



Mitochondrial DNA damage and brain ageing in HIV

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Background

- NCI in PLWH incompletely understood
- Limited data on role of ART toxicity in NCI

- Mitochondrial dysfunction implicated in ageing and in neurodegeneration (AD, PD etc.)
- Mitochondrial dysfunction well-recognised in PLWH
 - prior data largely associates with historical NRTI exposures

Methods

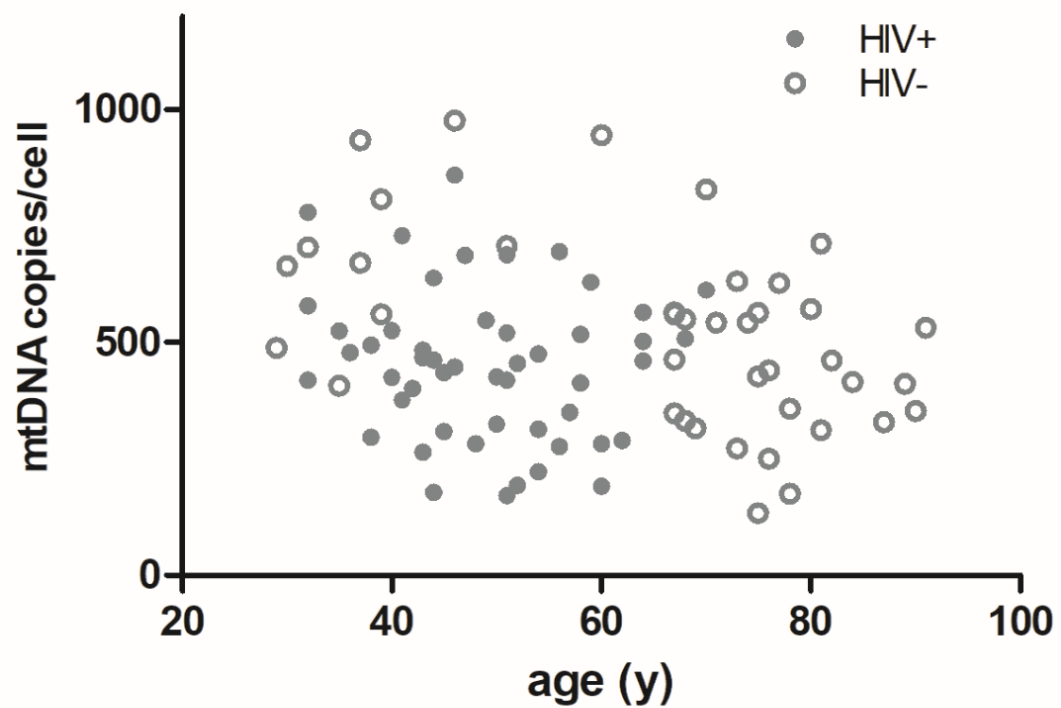
- Post-mortem frozen frontal grey matter
- HIV+ cases (52) / HIV- controls (40)
- Ante-mortem neurocognitive data
- Molecular analyses of mtDNA (qPCR, Illumina MiSeq)

