Human BioMolecular HBRI Research Institute

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A Way to Safer New Drugs

San Diego, California – October, 2017. Medicinal chemists and biologists at the Human BioMolecular Research Institute (HBRI), in San Diego, CA, and Sanford-Burnham-Prebys Medical Discovery Institute (SBPMDI), in San Diego, CA, respectively, have reported on a technology to monitor action potential (AP) kinetics and arrhythmia phenotypes in human cardiomyocytes in a high throughput manner *in vitro.* This may have importance for heart disease and other drug discovery efforts. Previously, conventional methods have been too costly or technically challenging to execute in high throughput. In addition, human cardiomyocytes were limited. Now, the ability to produce unlimited numbers of patient-specific human induced pluripotent stem cell-derived cardiomyocytes (hiPSC-CMs) creates a new paradigm for modeling congenital heart diseases and predicting proarrhythmic liabilities of drug candidates. Writing in October, 2017, in the journal *Frontiers in Physiology,* the authors describe the first large-scale, fully automated and statistically robust analysis of AP kinetics and drug-induced proarrhythmia in hiPSC-CMs. With this new method, researchers are also enabled to do drug discovery.

The method combines optical recording of a small molecule fluorescent voltage sensing probe, an automated high throughput microscope and automated image analysis to rapidly generate physiological measurements of cardiomyocytes. The technique can be adapted to other high content imagers to evaluate patient-derived hiPSC-CMs and predict proarrhythmic effects of drug candidates. A high throughput method for determining arrhythmias enables development of compounds to treat patients with heart disease and to develop other safer drugs that do not induce arrhythmias.

"*We believe that the technology will lead to compounds that prove potent in vitro and efficacious in clinical trials, at lower doses, resulting in greater patient tolerance, and less side effects*"… explains co-author Dr. John Cashman. "*As drug development progresses,*

and less toxic drugs become available, patients will benefit from improved safety, possibly with significant cost-savings."

The chemists and biologists at HBRI and SBPMDI are the first group to apply high throughput methods to generate information on proarrhythmic liabilities of drug candidates. Armed with this expertise, the researchers will apply similar strategies to development of other drugs, where new drug candidates may show increased efficacy.

Wesley L. McKeithan, Alex Savchenko, Michael S. Yu, Fabio Cerignoli, Arne A. N. Bruyneel, Jeffery H. Price, Alexandre R. Colas, Evan W. Miller, John R. Cashman and Mark Mercola (2017) An Automated Platform for Assessment of Congenital and Drug-Induced Arrhythmia. *Frontiers in Physiology* **8**:766.

Media contacts: To arrange on-site, phone, or Skype interviews with the researchers involved in this study, please contact John Cashman at (858) 458-9305 / JCashman@hbri.org or Mark Mercola at Sanford-Burnham-Prebys Medical Discovery Institute at 858-795-5242 or Stanford University at mmercola@stanford.edu

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About Human BioMolecular Research Institute

The Human BioMolecular Research Institute is a non-profit research institute conducting basic research focused on unlocking biological and chemical principles related to diseases of the human brain, cardiovascular disease and cancer. The Institute conducts fundamental studies of central nervous system disorders, heart disease and cancer including stem cell approaches and translates findings into new drug development to address human illness. In addition, the institute promotes scientific learning through community service and public access by disseminating information and sharing research with collaborators, colleagues and the public. For more information, visit us at www.HBRI.org.

About Sanford Burnham Prebys Medical Discovery Institute

Sanford Burnham Prebys Medical Discovery Institute (SBPMDI) is dedicated to discovering the fundamental molecular causes of disease and devising the innovative therapies of tomorrow. The Institute consistently ranks among the top five organizations worldwide for its scientific impact in the fields of biology and biochemistry (defined by citations per publication) and currently ranks third in the nation in NIH funding among all laboratory-based non-profit research institutes. SBPMDI utilizes a unique, collaborative approach to medical research and has established major research programs in cancer, neurodegeneration, diabetes, and infectious, inflammatory, and childhood diseases. The Institute is especially known for its world-class capabilities in stem cell research and drug discovery technologies. SBPMDI is a U.S.-based, non-profit public benefit corporation, with operations in San Diego (La Jolla), California and Orlando (Lake Nona), Florida. For more information, news, and events, please visit us at http://www.sbpdiscovery.org.