Exploring the impact of alcohol and SIV on skeletal muscle mitochondria in western diet-fed Rhesus Macaques

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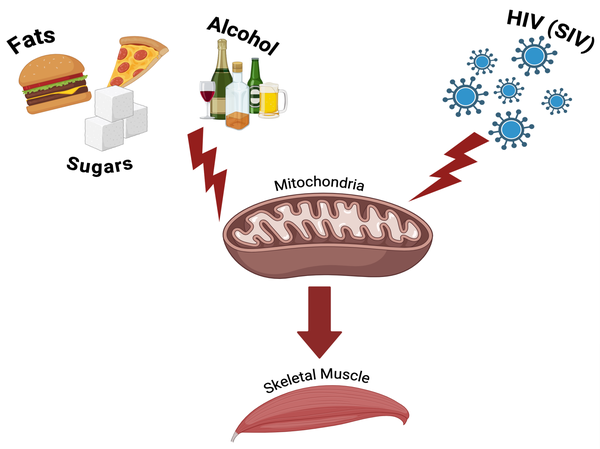
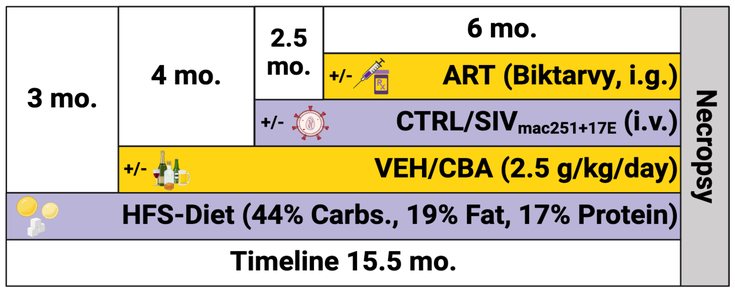
Background

- Skeletal muscle (SKM) is responsible for all movements performed by the body
- Along with structural support, the skeletal muscle also acts as storage for glucose, in the form of glycogen
- Human immunodeficiency virus (HIV/SIV) weakens the skeletal muscle
- Alcohol has also been linked to dysfunctions found in SKM mitochondria
- When combined, HIV and chronic binge alcohol (CBA) can prevent the mitochondria found in SKM from meeting the bioenergetic demand of the cell
- Without functioning mitochondria, SKM does not receive the energy needed to perform everyday function
- The lab studies the biogenetic dysfunction associated with SKM using preclinical CBA models in SIV infected Rhesus Macaques



Hypothesis: We hypothesis that alcohol and SIV, when combined with high fats and high sugars, will disrupt mitochondrial health.

Methods



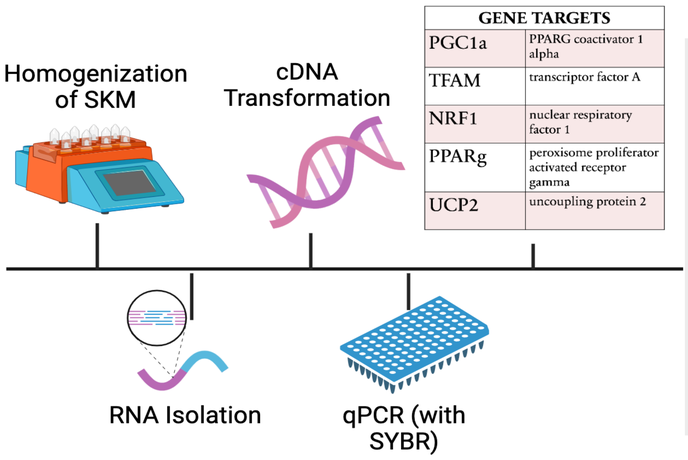
Experimental Design

Model: Adult male Rhesus Macaques on a western high fat/high sugar diet (HFSD)

