A polymorphic synonymous mutation in human ornithine- δ -aminotransferase (N378N)

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Source/Description: We examined the 10th exon of the human ornithine- δ -aminotransferase (OAT) gene (Mitchell *et al.*, 1988) by PCR amplification and sequencing of genomic DNA from a series of controls and individuals with gyrate atrophy of the choroid and retina.

Polymorphism: We detected a C→T transition at OAT cDNA residue 1134 (codon 378) in the context AACGCT. The mutation was confirmed by sequencing cloned cDNAs from a heterozygote. Because AAC and AAT both code for asparagine, this CpG dinucleotide alteration produces a synonymous mutation (N378N). The published human OAT cDNA sequences all have a C at this position (Inana *et al.*, 1986; Ramesh *et al.*, 1988; Mitchell *et al.*, 1988), whereas the normal rat sequence has a T.

Frequency: In 31 unrelated Caucasian controls we found the following frequencies:

(H1) AAC: 0.71

(H2) AAT: 0.29

There were 15 AAC homozygotes, 14 AAC/AAT heterozygotes and 2 AAT homozygotes.

Enzymes Tested: This transition does not alter a known restriction endonuclease site.

Chromosomal Location: 10q26.

Mendelian Inheritance: Codominant segregation was observed in 7 two generation families (22 meioses).

Probe Availability: Contact David Valle.

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References: 1) Mitchell *et al.* (1988) *J. Biol. Chem.* **263**, 14288–14295. 2) Inana *et al.* (1986) *Proc. Natl. Acad. Sci. USA* **83**, 1203–1207. 3) Ramesh *et al.* (1986) *DNA* **5**, 493–501.

PCR AMPLIFICATION AND DIRECT SEQUENCING OF GENOMIC DNA:

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A rare mitochondrial DNA BstNI polymorphism in a family with type II diabetes

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Source/Description: Mitochondrial DNA (mtDNA) of a family with a maternally inherited form of type II diabetes associated with a sensorineural hearing loss was analyzed by RFLP. Southern blot analysis of leucocyte DNA showed an unusual pattern when digested with restriction enzyme BstNI. Besides a site loss located in the ATPase 6 gene, as reported previously (1), also a site gain is present located in the ND 3 gene. Sequencing analysis revealed a synonymous substitution of A for G at position 10.097 (2).

Polymorphism: With BstNI digestion of a PCR amplified fragment encompassing the polymorphic site (forward primer (9.375–9.394); reverse primer (10.254–10.273)), only homoplasmy was detected when visualized on ethidium stained agarose gels.

Frequency: All 260 controls tested, including 60 regional samples (25 diabetes), were wild-type for this BstNI morph.

Not Polymorphic For: Not applicable.

Chromosomal Localization: Not applicable.

Mendelian Inheritance: Strictly maternal inheritance in a pedigree of 30 individuals.

Probe Availability: Not applicable.

Other Comments: Not applicable.

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References: 1) Holt, I.J. *et al.* (1988) *Hum. Genet.* **79**, 53–57. 2) Anderson, S. *et al.* (1981) *Nature* **290**, 457–465.

Southern blot analysis of leucocyte DNA digested with BstNI, probed with purified HeLa cell mtDNA. (P)patient; (C)control. Fragment sizes (kb) are indicated.

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