Opinion

Biology

Is Mitochondrial Dysfunction the Underlying Causal Reason for Human Diseases?

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Mitochondria, the cellular powerhouses, have emerged as pivotal players in human health and disease. Recent advances suggest mitochondrial dysfunction is implicated in a broad spectrum of disorders, ranging from neurodegenerative diseases, metabolic syndromes, cardiovascular conditions, to aging-related decline. This article explores the hypothesis that mitochondrial dysfunction may be a central underlying cause driving many, if not all, human diseases. By integrating evidence from molecular biology, clinical studies, and evolutionary theory, I argue that mitochondrial health is fundamental to cellular and systemic function. However, while mitochondrial dysfunction contributes significantly to disease pathogenesis, it is unlikely to be the sole cause of all human diseases due to the complexity of genetic, environmental, and lifestyle factors. Understanding mitochondria's multifaceted role could revolutionize diagnostics and therapeutics, positioning mitochondrial medicine at the forefront of future healthcare. This opinion advocates for a balanced yet focused research approach to uncover how mitochondrial dysfunction intersects with other pathogenic mechanisms.

Keywords: Mitochondrial Dysfunction; Human Diseases; Causal Relationship; Molecular Mechanisms; Outcomes

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THE HUMAN body is a marvel of biological complexity, a symphony of interacting systems each essential to our survival and well-being. Among these, mitochondria stand out as unique organelles—tiny power plants within nearly every cell—that generate the bulk of cellular energy through oxidative phosphorylation (Li et al., 2025). For decades, mitochondria were thought of primarily as energy producers, their role confined to bioenergetics. However, growing evidence reveals mitochondria as multifaceted regulators of cellular homeostasis, apoptosis, reactive oxygen species (ROS) production,

calcium signaling, and metabolic integration (Prates, 2025). This expanded view has led to a provocative question in contemporary medicine and biology: Is mitochondrial dysfunction the underlying reason for all human diseases?

At first glance, this question may appear reductionist, perhaps even overly simplistic given the staggering diversity and complexity of human diseases. Yet, it is rooted in compelling scientific observations and the undeniable centrality of mitochondria in cellular physiology. Mitochondrial dysfunction—broadly defined as any impairment in mitochondrial bioenergetics, dynamics, biogenesis, or signaling—has been implicated in a wide array of pathological states (Picard et al., 2016). From neurodegenerative diseases like Parkinson's and Alzheimer's, to metabolic disorders such as diabetes and obesity, cardiovascular diseases, cancer, and even psychiatric conditions, dysfunctional mitochondria are recurrent culprits (Aran & Singh, 2023). Could this shared thread indicate that mitochondria serve as a common nexus for disease development?

One of the strongest arguments supporting this view lies in the evolutionary origins and fundamental roles of mitochondria. Descended from ancient symbiotic bacteria through endosymbiosis, mitochondria carry their own DNA and reproduce independently within cells (Atlante & Valenti, 2023). They generate adenosine triphosphate (ATP), the chemical currency of energy, indispensable for all cellular processes. Given the enormous energy demands of human tissues—especially the brain, heart, and muscles—mitochondrial efficiency is critical (Dunn & Grider, 2021). When mitochondria falter, energy deficits ripple across cellular functions, potentially triggering disease cascades.

Mitochondria are also central to programmed cell death pathways and the regulation of oxidative stress. Excessive or dysregulated production of reactive oxygen species (ROS) can damage mitochondrial DNA (mtDNA) and cellular components, creating a vicious cycle of mitochondrial injury and cellular dysfunction (Li et al., 2025). This oxidative damage has been linked to aging and various chronic diseases. Indeed, mitochondrial DNA mutations accumulate with age and correlate with decreased mitochondrial function, suggesting a fundamental role in age-related decline and diseases (Somasundaram et al., 2024).

Neurodegenerative disorders offer vivid illustrations of mitochondrial dysfunction's impact. Parkinson's disease (PD), for example, is characterized by selective loss of dopaminergic neurons in the substantia nigra, with multiple studies documenting mitochondrial complex I deficiencies and increased oxidative stress in affected brain regions (Hauser & Hastings, 2012). Similarly, Alzheimer's disease (AD) pathology includes disrupted mitochondrial dynamics and bioenergetic failure, which may precede hallmark amyloid-beta plaques and tau tangles (Adamu et al., 2024). These findings suggest mitochondrial impairment is not a mere consequence but potentially a driver of neuronal death.

