Approaches to Defining Mitochondrial Protein Function Using Systems Biochemistry

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Introduction

In the post-genomic era, de ning functions for the whole complement of proteins is a major task, but it is critical for our understanding of basic biology and disease causation. In recent years, a mix of current large-scale and classical reductionist approaches—a process we call "systems biochemistry"—has aided in the characterization of poorly understood proteins, overcoming previous hurdles.   is method is proven particularly successful for mitochondria, whose well-de ned proteome has allowed for extensive analysis of the entire mitochondrial system, allowing understudied proteins to be positioned for bene cial mechanistic investigations. Recent advances in systems biochemistry have aided in the discovery of new disease-related mitochondrial proteins as well as long-sought "missing" proteins that perform critical activities.   ese researches, taken together, are leading to a better knowledge of mitochondrial functions and a molecular foundation for investigating mitochondrial disease [1].

Mitochondrial Dark Matter

Revolutions in imaging and structural biology allow us to observe subcellular components at stunning resolution, and gene editing technologies allow us to manipulate DNA seemingly without restriction. Our ability to measure, observe, and modify biological systems, on the other hand, has perhaps overtaken our basic knowledge of the gene activities that underpin them.

ere are a variety of reasons why so many proteins are still poorly understood. Many are justrly restrictindicated that the latter group was similarly represented in genome-wide association studies (GWASs) and was equ illnesses. Because of this "inspection bias," it's possible to make the mistake of concluding that well-studied proteins are more responsible for a certain impact just because they're more familiar [3].

is paradigm also applies to mitochondria, whose distinctive cellular "powerhouse" label has led to the erroneous assumption that this organelle is a completely de ned system with a fully de ned purpose. In reality, hundreds of mitochondrial uncharacterized (x) proteins (MXPs) have been discovered recently, and novel mitochondria-related processes are still being discovered.   e introduction of several large-scale approaches has hastened progress in de ning the functionalities of MXPs. Such "omics-level" analyses risk being nothing more than data gathering exercises on their own. When used correctly, these tests can lead to more precise, well-informed theories about protein function [4].

"Systems biochemistry" is the term we use to describe the combination of "systems" studies and traditional mechanistic biochemical and bioenergetics techniques.   e well-known proteome of mitochondria, as well as its controllable complexity and pro tability,