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### **ACCEPTED MANUSCRIPT**

#### Mitochondrial Network Responses in Oxidative Physiology and Disease<sup>1</sup>

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#### ABSTRACT

Mitochondrial activities are linked directly or indirectly to all cellular functions in aerobic eukaryotes. Omics methods enable new approaches to study functional organization of mitochondria and their adaptive and maladaptive network responses to bioenergetic fuels, physiologic demands, environmental challenges and aging. In this review, we consider mitochondria collectively within a multicellular organism as a macroscale "mitochondriome", functioning to organize bioenergetics and metabolism as an organism utilizes environmental resources and protects against environmental threats. We address complexities of knowledgebasedriven functional mapping of mitochondrial systems and then consider data-driven network

<sup>&</sup>lt;sup>1</sup> Based upon a lecture by DP Jones given at the Oxygen Club of California meeting in Berlin, Germany, June 2017.

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