(FBrf0086241)

From: ma11 [redacted]
Date: Thu, 2 Nov 95 09:18:07 GMT
To: [redacted]
Subject: Re: cytochrome P450s in FlyBase

----- Begin Included Message -----

>From [redacted] Thu Nov 2 00:15:35 1995
Date: Thu, 2 Nov 95 00:15:19 GMT
Mime-Version: 1.0
Content-Type: multipart/mixed;
boundary="==========_3479936==_"
To: [redacted]
From: [redacted] (Rene' Feyereisen)
Subject: Re: cytochrome P450s in FlyBase
Content-Length: 50308

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Content-Type: text/plain; charset="us-ascii"

Dear Rachel and Michael:
I am at last sending the P450 nomenclature text, as well as the annotated
entries for FlyBase. Because it is difficult to determine which P450 enzyme
catalyzes which biochemical reaction, or which P450 is responsible for which type of metabolic resistance, I have also made some commnets about references that might be confusing and that I would suggest to delete.
I also added 9 new P450 gene entries.
Most is self explanatory. The allele designation is a bit tricky, but it can be accomodated in a reasonable way, I think.
I have added a $$ sign above each alteration of the record. I hope I didn't
make too much of a mess.

The file is attached as a BinHex file (I think). If this presents a problem, I'll incorporate it into an E-mail message.

Thank you so much for your interest in keeping us P450 people organized. The latest Science issue on genome mapping claimed that there would be 60
P450 genes in C. elegans ! I don't know if we'll go this high in Drosophila, but if we do, implementing a nomenclature early will not have
been in vain.

Best regards from the land of the cactophilc Drosophila,
Rene

--==========_3479936==_
Content-Type: application/mac-binhex40; name="droso_e-mail_#1"
Content-Disposition: attachment; filename="droso_e-mail_#1"

--==========_3479936==_
Content-Type: text/plain; charset="us-ascii"

.Rene' Feyereisen
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.Tucson AZ 85721

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--==========_3479936==_--

----- End Included Message -----

Attachment converted: JANE:droso e-mail #1 (WDBN/MSWD) (00000676)

Drosophila P450 gene nomenclature:

The large number of cytochrome P450 genes (more than 50 in the human genome) and the possible confusion in nomenclature caused by the use of trivial names or laboratory-specific idiosyncrasies has led a nomenclature committee to recommend an official nomenclature of P450 names (latest update : NELSON *et al.* 1993, DNA and Cell Biology 12: 1-51.; Next update: NELSON *et al.* Pharmacogenetics, first issue of 1996). This nomenclature is almost universally accepted, and depends mostly on the efforts of Dr. David Nelson who assigns names upon submission of sequence information to him. This nomenclature calls for the CYP prefix followed by a family designation (arabic numeral), subfamily designation (letter) and gene number. These are in capitals and italics for genes (e.g. "the *CYP1A1* gene"), and in capitals for cDNA, mRNA and protein products (e.g. "the CYP1A1 protein"). The rules of the human nomenclature are followed in all species. In the mouse, the nomenclature has been adapted for gene names to conform to the nomenclature of mouse genes (e.g. "*Cyp1a1*").

As work on *Drosophila* P450 increases, there is a need to prevent confusion and to facilitate diffusion of information on P450 genes. FlyBase has become the repository of information on *Drosophila* genetic loci, rapidly replacing the "red book". It has come to our attention that FlyBase lists P450 genes in a way that differs from the P450 nomenclature and this may be the source of unneccessary confusion. On the other hand, the P450 nomenclature differs in minor details from the accepted nomenclature of *Drosophila* genes. In order to conform to the P450 nomenclature AND to the nomenclature of *Drosophila* genes, we propose a nomenclature system for Drosophila cytochrome P450 genes and urge for its dissemination through FlyBase and through publications of the authors who have reviewed and approve this communication.