Results: Sample characteristics

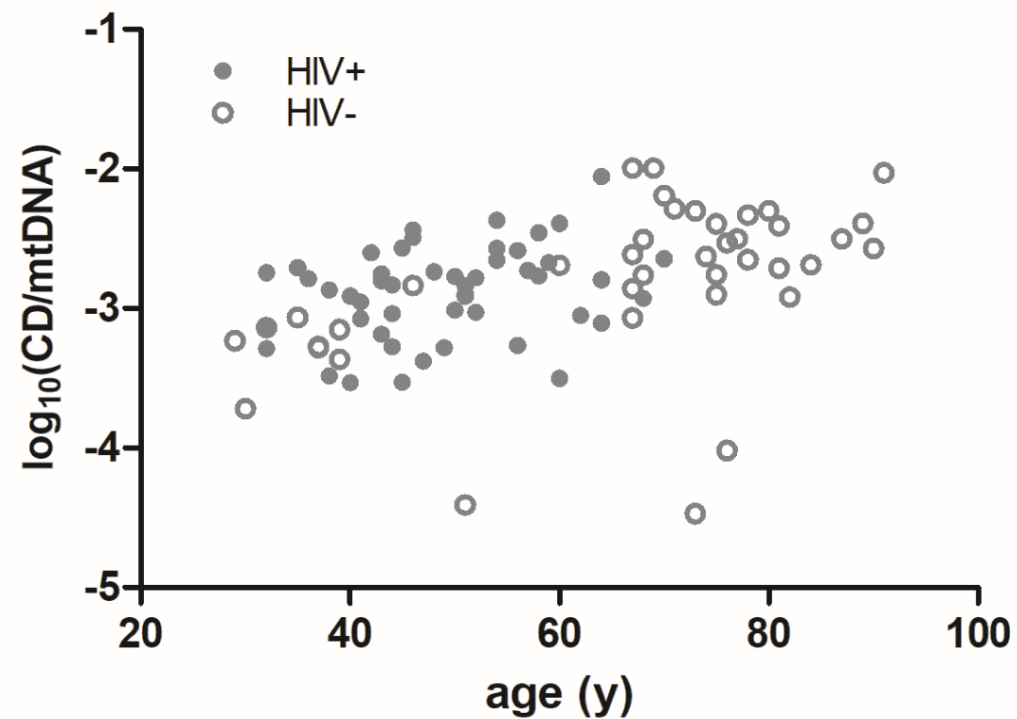
	HIV+	HIV-
n	52	40
Male	85%	70%
Age, mean (range)	49 (32,70)	66 (29, 91)
On ART at last antemortem study visit	74%	-
Ever ART treated	93%	-
Current CD4 count (cells/μL), median (IQR)	71 (25, 203)	-
HAND category (NN, ANI, MND, HAD)	9, 6, 14, 11	-

