

### Letters to the Editor

## Human Cytochrome P-450 (CYP) Genes: A Web Page for the Nomenclature of Alleles

### Letter

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The human cytochromes P-450 active in xenobiotic polymorphism are highly polymorphic (1). The current explosion in SNP<sup>1</sup> discovery emphasizes the need to have databases in the field that are frequently updated with respect to the nature and functional consequences of the different allelic variants, and that contain a consensus nomenclature system commonly accepted and used by all colleagues in the field. To fulfill these requirements with regard to the different human cytochrome P-450 (CYP) alleles encoding enzymes active in xenobiotic metabolism, a Web page has been constructed that contains a continuously updated list of allelic variants of cytochrome P-450 genes with Mikael Oscarson as Webmaster; Magnus Ingelman-Sundberg, Ann Daly, and Dan Nebert as Editors; and an International Advisory Committee with Jürgen Brockmöller, Michel Eichelbaum, Seymour Garte, Joyce A. Goldstein, Frank J. Gonzalez, Fred F. Kadlubar, Tetsuya Kamataki, Urs A. Meyer, David R. Nelson, Michael R. Waterman, and Ulrich M. Zanger. The Web page, which can be found at <http://www.imm.ki.se/CYPalleles/>, contains the latest updated knowledge about the allelic variants of genes in the human *CYP1*, *CYP2*, *CYP3*, *CYP5*, and *CYP8* families. There are also relevant online links to the papers describing each allele. Inclusion of information on allelic variants of the cytochromes P-450 involved in steroidogenesis is being planned soon. Ultimately, we would hope to include a listing of the common alleles of all 58 human CYP genes that are presently known and have the page continuously updated as new allelic variants of each CYP gene are described.

The principal function of this Web homepage is to encourage scientists worldwide to speak the same language and to avoid “home-made” allelic designations that would only confuse the nomenclature system and the scientific literature. An important additional function of this Web site is to rapidly update everyone about the progress in this rapidly moving field, thereby avoiding unnecessary work characterizing alleles that have already been described. All scientists are encouraged to submit their newly identified allelic variants to the CYP Allele

Nomenclature Committee, using the instructions given on the Web homepage.

In the nomenclature system for CYP alleles, the same general rules as have already been described for the human *CYP2D6* gene (2) are used, as further discussed by Nebert (3), to take into consideration the SNP explosion. These rules are also consistent with those of the Human Allele Nomenclature Working Group (4, 5).

It would be a disadvantage to rename existing alleles that have already been named, and in the Web page the established nomenclature for some P-450 genes have been kept. Regarding *CYP1A1* and *CYP2E1*, two different nomenclature systems were simultaneously proposed (6). At a meeting in July 2000 between members of the human CYP allele nomenclature committee and editors of the IARC Scientific publication (7), it was decided to recommend that all scientists use the system provided in the CYP alleles Web page.

The designation of a new unique allele (e.g., *CYP2D6\*34*) requires identification of one or more SNPs never before seen in all of the allelic series from \*2 through \*33. If a new allele has been detected at the cDNA level, verification of the SNP(s) in genomic DNA is required. Additional nucleotide changes and combinations of nucleotide changes in the gene are given letters (e.g., \*34A, \*34B). In cases where silent SNPs occur or SNPs are present in regulatory sequences or introns with unclear function, the allelic name should adhere to the closest functionally characterized allele by subgroup assignments (e.g., *CYP2D6\*4A*).

The protein is named after its allele but nonitalicized and with a period between the name of the gene product and number (e.g., *CYP2D6.4A*). Unless the 5'-most transcription start site has been well defined for a CYP gene, the nucleotide A in the initiation codon ATG should be denoted +1 and the base before A is numbered -1 (5).

The first alleles sequenced (or which are very similar in sequence and enzymatic activity to that of the reference allele) are to be designated as \*1 (or \*1A, \*1B, etc.). The references (or consensus or wild-type) allele will thus not necessarily be the major allele in every ethnic group. The inclusion of information on allele frequencies in different ethnic groups on the Web site will be considered in the future.

Thus, we encourage everyone to follow the guidelines provided on the Web page when describing and naming new CYP alleles. These guidelines include discussion with, and approval by, members of the Human Cytochrome P-450 (CYP) Allele Nomenclature Committee before publishing any paper with a new allele. This standardized nomenclature system will facilitate research in this field, decrease the confusion about allelic names, and be important for the future development of molecular epidemiology, ecogenetics, and pharmacogenetics.

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<sup>1</sup> The abbreviation used is: SNP, single nucleotide polymorphism.

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