Metabolic diseases further underscore mitochondrial significance. Type 2 diabetes is linked to impaired mitochondrial oxidative capacity in skeletal muscle and pancreatic beta cells (Li et al., 2024). Obesity and metabolic syndrome feature mitochondrial dysfunction that exacerbates insulin resistance and systemic inflammation (Pliouta et al., 2025). The interplay between nutrient excess, mitochondrial overload, and ROS generation forms a pathophysiological foundation for metabolic derangements.

In cardiovascular diseases, mitochondrial dysfunction compromises cardiac myocyte energy supply and promotes apoptosis, contributing to ischemic injury, heart failure, and arrhythmias (Yang, 2025). Cancer cells often exhibit altered mitochondrial metabolism, known as the Warburg effect, demonstrating mitochondrial roles in tumor growth and survival (Pliouta et al., 2025). Psychiatric disorders like depression and bipolar disorder are increasingly associated with mitochondrial abnormalities affecting neuronal function and plasticity.

Despite this wide-ranging evidence, the proposition that mitochondrial dysfunction is the underlying cause of all human diseases requires cautious consideration. Many diseases have distinct etiologies—genetic mutations unrelated to mitochondria, infectious agents, autoimmune attacks, or environmental toxins—that initiate pathology (Wen et al., 2025). For example, infectious diseases caused by bacteria, viruses, and parasites primarily involve pathogen-host interactions independent of mitochondrial defects, although secondary mitochondrial impairment can occur.

Moreover, the complexity of multifactorial diseases involves genetic predispositions, epigenetic modifications, environmental exposures, lifestyle factors, and immune responses (Changaei et al., 2025). These elements interact in networks far beyond mitochondrial function alone. While mitochondria may serve as amplifiers or integrators of cellular stress and damage, it is reductive to assign them as the sole root cause (Liu et al., 2024).

Another consideration is the variability in mitochondrial health among individuals and tissues. The threshold effect in mitochondrial diseases shows that a certain degree of mitochondrial dysfunction may be tolerated without clinical symptoms, and some individuals possess compensatory mechanisms to mitigate mitochondrial defects (Da et al., 2024). This variability complicates attributing causality universally.

The conceptual framework of mitochondrial dysfunction as a common denominator aligns with the emerging field of "mitochondrial medicine," which seeks to target mitochondrial pathways for therapeutic gain (Hong et al., 2024). Interventions such as antioxidants, mitochondrial biogenesis stimulators, metabolic modulators, and gene therapies hold promise. Importantly, recognizing mitochondrial dysfunction's role enables earlier diagnosis, biomarker development, and personalized treatment strategies.

However, embracing a holistic view that integrates mitochondrial dysfunction with other pathogenic mechanisms is essential. Diseases often reflect a convergence of insults—genetic, environmental, infectious, immunological—that collectively disrupt homeostasis (Li et al., 2024). Mitochondria, due to their central role in energy and signaling, are often caught in this storm, sometimes as initiators, sometimes as victims, and often as mediators of disease progression.

Future research should focus on elucidating the precise mechanisms by which mitochondria interact with other cellular systems and environmental factors to initiate and propagate disease. A systems biology approach will be instrumental in

dissecting these interactions. Clinically, integrating mitochondrial biomarkers and targeted therapies can transform patient care. Ultimately, mitochondria stand as both a beacon and a battleground in medicine. They remind us that life depends on the smallest engines within us and that preserving their function could hold the key to combating a vast array of diseases. While mitochondrial dysfunction may not explain every illness, its role as a foundational player in human pathology is irrefutable and demands ongoing scientific attention.

In conclusion, mitochondrial dysfunction is undeniably a critical factor underlying many human diseases. Its central position in cellular energy metabolism, signaling, and apoptosis makes it a linchpin in health and illness. The breadth of conditions linked to mitochondrial impairment—from neurodegeneration and metabolic syndrome to cancer and aging—highlights its importance. Yet, to assert that mitochondrial dysfunction alone causes human diseases overlooks the complexity and heterogeneity of pathological processes. ■

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