Results (1): Age

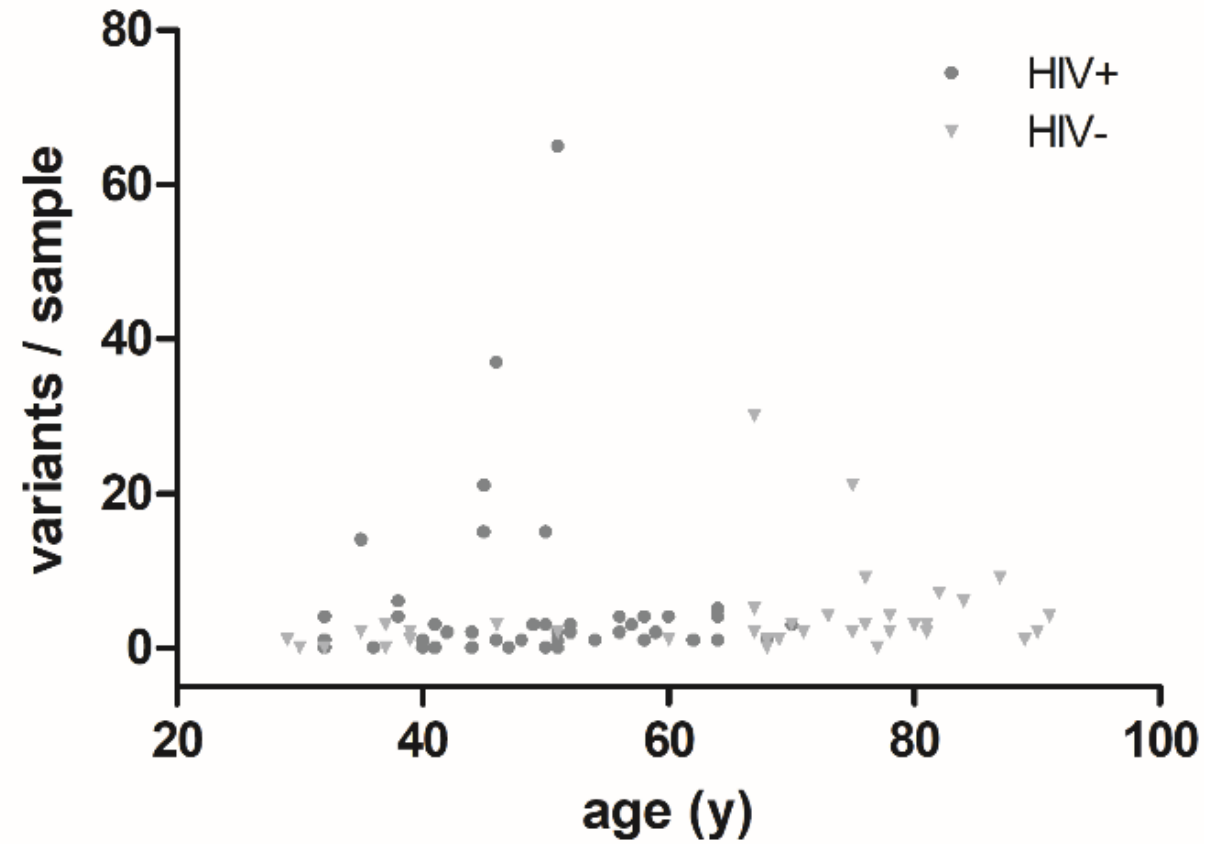
mtDNA content



mtDNA deletions

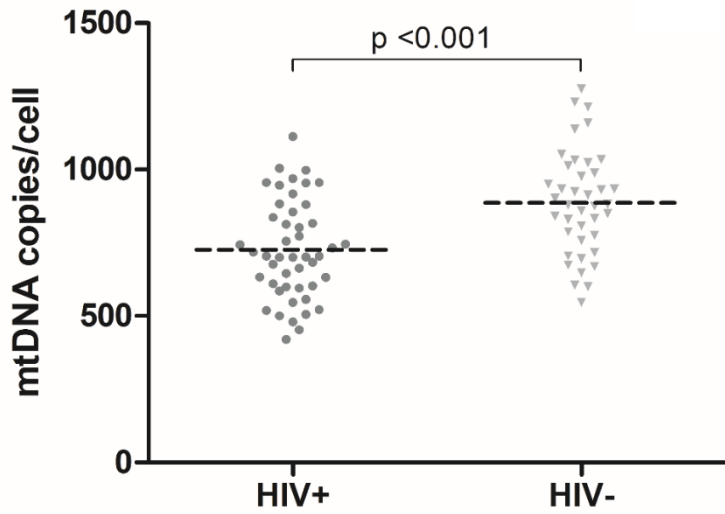


mtDNA point mutations

