to the possibility of a peripherin/RDS mutation at codon 172.

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Cystic Fibrosis Transmembrane-Conductance Regulator Mutations among African Americans

To the Editor:

Cystic fibrosis (CF) is less common in African Americans than in Caucasians of northern European descent, with an estimated incidence of 1/15,300 (Hamosh et al., in press), although the severity of the disease is comparable across racial lines. Macek et al. (1997) recently reported in the *Journal* the identification of several CF transmembrane conductance regulator (CFTR) mutations of noteworthy prevalence in blacks. This information will help clinical laboratories to improve the sensitivity of CF mutation testing for African American patients.

We have identified a CFTR mutation in exon 7 in two unrelated individuals of African American descent who were not included in the study by Macek et al. The mutation, ΔF311, results in the loss of a phenylalanine residue in the fifth transmembrane domain of the CFTR protein. One of our patients is a 4-year-old African American female who presented, at age 7 mo, with hypochloremic metabolic alkalosis and dehydration. She was subsequently found to have sweat chloride values on two occasions of 75 and 83 mEq/liter. Her lung disease is mild, with only slight peribronchial thickening on chest x-ray, and she had *Staphylococcus aureus* in her sputum at age 3 years. She is considered pancreatic sufficient, on the basis of qualitative fecal fat analysis. Without pancreatic-enzyme supplementation, she has maintained a normal growth pattern, with height and weight at the 50th percentile. Mutation testing determined her genotype to be ΔF508/ΔF311. The ΔF311 allele was first detected by the appearance of a distinct heteroduplex pattern when PCR product encompassing exon 7 was electrophoresed on 10% polyacrylamide. The mutation was identified as ΔF311 by dideoxy sequencing. No additional ΔF311 alleles have been found after a screening of a further 271 patient samples (~8.5% African American) at the University of North Carolina in Chapel Hill.

The second patient was referred for genetic testing because of abnormal fetal ultrasound findings. The patient was a 25-year-old (G2 P0 SAB1) African American. An ultrasound performed at 17 wk gestation identified a fetus with a Dandy-Walker malformation and an echogenic bowel. Follow-up ultrasound at 18.2 wk gestation confirmed the CNS abnormalities and a grade II echogenic bowel. The patient was counseled with regard to the numerous causes of Dandy-Walker malformations, as well as with regard to the causes of echogenic bowel, including CF. The fetal karyotype was normal, but maternal and fetal CF testing identified a heteroduplex pattern identical to the ΔF311 heterozygote pos-

itive control (Mutation Detection Enhancement gel system; FMC BioProducts). Patient DNA mixed with equal amounts of ΔF311 control DNA showed the same heteroduplex pattern as did either the patient DNA sample or the ΔF311 heterozygote DNA sample alone, suggesting that these abnormal alleles were identical. DNA sequencing using the ABI 377 nucleic acid sequencer subsequently confirmed this sequence change to be the ΔF311 mutation in heterozygous form.

Maternal cell contamination was ruled out by MCT-118 genotyping. The father of the fetus was not available for testing, and no other CF mutation or abnormal heteroduplex pattern was detected in the fetal sample. Because of the presence of the Dandy-Walker malformation, and prior to the CF results being provided to the patient, the patient elected to terminate the pregnancy. An autopsy was not performed, and fetal tissue was not available for confirmation of the amniocentesis results.

ΔF311 was first reported in a 2-year-old boy with a positive albumin-meconium test at birth and with repeatedly elevated sweat tests by age 4 mo (Meitinger et al. 1993). His other mutation is ΔF508. Prophylactic treatment with both pancreatic enzymes and mucolytic agents to deter lung disease has prevented the onset of either pulmonary or pancreatic symptoms in his first 6 years. The authors of that study did not identify any other individuals with this mutation, after screening an additional 205 CF chromosomes by SSCP (T. Meitinger, personal communication). This patient is of Bavarian Caucasian descent, and his pancreatic disease is distinct from that of the patient seen at the University of North Carolina in Chapel Hill (UNC), obscuring any correlation between ΔF311 and a particular phenotype. Apparent clinical dissimilarities among these three patients might be attributable to undefined aspects of either the genetic background or the environment, but low numbers prevent the drawing of conclusions along racial or other lines. Interestingly, the two individuals whom we describe, as well as the index case, each harbor a distinct ΔF311-associated haplotype (1 1 2, 1 2 2, and 2 1 2) defined by the flanking markers, XV2c-KM19-J3.11, suggesting that this mutation has occurred more than once. The multiple origins of ΔF311 suggest that it might be found on additional chromosomes, but this would not be limited to African American patients.

ΔF311 has thus been identified in two individuals of African American ancestry. In this racial group, this mutation appears to be more common than any CFTR mutation except DF508, compared with other alleles also identified in Caucasians. Among the 23 African American CF patients genotyped at UNC, the inclusion of ΔF311 increased total mutation-detection rates by ~2%. On the basis of the criteria established by Macek et al., we feel that molecular diagnostic laboratories should consider the inclusion of ΔF311 in the development of CF mutation-testing panels tailored to African Americans.

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mtDNA Mutations That Cause Optic Neuropathy: How Do We Know?

To the Editor:

Leber hereditary optic neuropathy (LHON) is an inherited form of bilateral optic atrophy in which the primary etiological factor is a mutation in the mitochondrial genome (mtDNA) (reviewed in Johns 1994; Riordan-Eva et al. 1995; Nikoskelainen et al. 1996; Howell 1997). Wallace et al. (1988) were the first group to identify a LHON mutation, when they showed that a high proportion of LHON families carried a mutation, at nucleotide 11778, that results in the substitution of histidine for the highly conserved arginine at amino acid position 340 of the ND4 subunit of complex I (NADH–ubiquinone oxidoreductase). The 11778 mutation is found in 50%–70% of all LHON pedigrees (e.g., see Mackey et al. 1996). Since the study by Wallace et al. (1988), hundreds of LHON patients from around