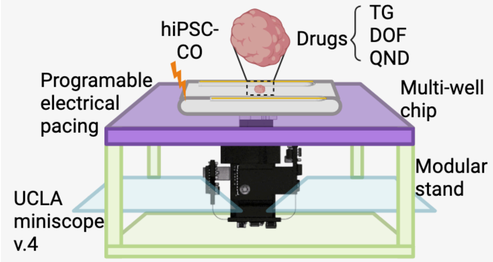
Using the Heart-on-a-Miniscope System to Investigate the Calcium Signal Dynamics of Human iPSC-derived Cardiac Organoids

Sanskriti Shindadkar[1], Michelle Phan[1], Karley Tioran[1], Dyala Omar[1], Yuqi Zhang[1], Liang Gao[1,3], Jijun Huang[2,3]

[1] UCLA Samueli School, Bioengineering, equal contributors, [2] Department of Medicine, UCLA David Geffen School of Medicine, [3] Co-senior author.

Introduction

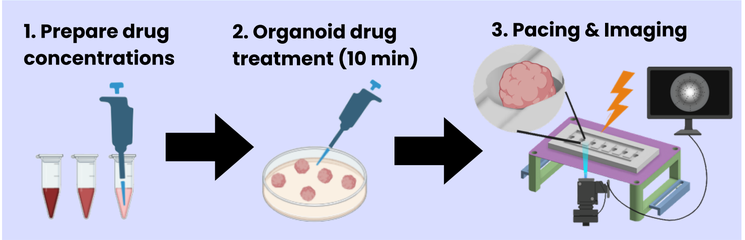
Our Goal: Develop the Next-Generation Heart-on-a-Miniscope: An Integrated Platform for Human Induced Pluripotent Stem Cell derived Cardiac Organoids (hiPSC-CO)



- **Improvements:** Updated imaging, housing, pacing, analysis, and validation.
- **Application:** drug testing, complex disease modeling: Heart Failure (HF-pEF)

Methodology

Data Collection



Fluoresence Raw Data

Ca^{2+} influx data

Mechanical Raw Data

Δ Area data

Data Processing

Denoising

Raw data

Filtered trace

Hypothesis for Drug Effects

Drug	Thapsigargin	Dofetilide	Quinidine
Full Width at Half Maximum (FWHM)	↑	↑↑	↑
Variability	↑↑	↑↑	↑
Contraction time	↔ or ↑	↑↑	↔ or ↑
Relaxation time	↑	↑↑	↑

Results

ROI auto-selected by Cellscope neural network

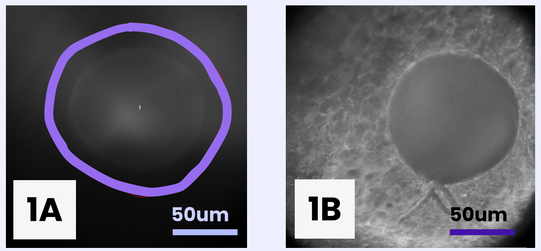


Figure 1: Successful capturing of the morphology of the hiPSC-COs on the miniscope. Visualized in fluorescence (A) and brightfield (B); Edges are brighter due to dye diffusion limits.

Measurement of Alterations in Calcium Transients (F/F0)

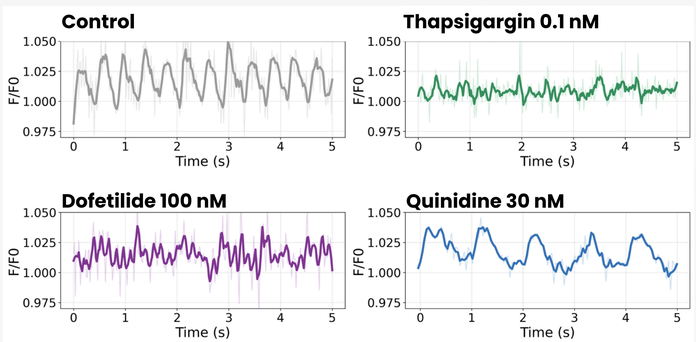


Figure 2: Quantification of fluorescence signals of the control group (untreated), Thapsigargin, Quindine, and Dofetilide.

