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Elevated Urinary Mitochondrial DNA Copy Numbers in IgA Nephropathy

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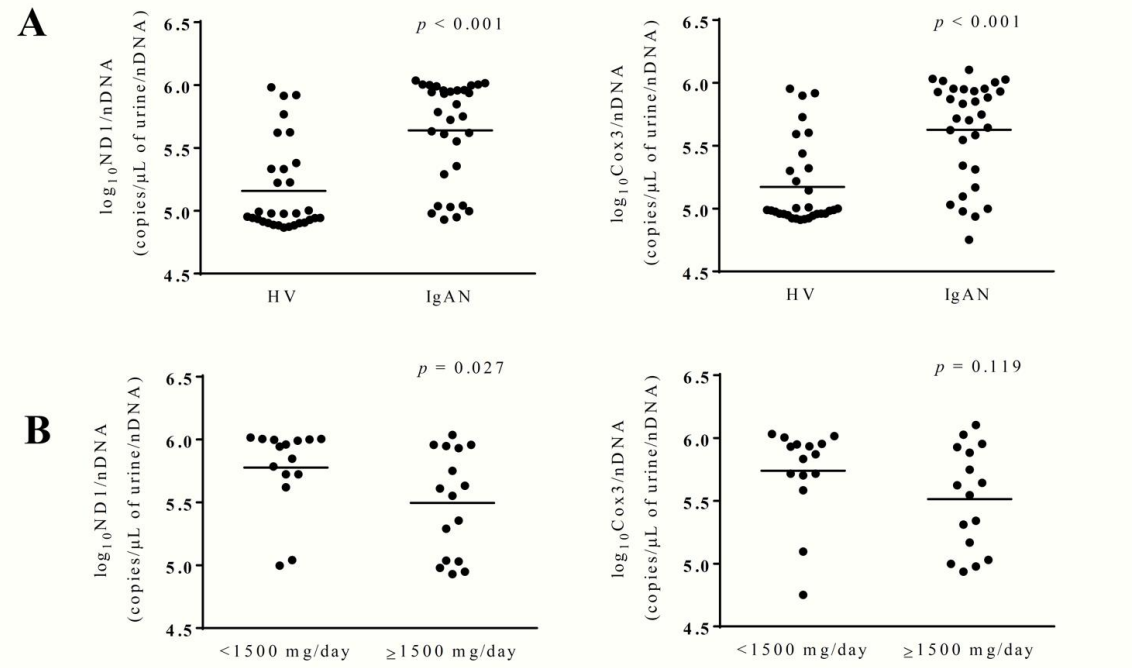
Objectives: Mitochondrial injury plays important roles in the pathogenesis of various kidney diseases. However, mitochondrial injury in IgA nephropathy (IgAN) has not been evaluated. Here, we examined the associations among mitochondrial injury, IgAN, existing prognostic markers, and treatment outcomes.

Methods: We prospectively enrolled patients with IgAN and age-/sex-matched healthy volunteers (HVs) as controls (n = 31 each). Urinary copy numbers of the mitochondria DNA (mtDNA) genes cytochrome-c oxidase-3 (*COX3*) and nicotinamide adenine dinucleotide dehydrogenase subunit-1 (*ND1*) were measured. We also measured urinary mtDNA levels at 6 months after medical treatment in patients with IgAN (n = 19).

Results: Urinary mtDNA levels were elevated in the IgAN group compared with that in HVs ($p <$ 0.001). Urinary mtDNA levels did not correlate with existing prognostic markers. However, urinary ND1 levels were significantly higher in the low proteinuria group than in the high proteinuria group ($p = 0.027$). Although urinary mtDNA levels did not change after medical treatment, changes in urinary levels of ND1 and COX3 were positively correlated with changes in proteinuria ($p = 0.038$ and 0.024, respectively) and inversely correlated with changes in the estimated glomerular filtration rate ($p = 0.033$ and 0.017, respectively) after medical treatment.

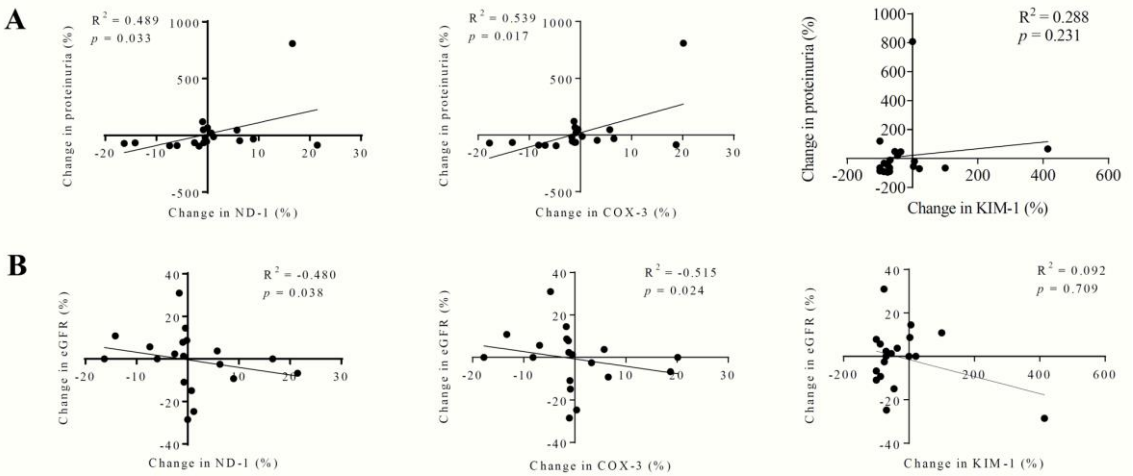
Conclusions: Mitochondrial injury played important roles in IgAN pathogenesis and may be involved in early-stage glomerular inflammation, prior to pathological changes and increased proteinuria. The correlation between changes in urinary mtDNA and proteinuria suggest that these factors may be promising biomarkers for treatment outcomes in IgAN.

Figure 1. Urinary mitochondrial DNA copy numbers at baeline.



(A) Urinary mitochondrial DNA copy numbers were elevated in the IgA nephropathy (IgAN) group compared with those in healthy volunteers. (B) Urinary copy numbers of nicotinamide adenine dinucleotide dehydrogenase subunit-1 (*ND1)* were higher in the low proteinuria group than in the high proteinuria group. Data were analyzed by Mann-Whitney tests. *COX3*, cytochrome c oxidase subunit 3.

Figure 2. Changes in urinary mitochondrial DNA copy numbers and kidney injury molecule-1 (KIM-1) levels at 6 months after medical treatment.



Changes in urinary levels of mitochondrial DNA showed positive correlations with changes in proteinuria at 6 months (A) and were inversely correlated with changes in eGFR at 12 months after medical treatment (B). Data were analyzed by Spearman's rank correlation coefficient. *ND1,* nicotinamide adenine dinucleotide dehydrogenase subunit-1; *COX3*, cytochrome c oxidase subunit 3.