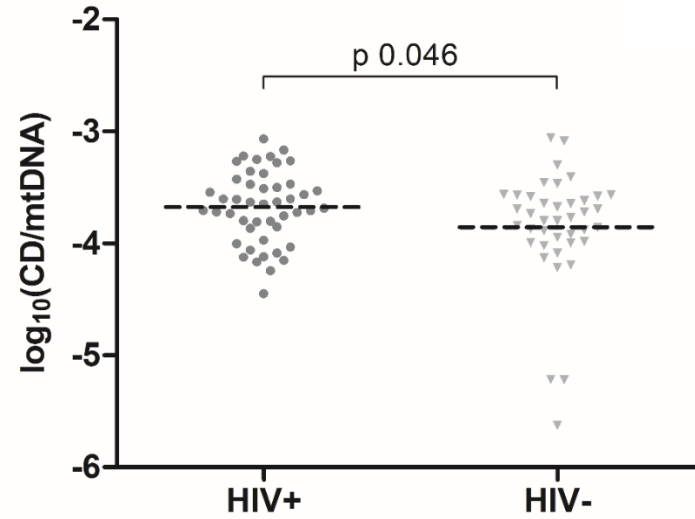


Results (2): HIV

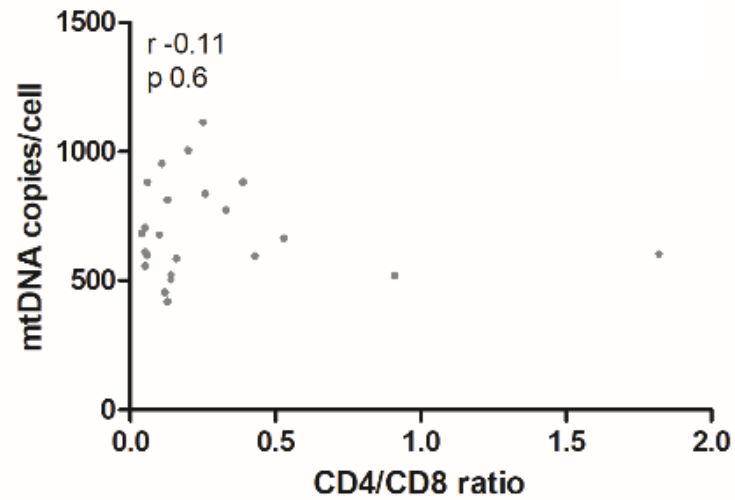
mtDNA content



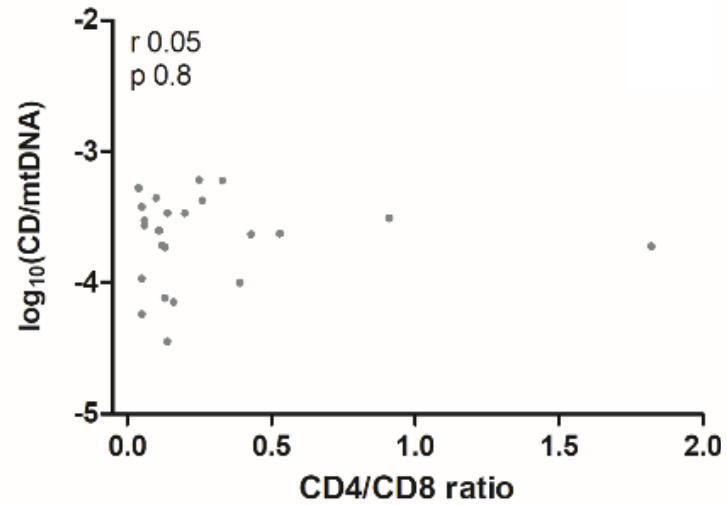