Measurement of Mechanical Contractions Using Change in Area (Fractional Change)

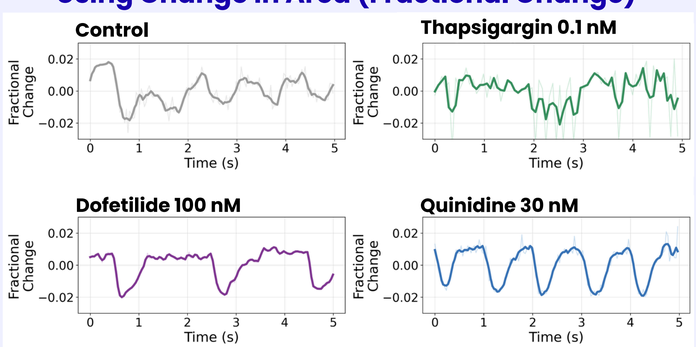


Figure 3: Quantification of mechanical movement of the different treatment groups.

Analysis and Discussion

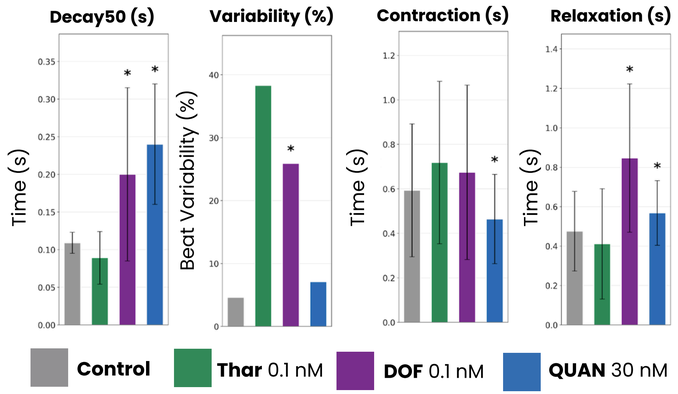


Figure 4: Visualized metrics of the different treatment groups.

Figure 4.
- **Thar,** Thapsigargin (SERCA Inhibitor)
- **DOF**, Dofetilide (IKr Blocker)
- **QUAN**, Quinidine (Na^+ and K^+ Channel Blocker)
- One-Way ANOVA with post-hoc pairwise comparisons (each drug vs Control) was calculated and labelled * on the bar chart if $p < 0.05$, for Decay50, Contraction, and Relaxation Time. To determine whether variability itself differs, we used Levene's test (variance-comparison test). These were paced at 0.5Hz.

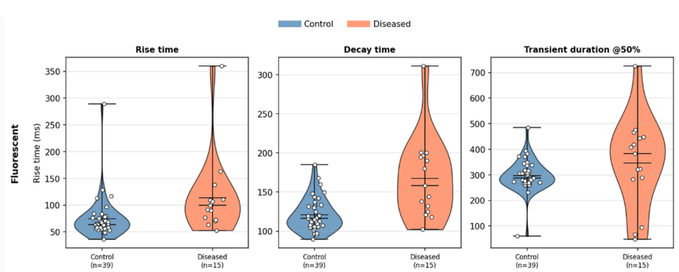


Figure 5: Comparison of the fluorescence rise time and decay time, as well as transient duration of the control vs diseased organoids.

Figure 5, Comparison of the fluorescence rise time and decay time, as well as transient duration of the control vs diseased organoids. Error bars were shown as standard deviation. The trend is that diseased cells have a larger range.

Limitations:
- Tradeoffs between image quality (brightness) and glare (Harder for signal processing)

Conclusion

Our Findings
- ☑ Drug response followed hypothesized trend
- ☑ Designed miniscope system successful

What is in Progress
- ☐ Increase sample size
- ☐ Test drugs in HFpEF-modeled organoids

Applications

Organoid analysis in many research areas

Disease Modeling | Drug Screening | Precision Medicine

Acknowledgements

Thank you to Dr. Huang, to the Aharoni lab, particularly Federico Sangiuliano, and Pouria Tirgar (author of the original Heart-on-the-Miniscope), Dr. E. Dale Abel lab, and the Capstone team. Our GitHub repository is available for everyone working on contractility and calcium transience, linked in the QR Code along with our results.