Mitochondrial diseases are heterogenous conditions related to mitochondrial respiratory chain dysfunction due to mitochondrial DNA or nuclear gene variants. Clinical manifestations range from early-onset, acute metabolic dysfunction to intermittent, and progressive, neuromyopathic decline. As manifestations are variable, clinicians need more sensitive and specific biomarkers.

**EVIDENCE SUPPORTING GDF15 IN CORRELATION TO MITOCHONDRIAL DISEASE**

GDF15 has been shown by studies on mitochondrial-disease patients to be significantly elevated in plasma or serum. An analysis of 33 individuals with confirmed mitochondrial disease demonstrated higher GDF15 concentrations (median: 1163 pg/mL; 1st-99th%-iles: 491-6817 pg/mL) than 120 normal age-matched donors (GDF15 median: 423 pg/mL; 1st-99th%-iles: 230-1560 pg/mL), and GDF15 levels showed a specificity of 92% for mitochondrial disease at a concentration threshold of 750 ng/mL.

Additionally, in seven months of clinical testing 216 patients were assayed for GDF15 levels (median: 510 pg/mL; 1st-99th%-iles: 221-6000) and 29% (62/216) displayed GDF15 concentrations above the threshold value. MELAS patients displayed higher GDF15 levels (median: 3290 pg/mL) than other mitochondrial disease patients (GDF15 median: 921 pg/mL).

However, NARP and PDHC-deficient patients presented with GDF15 levels in the normal range. Recent publications support our findings that NARP and PDHC-deficient patients have normal GDF15 levels and that MELAS patients’ median GDF15 levels are significantly elevated, yet in all studies, a small number of MELAS patients have presented with GDF15 levels within the normal range.1-5

**A BIOMARKER FOR MITOCHONDRIAL DISEASE**

Based on our experience and review of recent publications, GDF15 demonstrates high specificity and sensitivity for mitochondrial disease with the exception of NARP and PDHC-deficient patients and a small subset of MELAS patients. GDF15 appears to have a useful role, alongside other mitochondrial disease biomarkers, such as blood lactate, in the evaluation of patients suspected of mitochondrial disease. However, the role that this signal transducer has in the pathology of mitochondrial disease remains to be completely elucidated.

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REFERENCES


