges with developing new medications is testing to make sure we are treating a problem without causing any cardiac toxicity. This technology helps us to ensure that we are doing just that."

In order for medications to be approved by the FDA, they must be vetted to make sure they do not pose a danger to the heart or any other part of

the body. In the earliest phases of testing, cells are treated with the medication to see how they react. Traditionally, the most reliable method is to measure their response manually, by directly sticking probes into the cell. New high-throughput technologies speed up this practice. However, until now no such high-throughput system has been available for work with actual heart cells. Dr. Entcheva's research helps provide a more complete picture of how the drug could affect the heart early in the drug development process, saving time and resources that can be spent on other new drug candidates.

"The benefit of optical stimulation and optical recording is that it provides a way to dynamically control millions of cells simultaneously without needing to come into contact with the sample," said Aleks Klimas, first author on the paper and Dr. Entcheva's Ph.D. student. "This not only allows you to perform faster testing but also provides a safer way to do measurements if you're testing hazardous materials."

Separate from its uses in the drug discovery arena, the method can also be used by scientists to confirm that stem cells have properly matured into heart cells. The new technique will help them improve the quality of these newly created heart cells and speed up their deployment in the clinic.

The technology has the potential to be adopted by pharmaceutical companies to expedite the drug development process. Following the completion of her Ph.D. in biomedical engineering at GW, Ms. Klimas hopes to commercialize the idea and develop a business to market the device.

More information: Aleksandra Klimas et al. OptoDyCE as an automated system for high-throughput all-optical dynamic cardiac electrophysiology, *Nature Communications* (2016). DOI: 10.1038/ncomms11542

Provided by George Washington University

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