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"Alcohol-mediated changes in mitochondrial dynamics proteins in skeletal muscle of SIV-infected female rhesus macaques"

In the United States, there are approximately 1.2 million people living with HIV (PLWH). With advancements in antiretroviral therapy (ART), PLWH have similar life expectancies as unaffected individuals, increasing risk for multimorbidity. Age-related comorbidities may be complicated by at-risk alcohol use, which is twice as prevalent among PLWH compared to the general population. Myopathy is common with at-risk alcohol use and dysfunction of mitochondria may contribute to its pathophysiology. Mitochondrial quality is maintained by the dynamic processes of fusion and fission. During fusion, mitochondria join and exchange material; during fission, mitochondria are separated to remove damaged portions of the network. Our recent work shows that mitochondrial quality is poorer in myoblasts from PLWH with higher Alcohol Use Disorders Identification Test (AUDIT) score and this was associated with decreased skeletal muscle (SKM) expression of mitochondrial dynamics genes: mitofusin 1 (*MFN1*), mitochondrial fission factor (*MFF*) and dynamin-related protein 1 (*DRP1*). Similarly, preliminary data for this study show that chronic binge alcohol (CBA) decreased SKM gene expression of optic atrophy 1 (*OPA1*) and *MFF* in a non-human primate model of HIV infection (SIV). We hypothesized that CBA decreases SKM expression of mitochondrial dynamics proteins in HIV/SIV infection.

Female rhesus macaques (4-10 years old) received CBA (50-60mM peak blood alcohol concentration) or isovolumetric water (VEH) five days per week, starting three months prior to infection with SIV_{mac251}. CBA was continued throughout the duration of the study. Daily ART was initiated 2.5 months after SIV infection, and macaques were euthanized 9 months later. SKM samples were collected before initiation of CBA or VEH (naïve, N=8) and at the time of euthanasia (VEH/SIV, N=8; CBA/SIV, N=7). Protein was extracted from flash-frozen SKM and quantified using a bicinchoninic acid assay, then 20 mg of protein was separated using SDS-PAGE according to molecular weight and transferred to polyvinylidene fluoride (PDVF) membranes. After immunoblotting, specific amounts of dynamics proteins (*OPA1*, *MFF* with others in progress) in SKM were visualized using enhanced chemiluminescence and quantified relative to β-tubulin. Data were analyzed using a Kruskal-Wallis test with an alpha level set to 0.05.

Neither OPA1 ($p=0.21$) nor MFF ($p=0.60$) expression was significantly altered by CBA. It is possible that expression of other mitochondrial dynamics proteins are more robustly affected by CBA or that alcohol alters protein activity via post-translational modifications. This is currently under investigation. Protein measurements will compliment ongoing studies examining the effects of CBA on SKM mitochondrial quality in the context of SIV/HIV.