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 Mitosciences LLC, Eugene, OR, USA¹ University of Oregon, Eugene, OR, USA² and
 University of Hawaii, Honolulu, HI, USA³ "Mitochondrial Dysfunction in HAART
 Detected with Simple Quantitative Dipstick Assays for Mitochondrial Proteins", Abstract
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The above poster is available at the 2006 CROI conference website:
<http://www.retroconference.org/2006/PDFs/667b.pdf>

Background:

There is mounting evidence that metabolic complications of HAART result from mitochondrial dysfunction. NRTIs inhibit mitochondrial DNA pol- γ and mtDNA depletion has been observed in subcutaneous fat of HIV+Lipoatrophy (LA) patients. However, studies on mtDNA levels in tissues used for routine sampling, such as PBMCs, are equivocal and controversial. Consequently there has been a call for simple tests of mitochondrial function more suitable for the study and diagnosis of metabolic complications. We have developed simple dipstick tests to measure levels of key enzymes of the mitochondrial oxidative phosphorylation (OXPHOS) system, which is responsible for >95% of ATP production in normally functioning cells. We show here that the tests have clinical utility to monitor adverse effects of HAART in both fat and PBMCs.

Methods:

Quantitative 2-site immunoassay dipstick tests were used to measure levels of OXPHOS enzyme complexes I (CI: NADH dehydrogenase) and IV (CIV: cytochrome *c* oxidase) in gluteal subcutaneous adipose tissue and PBMCs of 26 patients forming 3 cohorts: 1) HIV-, 2) HIV+LA-, and 3) HIV+LA+ (cohorts 2&3 on HAART). LA was determined by patient report and physician concurrence. MtDNA copies/cell were assayed by RTPCR using primers for the mtDNA NADH dehydrogenase 2 and the nuclear Fas gene.

	HIV-	HIV+LA-	HIV+LA+
N	7	4	15
	% of HIV- cohort mean		
Fat CI	100	61	44*
Fat CIV	100	93	58*
PBMC CI	100	95	78*
PBMC CIV	100	91	63‡
Fat mtDNA	100	24*	30*
*p<0.05 vs HIV- cohort, t-test			
‡p=0.08 "			

Results:

Both CI and CIV were reduced significantly in fat and PBMCs of the HIV+LA+ cohort compared to the HIV- cohort. Intermediate levels of both enzymes were also seen in fat

and PBMCs of the HIV+LA- cohort, but these differences were not statistically significant, possibly due to low sample number of the HIV+LA- cohort. MitDNA levels in fat were reduced significantly in the HIV+LA- and HIV+LA+ cohorts.

Conclusions.

The results show that these simple dipstick assays for mitochondrial enzymes have clinical utility to monitor adverse effects of HAART, i.e., they reveal mitochondrial dysfunction in LA+ patients. As the tests work on easily accessed tissue samples, they will facilitate study of HAART-associated mitochondrial dysfunction and may be useful theranostic aids to guide therapy. Moreover, because they are simple, robust and inexpensive, the tests hold promise for use in resource-poor settings.