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mtDNA: Pathogenic or Nonpathogenic Sequence Changes

To the Editor:

Tatuch et al. (1992) have reviewed the literature on the 8993 mtDNA mutation in a recent case report in this *Journal*. Their evidence that this point mutation causes Leigh disease is strong, even though it has not yet been possible to document the predicted biochemical defect. Their case does not need the spurious support they infer from our data (Poulton et al. 1988). We reported a patient with Kearn-Sayre syndrome (KSS; see Petty et al. [1986]), which we described as group I mitochondrial myopathy, in whom we found two restriction-site losses in the region of the 8993 mutation. Unlike the family they described, our patient was homoplasmic for the point mutation, as were his asymptomatic maternal relatives. Sequence analysis now confirms that there is a G-to-A transition at bp 8994 that does not cause an amino acid substitution. We conclude that this mutation is not pathogenic. Furthermore, this boy has an mtDNA deletion (fig. 1) that is sufficient to explain his clinical syndrome.

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TACCACCTACCTCCCTCACCAAA  ATPase 8
          **********
TACCACCTACCTCCCTGACAAGC  Patient
          **********
TCATCGCTACCTCCCTGACAAGC  ND5
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Figure 1 Exact homology between bp 8468–8477 (*top strand*) and bp 13580–13589 (*bottom strand*). Asterisks (*) indicate the homologous region.

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