Redox Biology 13 (2017) 418–420

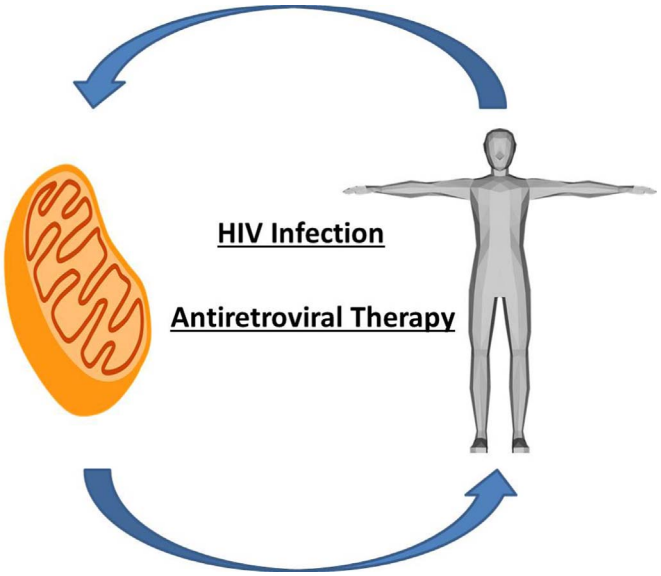
Contents lists available at ScienceDirect

Redox Biology

journal homepage: www.elsevier.com/locate/redox

Invited Commentary

Blood-based bioenergetic profiling: A readout of systemic bioenergetic capacity that is related to differences in body composition



Mitochondrial bioenergetics and body composition in HIV infected women on antiretroviral therapy – Blood-based bioenergetic profiling is a minimally invasive tool that can be utilized to examine mitochondrial alterations associated with HIV infection, its treatment, and its consequences

Circulating cells have been reported to exhibit mitochondrial alterations related to various health conditions. For example, changes in mitochondrial DNA content, enzyme activity, and electron transport chain activity, in multiple blood cell types, have been reported in HIV, diabetes, atherosclerosis, cardiovascular disease, Parkinson's, Alzheimer's, cancer, inflammation, cognition, Huntington's, sepsis, and fibromyalgia [1–14]. In recent years, respirometric profiling of blood cells has emerged as a robust and innovative approach for assessing mitochondrial function in a minimally invasive manner. These methodologies have helped to significantly expand translational bioenergetics research, and have been successfully implemented in a variety of human studies [15–21].

The manuscript by Willig et. al. builds upon a growing body of work demonstrating the ability of blood cells to report on differences in mitochondrial function across a wide range of human conditions. While previous studies have focused on skeletal muscle mitochondrial bioenergetics, this is the first to demonstrate that blood-based measures of mitochondrial function are related to body composition in any context. These findings are also significant based on the changes body composition associated with HIV infection, disease progression, and antiretroviral therapy (ART) [22–25]. Alterations in adiposity and lean mass are accompanied by systemic metabolic consequences, which may be associated with the bioenergetic capacity of circulating cells. The results of this study may also be generalizable beyond HIV infected individuals, and extend to other conditions that are accompanied by changes in body composition. In particular, changes in the ratio of lean mass to fat mass are evident in aging, weight cycling (loss/regain) and physical inactivity (i.e. bed rest/hospitalization) [26–34]. Such changes in body composition are likely related to worsening metabolic health and poor physical function.

The study by Willig et al. leads to new questions regarding the potential role of mitochondria in HIV infection, its treatment, and its consequences. The relationship between body composition and systemic bioenergetic capacity remains to be defined by future studies. For example, are

☆ Featured Article: Amanda L. Willig, Philip A. Kramer, Balu K. Chacko, Victor M. Darley-Usmar, Sonya L. Heath, E. Turner Overton, Monocyte bioenergetic function is associated with body composition in virologically suppressed HIV-infected women, Redox Biology, 12, 2017, pp. 648–656.

http://dx.doi.org/10.1016/j.redox.2017.06.012
Received 21 June 2017; Accepted 27 June 2017
Available online 30 June 2017

the bioenergetic differences among HIV-infected women related to the direct mitotoxic effects of ART? Indeed, it has been reported that peripheral blood mononuclear cells from HIV-infected patients on ART exhibit reduced mitochondrial membrane potential [35]. Future studies can address whether changes in body composition occur in parallel with mitochondrial alterations in this patient population, or if there a causal relationship. A possible interpretation of the reported results may be that systemic bioenergetic capacity, as reported by blood-based bioenergetic profiling, is responding to changes in metabolic demand that occur as a result of alterations in body composition. A major implication of this work is that these questions, and numerous others, can be addressed by using the blood-based bioenergetic profiling approach being utilized by this research group and others. Such assays are minimally invasive and therefore amenable for use in longitudinal studies. Using these approaches, it is possible to track HIV infected individuals through the course of disease progression and the treatment with ART. This current study by Willig et al., and future research stemming from this work, may also have important clinical implications. The ability to track the mitotoxic effects of ART in individual patients can support the development of more optimized treatment strategies that are able to balance the treatment of HIV infection with potential side-effects related to systemic mitochondrial toxicity.

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