For *Drosophila* P450 genes, we recommend that the italicized root symbol "*Cyp*" representing Cytochrome P450, be followed by an italicized Arabic number denoting the family, a italicized letter denoting the subfamily (when two or more exist), and an Arabic numeral representing the individual gene within the subfamily. The cDNA, mRNA and protein should include all capital letters without italics or hypens in accord with the P450 nomenclature.

Example: Gandhi et al 1992 DNA and Cell Biol 11: 397-404. The P450 gene identified by these authors should be called *Cyp4d1* and its product CYP4D1 (This gene is currently listed in FlyBase as Cyt-P450-4D1). The proposed nomenclature is in agreement with the *Drosophila* tradition e.g. *Adh* gene and ADH enzyme.

Synonyms: Genes named and characterized before their identity as a P450 was known can maintain their traditional name, but the Cyp designation becomes a *synonym*.

Allelic variants: The P450 nomenclature calls additional alleles of a known P450 gene by the suffix v1, v2 etc. while the "type" sequence has no suffix. In the *Drosophila* nomenclature, all alleles have an italicized superscript following the gene designation. The allele designations can be quite complex. We propose that coding sequence variants of P450 genes be named by superscripted v designations. For example, an allelic variant ($His^{29}Arg$) of *Cyp4u2* from a Timbuktu collection, would be $Cyp4u2^{v1}$ where *Cyp4u2* represents the sequence of the gene first isolated from the Oregon-R strain. The His^{29} mutation may or may not have a phenotype or a different catalytic activity. Alleles of unknown sequence or alleles varying in sequence outside the coding region may be named in the traditional *Drosophila* way (e.g. $Cyp4u2^{oboy}$).

Pseudogenes: Confirmed pseudogenes would have a p suffix, for instance *Cyp4e1p*

We would ask FlyBase curators to reserve *Cyp-number-letter-number* (e.g. *Cyp6a2*) to P450 genes, and to prevent possible confusions by accepting only P450 names that have been approved by the P450 nomenclature committee. To obtain a P450 name assignment, authors can contact Dr. David R. Nelson (fax 901 448 7360; E-mail "DNELSON@UTMEM1.UTMEM.EDU"). Dr. Nelson collates P450 sequences in strict confidence before publication and will make assignments after consultation with the P450 nomenclature committee.

We believe that rapid implementation of this nomenclature would benefit not only workers in the P450 field, but also all Drosophilists who sooner or later will stumble upon a P450 gene in their studies. We note that *Cyp4e1*, *Cyp4d1*, *Cyp4d2* and *Cyp18* (the Hurban & Thummel *Eig17-1* gene) were all characterized or sequenced in projects that were not aimed at P450 genes, and that perhaps twenty new *Drosophila* P450 genes are likely to be described in the coming year.

Current problems with P450 genes in FlyBase:

Flybase : Cyt-P450-17C: confusion is possible because there is a CYP17 in vertebrates (the gene for 17α hydroxylase / 17,20 lyase). The P450 gene identified originally by Hurban and Thummel (*Eig 17-1*) is not a member of the CYP17 family but a CYP18 (*Cyp18*).

Flybase: Cyt-P450-A1 and Cyt-P450-B1: The A1 and B1 designation are trivial names used by Waters and collaborators. The P450 nomenclature allows the use of trivial names as in "P450-B1" in publications but recommends that the official name (*Cyp6a2*) be used for easy identification.

Flybase: Cyt-P450-D2: This P450 is in fact *Cyp4d2* also listed as Cyt-P450-4D2 and Cyt-P450-X in FlyBase.

Flybase: Cyt-P450-X: cyt P450 on X. We know of at least 6 P450 genes on the X. This P450 is in fact *Cyp4d2*.

FlyBase: a (minor) problem is that one gene, *Cyp1*, is currently listed in FlyBase. It is a cyclophilin-1 gene. Because P450 genes would usually have at least a letter and a number in addition to the *Cyp-number* prefix, this would not cause a major problem (except for inadequately programmed computers). *Cyp1* would probably not be confused with CYP1A1 found (so far) only in vertebrates.