deletions



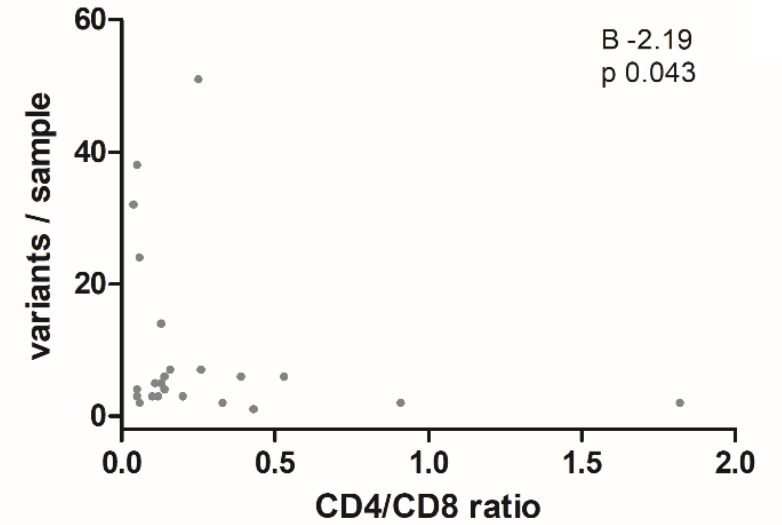
mtDNA
content



deletions

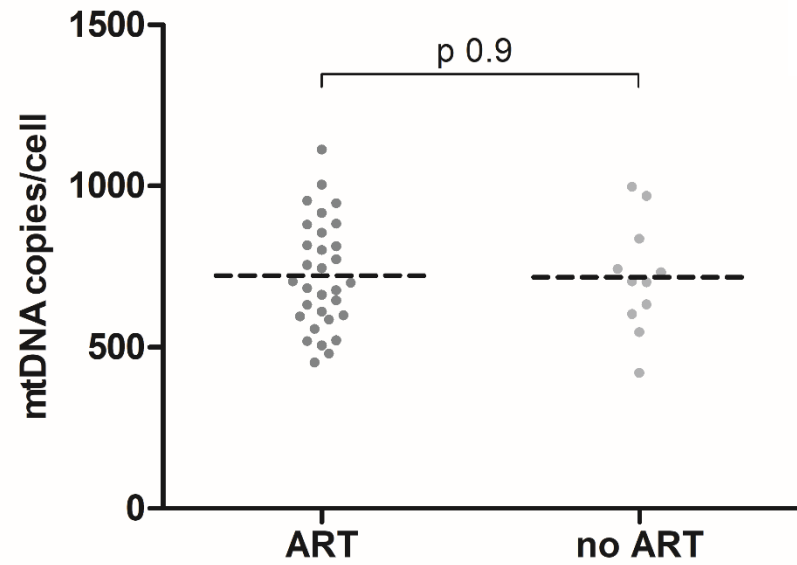


point mut.

