# High Resolution Respirometry of Heart Mitochondria in Healthy and Stressed States

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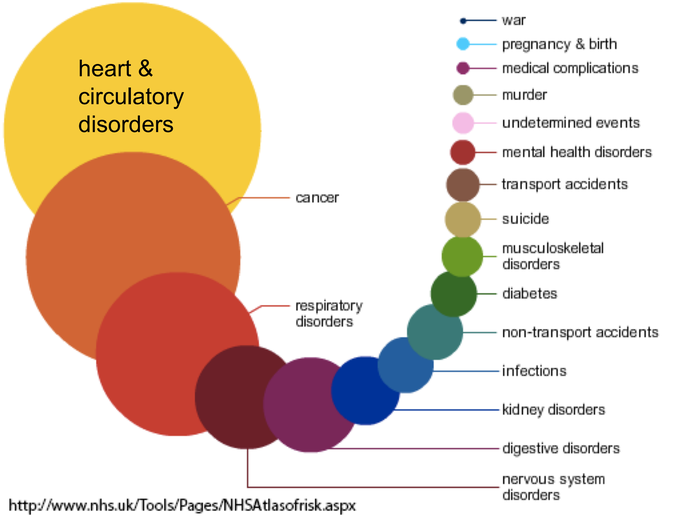
## Abstract

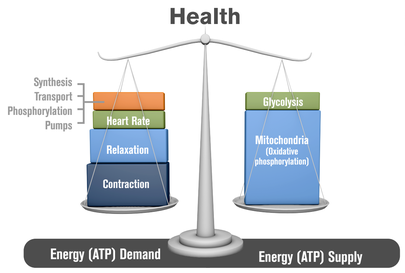
Heart disease remains the leading cause of death globally, claiming the lives of nearly 10 million people in 2016. Current standard-of-care therapies for heart disease patients reduce energy demands on the heart but do not treat underlying deficits in cellular energy production. Cardiac mitochondria are primarily responsible for the production of energy in the heart, and targeting dysfunctional mitochondria represents a promising solution to improving the prognosis of heart disease patients. Increased production of reactive oxygen species in heart disease damages mitochondrial function, ultimately decreasing cardiac energy supply. Isolated mitochondria exposed to hydrogen peroxide serves as a heart disease model where the reactive oxygen species damage the respiratory chain, a series of complexes responsible for the actual production of energy. N-acetylcysteine (NAC) is a drug precursor to glutathione, an endogenous antioxidant which reduces reactive oxygen species. In this project, isolated mitochondria are treated with hydrogen peroxide with or without NAC. If NAC is capable of rescuing the respiratory rate, that would suggest that NAC restores mitochondrial energy production in pathological states. If successful, these data would be the first step in determining if incorporation of NAC into heart disease treatment plans could begin to better treat the number of one cause of morbidity/mortality on the planet.