Flybase calls P450 gene products "mixed-function monooxygenase" and gives EC number 1.14.14.1. We recommend dropping the EC designation which is both outdated and formally incorrect (in some cases P450 are reduced by iron sulfur proteins, not flavoproteins). We also recommend calling these enzymes either monooxygenase (preferred) or mixed-function oxidase, in keeping with the original O. Hayaishi and H. Mason designations of these enzymes ("mixed-function monooxygenase" is at best a tautology). In some cases, P450 enzymes act as endoperoxide isomerases, thus are not formally oxygenases.

Signatories:

René Feyereisen : University of Arizona

Daniel W. Nebert : University of Cincinnati
(P450 nomenclature committee)
David R. Nelson : University of Tennessee, Memphis
(P450 nomenclature committee)

Marcel Amichot : INRA, Antibes, France
Jean B. Bergé :INRA, Antibes, France
Boris C. Dunkov : University of Arizona
James Fogleman : University of Denver
Richard ffrench-Constant : University of Wisconsin
Ranjan Ganguly : University of Tennessee, Knoxville
Patrick Hurban : Stanford University
Timothy J. Sliter : Southern Methodist University
Larry C. Waters : Oak Ridge Natl. Lab.

My EDITIONS are preceded by $$ and placed under the edited line

My ADDITIONS are also preceded by $$

Combine Cyt-P450-D2, Cyt-P450-4D2 and Cyt-P450-X as a single gene record > Cyp4d2
$$yes

Change Cyt-P450-17C to Cyp18
$$yes

Change Cyt-P450-B1 to Cyp6a2
$$yes

Change Cyt-P450-4D1 to Cyp4d1
$$yes

!!! Change Cyt-P450-A1 to ? Cyp6a1
$$ Cyp4g1 (CYP6A1 is a house fly gene)

!!! Change Cyt-P40-4E2 to ? Cyp4e2
$$yes

!!! Change Cyt-P450-rAF4 to ?
$$Cyp6a9

!!! Change Cyt-P450-rAF5 to ?
$$Cyp6a8

!!! Change Cyt-P450-rBF6-2 to ?
$$yet unnamed P450 gene fragment, at same cytological location as Cyp6a8 and Cyp6a9 (the three are part of a cluster at 51C)

Replace all
*F unspecific monooxygenase == EC 1.14.14.1
by
*F monooxygenase
with no EC number

$$ replace all
*f mitochondrion
by
*f endoplasmic reticulum / microsomes
[none of the currently known Drosophila P450 have been shown to be mitochondrial, and all are assumed to be microsomal. Note that mitochondrial forms of P450 will be discovered in

Drosophila in the near future. Some (e.g. CYP12) have already been characterized in the house fly].

!!! I await yr suggestions about renaming alleles:

*A Cyt-P450-B1[91C]
*A Cyt-P450-B1[91R]
$$ The question of allele names is a thorny one. I think it doesn't really matter how they are called, but it seems that giving the name of a strain (91C or 91R) is a poor precedent in the long term, and is in violation of the Lindsley &Zimm (p.1) statement warning against the use of elements of the genotype in allele designations. The 91C and 91R sequences are really polymorphisms. There are not "mutant alleles" in the usual Drosophila sense. There is no firm evidence that overexpression of the Cyp6a2 gene in the 91R strain is a trait linked in any way to the sequence of the gene. Instead, all evidence to date points to a regulation in trans (just like overexpression of the CYP6A1 gene in some strains of the house fly). Our proposal was to give v1,v2,v3 etc. superscript alleles designations for VARIANTS IN THE CODING SEQUENCE of the P450 gene. This would not have to conflict with the traditional way of doing things in Drosophila. There are examples where a single amino acid substitution will change the substrate specificity of a P450 protein, but the amount of work needed to prove such differences in catalytic activity will remain an obstacle for a long time (compared to the ease with which structural variants will be sequenced). Also the concept of "wild type" is a bit moot (I don't think many P450s will be discovered by the mutant allele route). I have no objection to calling the two alleles Cyp6a2[91R] and Cyp6a2[91C], but then which sequence will be the "wild type" and become Cyp6a2[+] or, commonly, Cyp6a2 ? Perhaps Larry Waters should be given the opportunity to name the alleles, since he first published their sequence ?

note that

*A Cyt-P450-4D1[+tGa]

is a rather special case as this is an engineered allele (Rachel adds, and does not represent a sequence variant, FlyBase systematically names such rescue construct alleles itself, for curational purposes).

