Research Summary: Mitochondria #2

As featured in Dr. Kenny Mittelstadt's video:
What Mitochondrial Dysfunction Looks Like Before Disease
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Research Context:

This week's topic explores how mitochondrial dysfunction can develop before a disease is officially diagnosed. Many people assume something is only "wrong" once a lab value falls outside the normal range, but biology rarely changes overnight. There is often a long period where the body adapts, compensates, and becomes less efficient while routine blood work still appears reassuring. Mitochondria, the tiny structures inside nearly every cell that produce most of your body's energy, are part of that story. The research below examines how mitochondrial function connects with insulin resistance, metabolic health, and chronic disease, while highlighting an important reality: researchers are still clarifying whether these changes are the cause, consequence, or part of a larger pattern unfolding.

Key Findings from the Research:

Study 1 (PMID 28551803):
Gonzalez-Franquesa and Patti reviewed the relationship between insulin resistance and mitochondrial dysfunction. Insulin resistance means the body's cells become less responsive to insulin, the hormone that helps move sugar from your bloodstream into your cells. The authors found that people with insulin resistance often show changes in mitochondrial energy production, mitochondrial turnover (the process of replacing old mitochondria with healthy new ones), and overall mitochondrial quality. Importantly, many of these changes appear before type 2 diabetes is formally diagnosed. The review also highlights an important limitation in the research: scientists still do not know whether mitochondrial dysfunction starts the process or develops because of earlier metabolic stress.

Study 2 (PMID 24732809):
Lu, Tan, and Cai reviewed what is known as the Warburg effect, a well-studied shift in how cancer cells produce energy. Instead of relying primarily on mitochondria, many cancer cells favor a much less efficient pathway called glycolysis, even when oxygen is available. This does not mean mitochondrial dysfunction causes cancer or that everyone with impaired mitochondrial function is developing cancer. Rather, the researchers use cancer biology as a clear example of how dramatically cellular energy metabolism can change. Their work highlights that mitochondria are not simply "powerhouses" producing energy; they also influence how cells grow, communicate, respond to stress, and survive. Understanding these shifts helps researchers appreciate why mitochondrial function matters across many chronic conditions and why subtle changes in cellular energy production may have broader effects on overall metabolic health long before disease becomes apparent.

Study 3 (PMID 19349201):
Dumas and colleagues examined whether mitochondrial dysfunction in skeletal muscle is a cause of insulin resistance or develops as a result of it. Skeletal muscle plays one of the largest roles in blood sugar regulation because it uses a significant amount of glucose after meals. The authors found that reduced mitochondrial function is consistently associated with insulin resistance, lower fat-burning capacity, and reduced oxidative phosphorylation, the highly efficient process mitochondria use to generate cellular energy. However, they also emphasize that the available human research cannot yet determine which comes first. Mitochondrial dysfunction may contribute to insulin resistance, result from it, or develop alongside other metabolic changes already underway.

Functional Medicine Connections:

Here's how these findings fit together: mitochondria do not work in isolation. They constantly communicate with systems involved in blood sugar regulation, inflammation, hormone signaling, nutrient status, detoxification, and cellular repair. When these communication networks become strained, your cells may produce energy less efficiently long before a disease is diagnosed.

This helps explain why two people with similar routine lab results can have very different day-to-day experiences. From a functional medicine perspective, the goal is not to assume mitochondria are the root cause of every symptom. Instead, they are one important clue within a larger investigation. Looking at mitochondrial function can help reveal where stress is accumulating, where the body may be compensating, and which upstream patterns may deserve closer attention before conventional disease thresholds are crossed.

In that gray zone, symptoms and subtle changes are not proof of disease, but they may be meaningful signals that the body's communication networks are under increasing strain. Understanding those patterns can help guide a more complete investigation rather than simply waiting until disease becomes obvious.

Practical Reflections & Takeaways:

Think about your own patterns for a moment. Have you noticed your energy, exercise recovery, or mental clarity changing even though you've been told your labs look normal? Do those changes seem to follow periods of poor sleep, chronic stress, illness, or changes in your nutrition?

These observations are not a diagnosis, but they are meaningful clues about how your body may be functioning beneath the surface. Rather than dismissing these experiences because they don't fit neatly into a diagnosis, consider them valuable information.

References:

- Gonzalez-Franquesa A, Patti ME. Insulin Resistance and Mitochondrial Dysfunction. Adv Exp Med Biol. 2017. PMID: 28551803.
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- Dumas JF, Simard G, Flamment M, Ducluzeau PH, Ritz P. Skeletal Muscle Mitochondrial Dysfunction and Insulin Resistance. Diabetes Metab. 2009. PMID: 19349201.