

# COULD SUCCINATION LEAD TO CARDIOTOXICITY?

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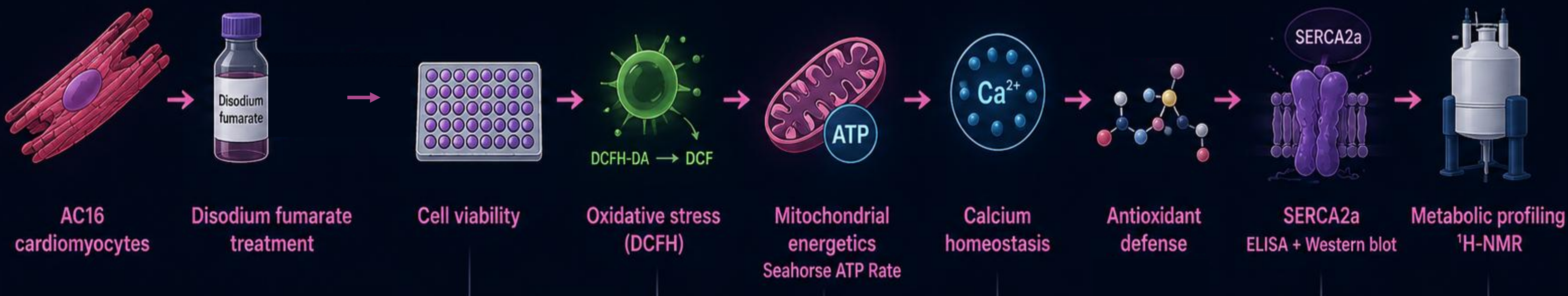
## Background

Cardiovascular disease is a leading global cause of mortality, and it leads to a reduced quality of life, driving the need to better understand the molecular mechanisms underlying disease progression. SERCA2a, a calcium pump essential for cardiomyocyte relaxation after each contraction, is a key regulator of cardiac function. Any impairment in SERCA2a activity is linked to cardiac dysfunction or even cardiotoxicity. A post-translational modification called succination that occurs when fumarate, a Krebs cycle intermediate, accumulates and reacts spontaneously and irreversibly with target proteins. This study investigates the role of succination in cardiac dysfunction/toxicity, with a focus on its impact on SERCA2a.

## Hypothesis

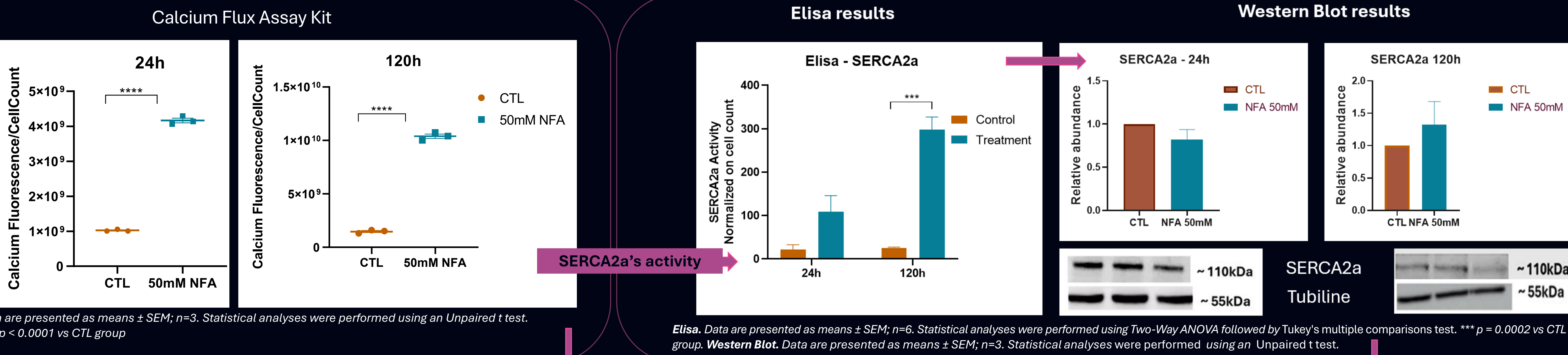
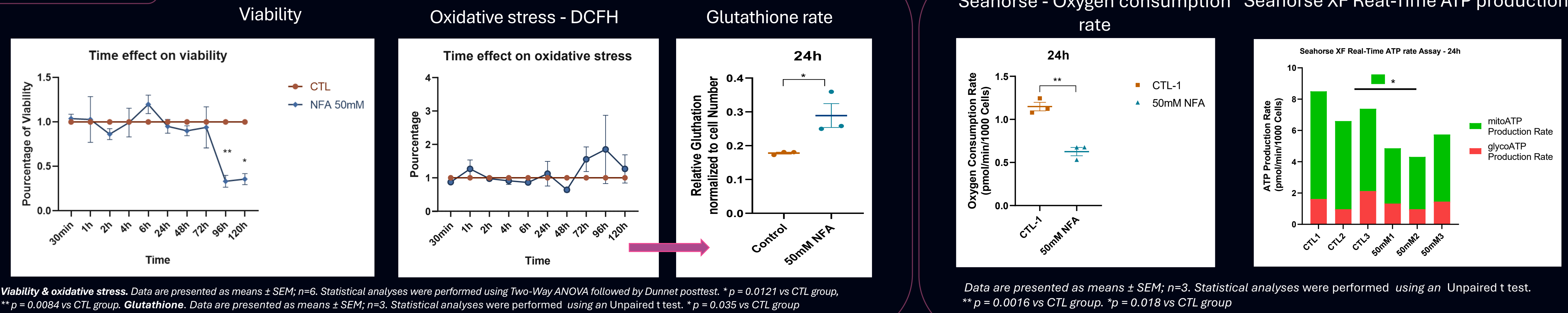
Fumarate accumulation and the subsequent succination could lead to cardiac dysfunction/toxicity in cardiomyocytes by impairing SERCA2a activity and calcium flux, as well as modifying other pathways such as oxidative stress and cellular energetics.

## Experimental design



**Objective:** To evaluate whether fumarate's accumulation/succination affects calcium handling and contributes to dysfunction in cardiomyocytes.

## Results



## Take home message

Fumarate accumulation may promote protein succination. This could alter calcium homeostasis and contribute to cardiotoxicity through mitochondrial dysfunction and impaired SERCA2a activity.

## Conclusion

## References

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