**Leading causes of death in perspective**

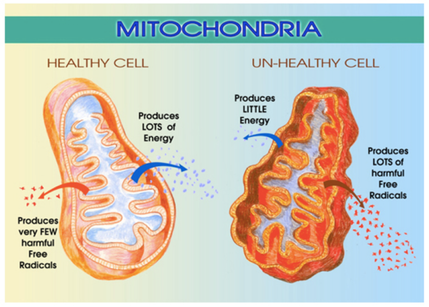



http://www.nhs.uk/Tools/Pages/NHSAtlasofrisk.aspx

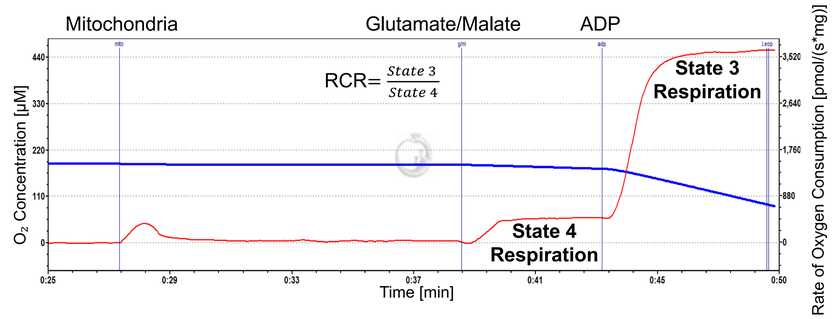
## Background

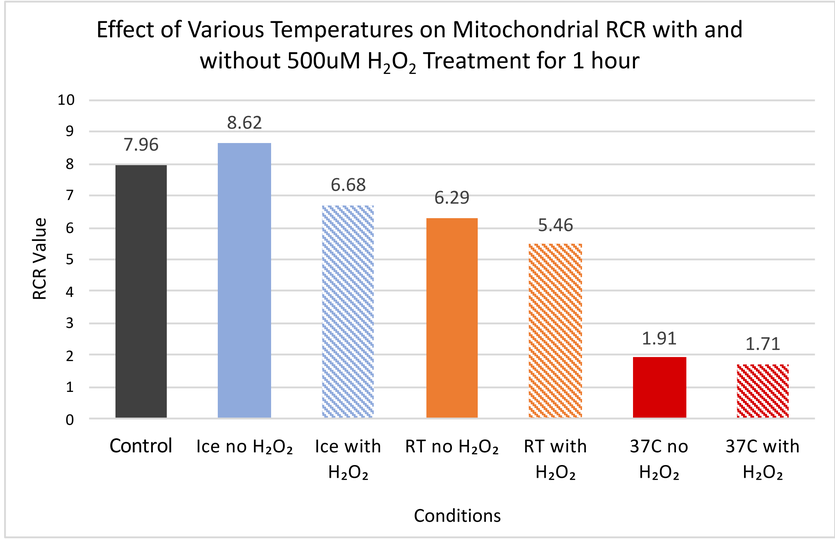



Current Treatments vs. Future Treatments



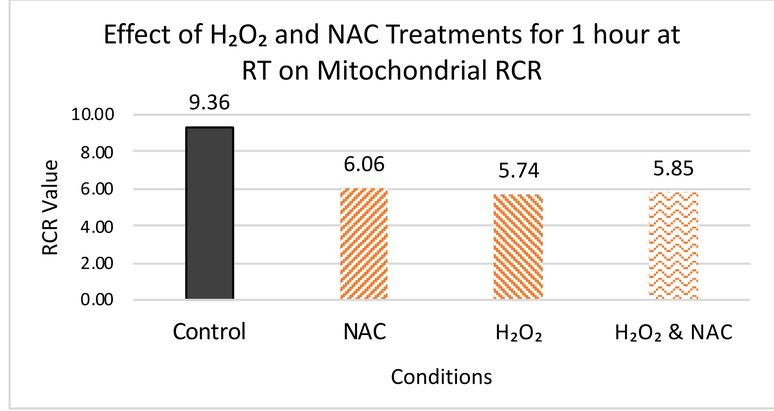

## Respiratory Stressors




| Percent Degree of Change in RCR Value Compared to Control | | | | | |
|---|---|---|---|---|---|
| Ice no $H_2O_2$ | Ice with $H_2O_2$ | RT no $H_2O_2$ | RT with $H_2O_2$ | 37C no $H_2O_2$ | 37C with $H_2O_2$ |
| +8.29 | -16.08 | -20.98 | -31.41 | -76.01 | -78.52 |

## NAC Decreases Damage




| Percent Degree of Change in RCR Value Compared to Control | | |
|---|---|---|
| NAC | $H_2O_2$ | $H_2O_2$ & NAC |
| -35.26 | -38.68 | -37.50 |

## Conclusion

- Further testing is needed to confirm the implications that NAC has the ability to restore respiratory capacity of cardiac mitochondria
- Future studies should focus on the potential of NAC as a heart disease treatment through testing with cells, whole hearts, and at the organismal level

## Acknowledgement

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Friedman, L. F. (2017). The things most likely to kill you in one infographic. Retrieved July 18, 2018, from https://www.independent.co.uk/news/health/the-things-most-likely-to-kill-you-in-one-infographic-a7747386.html

Brown, D. A., Perry, J. B., Allen, M. E., Sabbah, H. N., Stauffer, B. L., Shaikh, S. R., … Gheorghiade, M. (2016). Mitochondrial function as a therapeutic target in heart failure. *Nature Reviews Cardiology*, *14*, 238. Retrieved from http://dx.doi.org/10.1038/nrcardio.2016.203

Neustadt, J. (2018). Protect Your Mitochondria, Protect Your Health. Retrieved from https://nbihealth.com/protect-mitochondria-protect-health/

The top 10 causes of death. (2018). Retrieved July 18, 2018, from http://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death