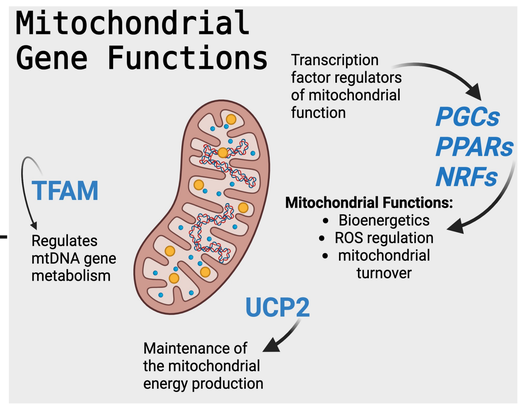
Groups

- **VEH/SIV**: Isovolumetric water vehicle (VEH) treatment + infected with SIV
- **CBA/SIV**: chronic binge alcohol treatment + infected with SIV

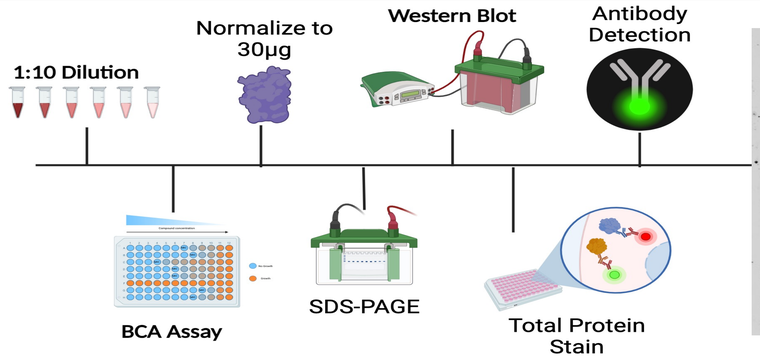
Relative mRNA Expression

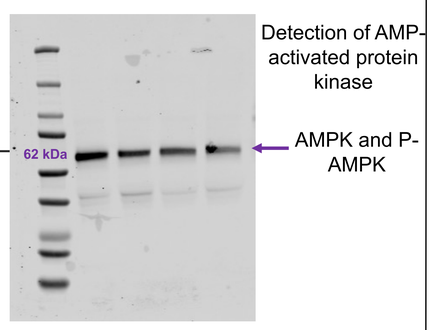


GENE TARGETS	
PGC1a	PPARG coactivator 1 alpha
TFAM	transcriptor factor A
NRF1	nuclear respiratory factor 1
PPARg	peroxisome proliferator activated receptor gamma
UCP2	uncoupling protein 2