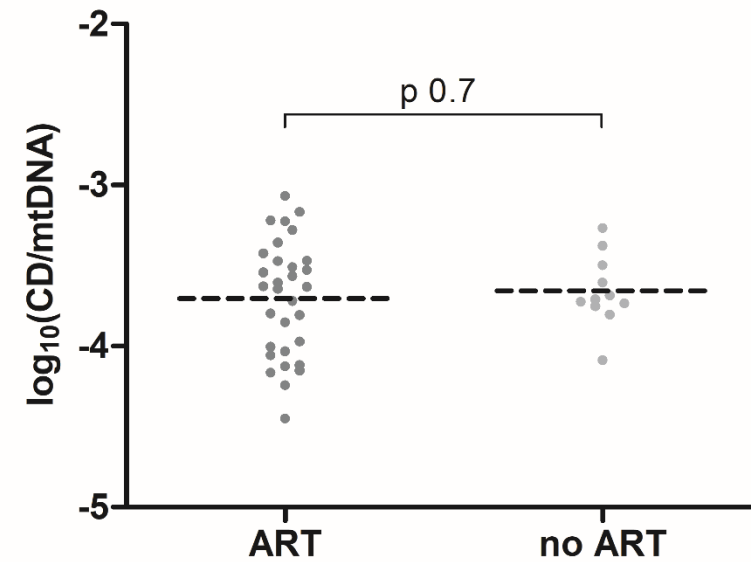


Results (3): ART

mtDNA content



mtDNA deletions

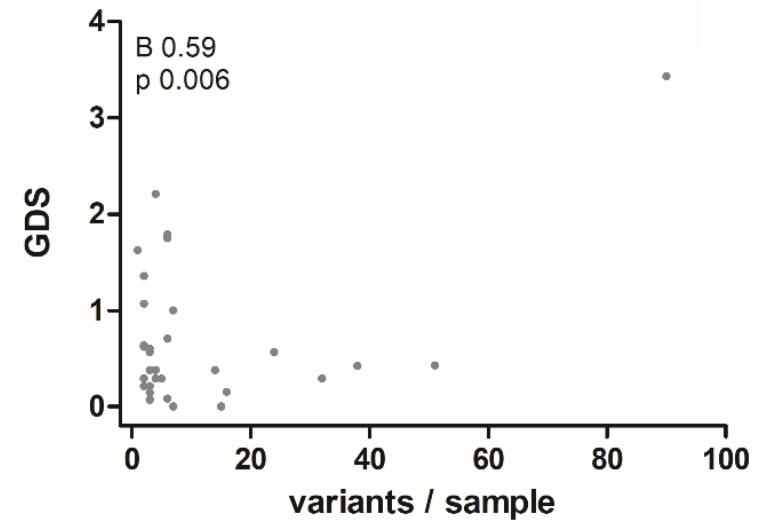
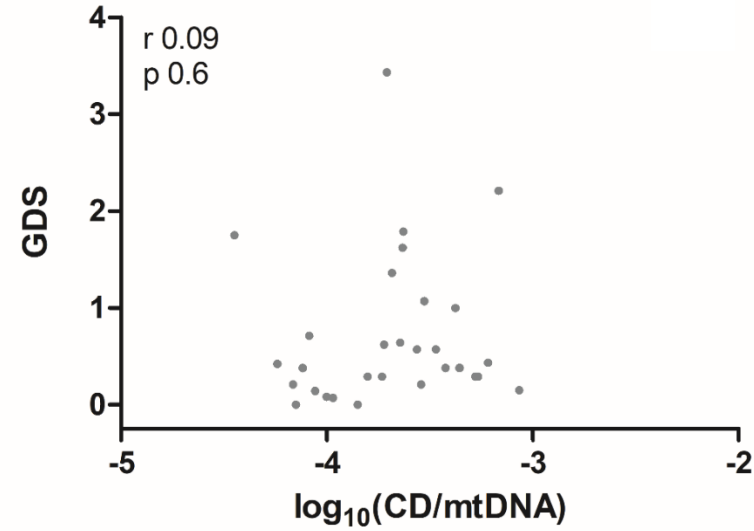
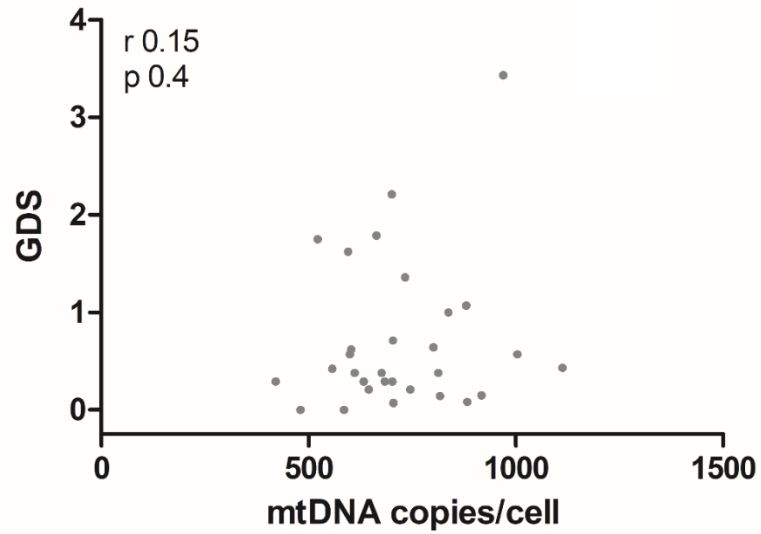


Results (4): NCI

mtDNA
content

deletions

point mut.



Conclusions

- As anticipated, increased age was associated with:
 - Decreased mtDNA content
 - Increased mtDNA deletions and point mutations
- HIV exacerbated all of these changes => 'age advancement' of:
 - mtDNA content, ~32 years
 - mtDNA deletions, ~12 years

Conclusions

- HIV effect rather than ART / NRTIs
 - Low concentration of ART in CNS?
 - Sensitivity of neurons to viral toxicity?
- Further research in well-controlled HIV needed:
 - Advanced HIV may limit generalisability
 - Association with NCI remains unclear
- *HIV may affect biological pathways of ageing*

Acknowledgments

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