Title: Exploring Doxorubicin-mediated Hypertrophy and Cell Death in Primary Human Cardiomyocytes

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Purpose: Doxorubicin used to treat cancer is dose-limited due to its adverse effect of cardiotoxicity. In this study, we observe hypertrophy and cell death caused by doxorubicin treatment, and we determine ways to prevent cardiotoxicity but still get an effective treatment for cancer.

Methods:

In this study, we used cell-based and bioinformatic approaches. For our cell-based approach, we treated primary human cardiomyocytes with doxorubicin or etoposide and assessed their sizes by tracing the area of the cells with a program called ImageJ. The average areas were expressed as a relative size to untreated cells. Using bioinformatic analysis, we searched for evidence that would suggest certain drugs would prevent the disruption of calcium homeostasis in cardiomyocytes by doxorubicin. We used Comparative Toxicogenomic Database to look at common genes between the ryanodine receptor and drugs used in cardiology.

Results:

Overall, we found that doxorubicin-mediated cardiotoxicity is due to hypertrophy and cell death. After 24 hours of treatment with doxorubicin, cardiomyocytes increased in size with a concentration dependent effect, and after 72 hours of treatment, cell death increased with increasing concentration. We also found evidence suggesting certain drugs may interact with the ryanodine receptor.

Conclusions

In conclusion, we performed cell-based and bioinformatic analysis on doxorubicin-treated primary human cardiomyocytes to examine cardiotoxicity. This study showed that hypertrophy and cell death occurred in cardiomyocytes that were treated with doxorubicin, and based on the bioinformatic results, there is a potential system that could counteract this cardiotoxicity. Based on the results, there is a potential system that could counteract doxorubicin-mediated cardiotoxicity. This means that cardiotoxicity may be prevented in patients being treated for cancer with doxorubicin.