Am. J. Hum. Genet. 66:744, 2000

The 1298(A→C) Mutation of Methylenetetrahydrofolate Reductase Should Be Designated to the 1289 Position of the Gene

To the Editor:

van der Put et al. (1998) recently reported that a second common mutation within the gene coding for the enzyme methylenetetrahydrofolate reductase (MTHFR; E.C. 1.5.1.20) results in significantly reduced catalytic activity. This mutation is important because MTHFR plays a significant role in the metabolism of folate and, ultimately, of homocysteine, which is implicated as a risk factor for neural-tube defects (Copp et al. 1990). van der Put et al. (1998) designated this mutation—MTHFR 1298(A→C)—as changing a glutamate into an alanine residue. A review of the human MTHFR mRNA sequence (GenBank accession number U09806) shows that this mutation is not present in the human sequence at position 1298 but may, in fact, be mutation 1289(A→C). There are two reasons why this may be so. First, the nucleotide at 1298 is a T (fig. 1). Second, the authors report that this mutation, 1298C, destroys an *Mbo*II restriction site. The recognition site for *Mbo*II is GAAGANNNNNNN/N/. There is no *Mbo*II restriction site at 1298; however, there is one at 1289 in the human MTHFR sequence (fig. 1). The enzyme *Mbo*II is expected to cut between nucleotides 1297 and 1298, whereas the mutation they describe is likely to be at position 1289. Although this does not affect the results of their study, it is important to accurately designate mutations to the proper nucleotide position, thereby avoiding errors in subsequent research concerning this important gene.

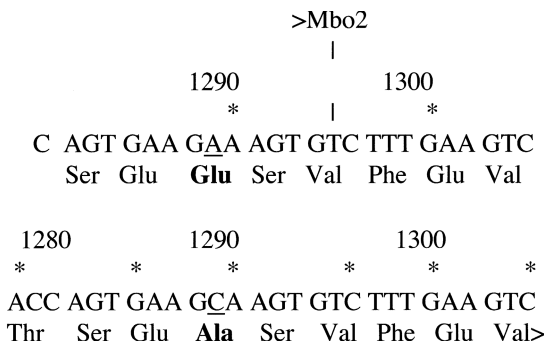

Figure 1 *Mbo*II restriction site on human MTHFR (GenBank accession U09806). *Mbo*II recognizes GAAGA (upper nucleotide sequence). MTHFR 1298C (lower sequence) abolishes the *Mbo*II site. Sequence data were obtained from GenBank (accession number U09806). The lower sequence is identical to the GenBank sequence.

JAMES G. DONNELLY
Department of Pathology and Laboratory Medicine, Ottawa Hospital, and Departments of Biochemistry, Immunology and Microbiology, and Pathology and Laboratory Medicine, Faculty of Medicine, University of Ottawa, Ottawa, Canada

Electronic-Database Information

Accession number and URL for data in this article are as follows:

GenBank, http://www.ncbi.nlm.nih.gov/Genbank/GenbankOverview.html (for human MTHFR mRNA sequence [accession number U09806])

References

Copp AJ, Brook FA, Estibeiro JP, Shum ASW, Cockroft DL (1990) The embryonic development of mammalian neural tube defects. Prog Neurobiol 35:363–403

van der Put NMJ, Fons G, Stevens EMB, Smeitink JAM, Trijbels FJM, Eskes TKAB, van den Heuvel LP, et al (1998) A second common mutation in the methylenetetrahydrofolate reductase gene: an additional risk factor for neural-tube defects. Am J Hum Genet 62:1044–1051

Address correspondence to: Dr. James G. Donnelly, Department of Pathology and Laboratory Medicine, Ottawa Hospital–Civic Campus, 1053 Carling Avenue, Ottawa, ON, Canada K1Y 4E9. E-mail: jdonnelly@civich.ottawa.on.ca

0002-9297/2000/6602-0045$02.00

Am. J. Hum. Genet. 66:744–745, 2000

Reply to Donnelly

To the Editor:

Donnelly comments, in his letter, on the confusing numbering used for the nomenclature of the second single-