Mitochondrial DNA in CSF is Associated with Inflammation and Defects of Neurocognitive Function in HIV Infection

Josué Pérez-Santiago1, Rachel D. Schrier1, Marta Massanella1, Sara Gianella1, Mariana Chernew2, Susanna R. Var3, Tyler R. C. Day1, Miguel Ramirez-Guana1, Davey M. Smith1, Ronald J. Ellis2, Scott Letendre3, and Sanjay R. Mehta1,4

1University of California San Diego, La Jolla, California, USA; 2Veterans Administration San Diego Healthcare System, San Diego, California, USA; and 3University of Alberta, Edmonton, Alberta, Canada

Objectives
To characterize the relationship between mitochondrial DNA (mtDNA) levels in cerebrospinal fluid (CSF) and neurocognitive function.

Methods
We quantified mtDNA levels in CSF of 28 HIV-infected patients by droplet digital PCR (ddPCR).

Conclusions
While mtDNA was not associated with the presence of NCI, higher levels of mtDNA were strongly associated with greater severity of impairment among those with NCI (Figure 1).

Higher levels of mtDNA were associated with more inflammation in the CNS and blood (Figure 2, 3), and was the strongest predictor of NCI severity (Table 2).

Levels of mtDNA in CSF preceded pleocytosis as mtDNA peak levels preceded pleocytosis (Figure 4).

Altogether these data suggest that mtDNA is a biomarker for severity of NCI. Given that mtDNA is pro-inflammatory and is strongly associated with other markers of inflammation in the CNS (IP-10, CD8+ T cells in CSF producing IFN-γ and IL-2), we hypothesize that either the source of mtDNA in individuals with NCI is from neurons or individuals with NCI have inflammatory mechanisms that are different than individuals who are NCI or NCD.

Table 1. Virologic, Immuneologic, and Neurocognitive Characteristics

Table 2. mtDNA in CSF is Strongest correlate of NCI severity

Table 3. mtDNA in CSF predicts pleocytosis

References

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Figure 1: Higher mtDNA in CSF is positively associated with worse neurocognitive performance among individuals with NCI.

Figure 2: Higher mtDNA in CSF is associated with inflammation in individuals with NCI.

Figure 3: Higher mtDNA in CSF is associated with inflammation if CSF VL is detectable in both NCI and NCD patients.

Figure 4: mtDNA in CSF precedes pleocytosis.

Figure 5: The relationship between mtDNA levels in CSF and levels of inflammatory cytokines in CSF and plasma was assessed using Spearman’s test.

Figure 6: In all cases mtDNA in the cerebrospinal fluid (CSF) of individuals with NCI was higher than in the cerebrospinal fluid of individuals without NCI.