SickKids
Industry Partnerships & Commercialization

TECHNOLOGY BRIEF

DIAGNOSTICS & RESEARCH TOOLS

MATCH: Machine learning algorithms for toxicity and cardiac health

BACKGROUND

Dysfunction of the heart due to unexpected toxicity can be related to problems with reduced contractility or adverse changes to cardiac rhythm. These complex actions make *in vitro* modeling of heart function challenging and preclinical animal models suboptimal, leading to significant problems in predicting the effect of pharmaceuticals on the heart. As a result, unexpected cardiac toxicity eliminates 30% of drug candidates from development pipelines and 16% of post-market drugs.

Current drug discovery and preclinical models of cardiac function do not accurately predict cardiac activity or toxicity, resulting in high rates of unexpected failure. To improve prediction and elimination of compounds with potential cardiotoxicity earlier in the drug discovery continuum, a test integrating multiple cardiac outputs with greater certainty and throughput is required.

DESCRIPTION OF THE INVENTION

Our cardiotoxicity platform incorporates multiple tests of cardiac function into a unified, multi-parametric system, providing predictive power. Our use of non-biased machine learning algorithms allows us to determine which metrics are most predictive of human cardiac activity, eliminating unnecessary tests and setting an industry standard for *in vitro* cardiac activity screening.

1. Multiple Electrode Array Analysis: determines the effect a compound may have on ion channel flux and cardiac electromechanical coupling, utilizing functional 2D monolayers of cooperatively beating iPSC-CM cardiac "tissue" (Fig 1) and analyzed using algorithms.

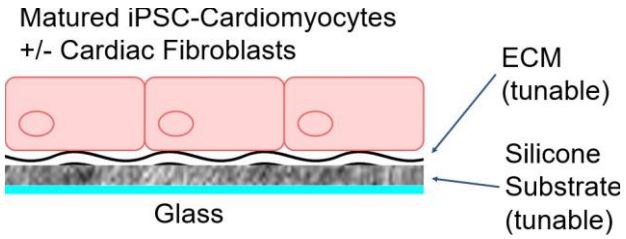

Fig 1: 2D monolayer of iPSC-CM cardiac tissue.

2. Beating and Contractility Analysis: determines how a compound alters tissue contractility and beating rate and rhythm using our carbon nanotube sensor device developed and patented for the purpose of determining drug effect on cardiac tissue composed of iPSC-CMs, which we have illustrated to be the first platform assay that recapitulates the *in vivo* effect of cardioactive drugs.

KEYWORDS
Cardiac, drug discovery, toxicity, platform, artificial intelligence, machine learning

3. Real-time Tissue Stiffness Analysis: determines how a compound alters tissue function in the context of a healthy (soft) and diseased (stiff) heart, using our advanced imaging and optical flow analysis to determine changes to cardiomyocyte function. This analysis is unique and illustrates how drug effect is dependent on the context of overall organ health.
The above three parameters are integrated through a proprietary cardiac activity machine-learning classifier against known drug classes (together called "MATCH") (Fig 3).

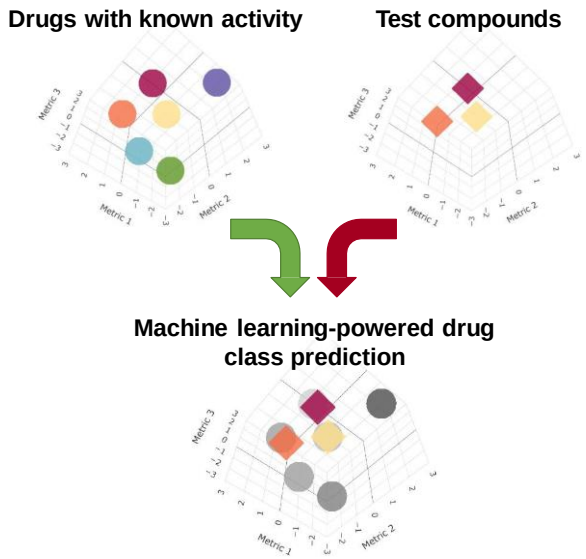

Fig 2: Our proprietary cardiac activity machine-learning algorithm called "MATCH"

MATCH identifies the cardiac activity/toxicity of the investigational drug(s) and generates a comprehensive report (Fig 3).

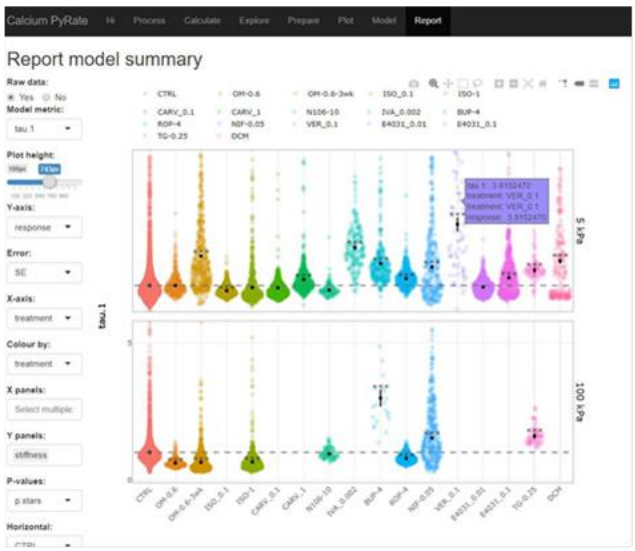

Fig 3: Comprehensive report generated by the MATCH platform

COMMERCIAL APPLICATIONS & ADVANTAGES

MATCH integrates multiple cardiotoxicity assays into a single a machine learning-based report designed to seamlessly integrate into contemporary preclinical drug discovery hit to lead validation. It provides a robust cardiotoxicity profile unparalleled in the industry translating to reduced cardiotoxicity of drug candidates, reducing failures and improving clinical trial success.

DEVELOPMENT STAGE

MATCH is a fully developed assay system validated through use in several drug discovery screens.

PATENT STATUS

PCT application filed.

IP&C is seeking partners to advance this technology.

LEAD INVENTORS:
Dr. Jason T. Maynes, MD, PhD, Chief, Anesthesia and Pain Medicine, Curtis Joseph and Harold Groves Chair in Anesthesia and Pain Medicine, The Hospital for Sick Children
Dr. Yu Sun, PhD, Professor, Canada Research Chair in Micro and Nano Engineering Systems; Director, University of Toronto Robotics Institute

LICENSING CONTACT:
Bradford T. Brinton, PhD, Senior Manager, Tel. 416.813.7654 ext. 309444, brad.brinton@sickkids.ca
IP&C Ref. | RDLP 1071