Ashton Szarnicki

Roche Award

Chemistry Major

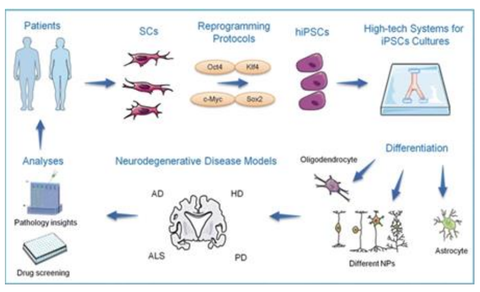
First Year ARCS Scholar

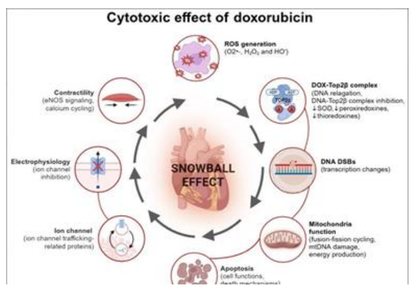
MOREHOUSE COLLEGE

Evaluating Dexrazoxane's Cardioprotective Efficacy Against Doxorubicin in Human Cardiomyocyte Models

Using both 2D and 3D hiPSC-derived cardiomyocyte platforms, we investigated whether dexrazoxane could mitigate doxorubicin-induced toxicity. These results validated the dose-dependent toxicity of doxorubicin and established the viability of hiPSC-based platforms to provide valuable insights into drug interactions within cardiac tissues.

Background





2D HiPSC/Materials

Figure 1. hiPSC -seeded microtissue Molds.

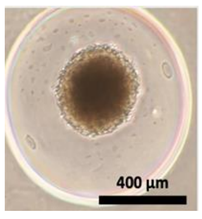


Figure 2. An individual microtissue.

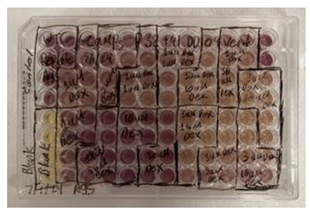
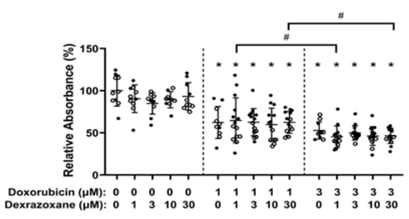


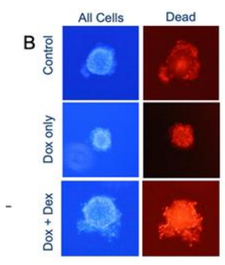
Figure 3. 96 well plate after being treated with MTT solubilization and thoroughly mixed.

Preparation of 2D cell culture. Cardiomyocytes were cultured for ~ 2 weeks along with lactate purification before use. Each 96 well plate was seeded with 35,000 Cardiomyocyte cells each well and cultured for 3 days.
Microtissue creation process. 5,985,000 hiPSC-cardiomyocytes and 315,000 fibroblast (5%) were seeded into 18 agarose molds with ~ 332,500 cells per each mold. After culturing for 7 days, the agarose molds were transferred over to a 6 well plate with PDMS holders, treated, and cultured for an additional 3 days.

Results



MTT cell viability response to dexrazoxane during 72-hour doxorubicin treatment in 2D hiPSC-derived cardiomyocytes. Effects of prolonged (72 hours) doxorubicin treatment at 1 μM and 3 μM concentrations on cardiomyocyte viability with co-administration of varying dexrazoxane doses (1, 3, 10, 30 μM). Circles represent individual data points with filled and empty circles representing two individual experiments (N = 9-14). Error bars represent mean ± standard deviation. * denotes statistical significance compared to non-doxorubicin treated group with same dose of dexrazoxane. # denotes statistical significance of the 1 μM and 3 μM doxorubicin treated group with same dose of dexrazoxane.



Live dead cell response to dexrazoxane after 72-hour doxorubicin treatment in 3D hiPSC-derived cardiac microtissues.
(B) Representative images of single microtissues with live/dead staining. Circles represent individual data points (N =4). Error bars represent mean ± standard deviation. *denotes statistical significance of the 1 μM and 3 μM doxorubicin treated group compared to the non-doxorubicin treated group.

Conclusion

In this study, we evaluated the cardioprotective effects of dexrazoxane against doxorubicin-induced cardiotoxicity in both 2D and 3D models simulating human cardiac tissue. Our results demonstrate:

- That dexrazoxane did not effectively prevent doxorubicin-induced loss of metabolic activity (Fig. 5).
- 3D microtissue models showed similar cell death between dexrazoxane treated cells and doxorubicin only controls. (Fig. 6 A-B).
- These results in both 2D and 3D models validate the dose-dependent toxicity of doxorubicin.

Scholar Awards Celebration

November 12, 2025

SCHOLAR AWARDS CELEBRATION ARCS FOUNDATION ATLANTA

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