Protein Expression Analysis





Results

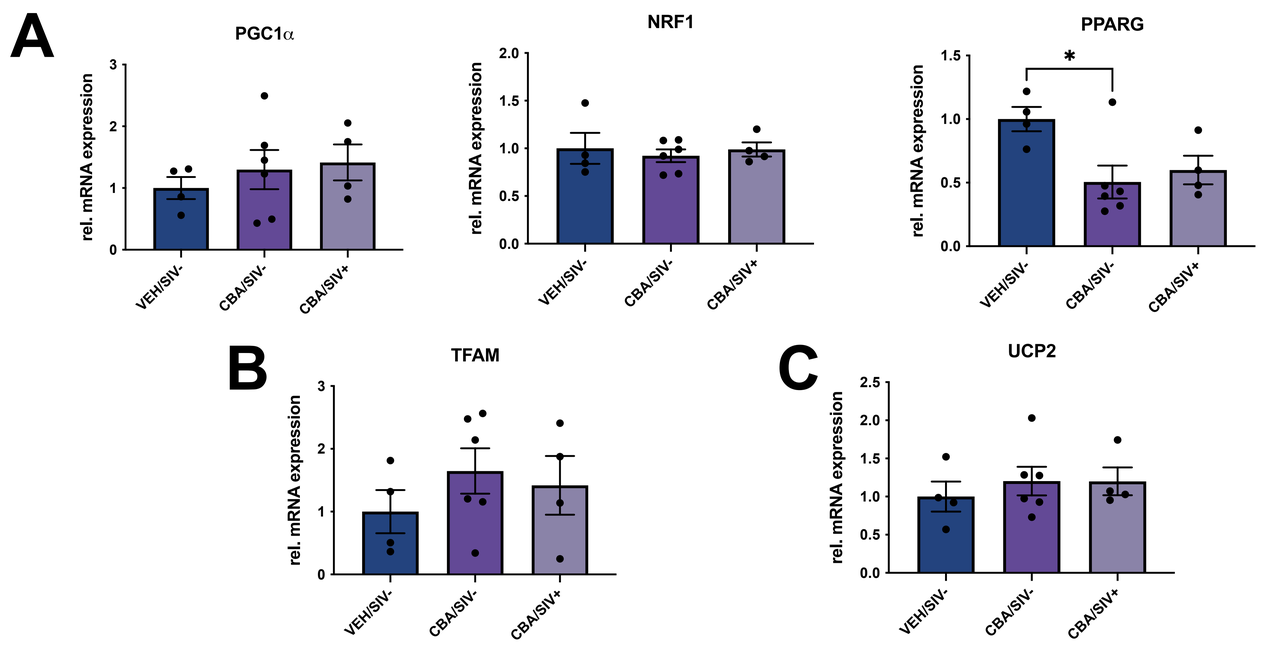


Figure 1. The effects of alcohol on mRNA expression in mitochondrial health associated genes derived from SIV-infected male rhesus macaques fed HFSD. (A) Transcription factor regulators of mitochondrial function (PPARG, PGC1α, NRF1). **(B)** Regulator of mtDNA gene metabolism (TFAM). **(C)** Maintains mitochondrial energy production (UCP2). n=4-6, *p<0.05. vs VEH/SIV-

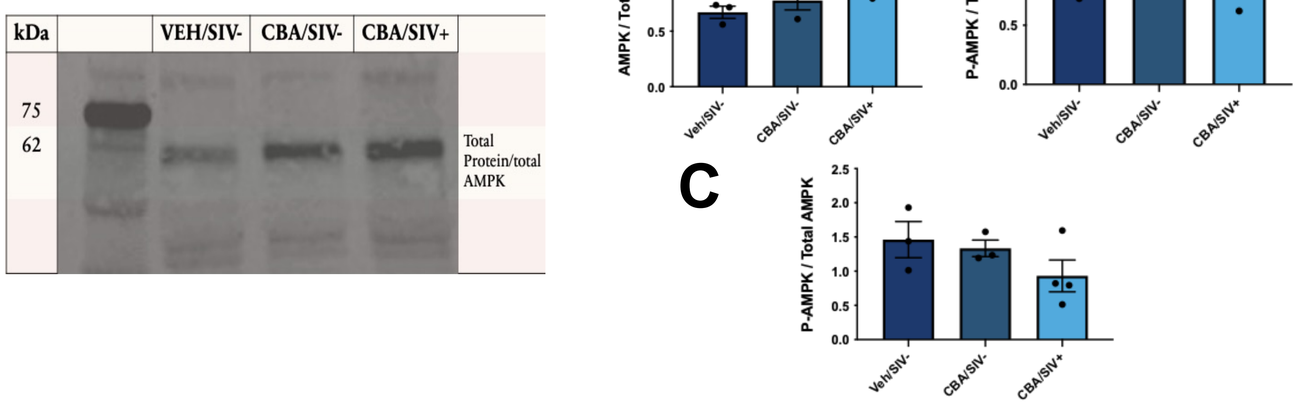


Figure 2. The effects of alcohol on AMPK protein expression in skeletal muscle derived from male rhesus macaques. (A) Representative immunoblot of total AMPK per group. **(B)** Relative protein expression of AMPK and P-AMPK normalized to total protein. **(C)** Relative protein expression of P-AMPK normalized to total AMPK. n=4-6, *p<0.05. vs VEH/SIV-

Summary

- Preliminary evidence shows that alcohol decreases mRNA expression of PPARg
- Preliminary study also shows an increase in total AMPK with alcohol in the SKM
- Since this is an on-going study, as more samples are added, the effects of alcohol on SKM mitochondrial health will be identified in HFSD fed SIV-infected macaques

Acknowledgements

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