In addition to the changes above, and the queries, if you send this file back with us annotated with any other corrections - if possible with references - we will implement them.

Michael Ashburner, for FlyBase

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==========================================================

*a Cyt-P450-17C
$$ Cyp18
*i Eig17-1
*e Cytochrome P450 17C
$$ Cyp18, a member of the cytochrome P450 superfamily
*z FBgn0010383
*b 1-[59]
*c 17C
*d cytochrome P450
*d dimethylnitrosamine demethylase \?
$$ no enzymatic evidence available. remove previous line.

$$
Eig17-1 is an ecdysone-inducible gene in larvae.

*F unspecific monooxygenase == EC 1.14.14.1
$$ monooxygenase
*g S66112
*x FBrf0064515 == Hurban and Thummel, 1993, Molec. Cell.
Biol. 13(11): 7101--7111
*f mitochondrion
$$ endoplasmic reticulum / microsomes
#
*a Cyt-P450-4D1
$$ Cyp4d1
*i Cyp4D1
$$ delete *i
*e Cytochrome P450 4D1
$$ Cyp4d1, a member of the cytochrome P450 superfamily
*z FBgn0005670
*y FBgn0010221
*b 1-[0.5]
*c 2D
*d cytochrome P450
*J PS00086 == Cytochrome P450 cysteine heme-iron ligand
signature.
*F unspecific monooxygenase == EC 1.14.14.1
$$ monooxygenase
*g X67645
*m PIR/S25707
*m SWP/P33269
*u Maps between Pgd and pn; does not correspond to any known
lethal complementation group.
*x FBrf0068050 == Alatortsev and Frolov, 1994, A. Conf. Dros.
Res. 35 : 181
*x FBrf0055783 == ew606.mg == Gandhi et al., 1992, DNA Cell
Biol. 11(5): 397--404
*f mitochondrion
$$ endoplasmic reticulum / microsomes
*E FBrf0055783 == ew606.mg == Gandhi et al., 1992, DNA Cell
Biol. 11(5): 397--404
*N 2D4,2D6
```

```
*Z 35
*T 1.7
*Y 1.7
*K High levels in 2nd & 3rd instar larvae
*S 500 aa
*i CYP4D1
*A Cyt-P450-4D1[+tGa]
*x FBrf0055783 == Gandhi et al., 1992, DNA Cell Biol. 11(5):
397--404
*E FBrf0055783 == Gandhi et al., 1992, DNA Cell Biol. 11(5):
397--404
*i unnamed
*o in vitro mutagenesis | rescue fragment
*k Mode of assay: Assayed in vivo (genomic allele of gene)
*P P{Cyt-P450-4D1[+tGa]}
#
*a Cyt-P450-4D2
$$ Cyp4d2
*e Cytochrome P450 4D2
$$ Cyp4d2, a member of the cytochrome P450 superfamily
*z FBgn0011576
*b 1-[0.5]
*c 2D
*d cytochrome P450
*F unspecific monooxygenase == EC 1.14.14.1
$$ monooxygenase

$$
*g Z23005
*g X75955
*m PIR/S41192

*x FBrf0068050 == Alatortsev and Frolov, 1994, A. Conf. Dros.
Res. 35 : 181
$$ Frolov and Alatortsev, 1994, DNA Cell Biol. 13(6): 663--
668
*f mitochondrion
$$ endoplasmic reticulum / microsomes
#
*a Cyt-P450-4E2
$$ Cyp4e2

$$
*e Cyp4e2, a member of the cytochrome P450 superfamily
$$
*c 44D1-2

*d cytochrome P450
*F unspecific monooxygenase == EC 1.14.14.1
$$ monooxygenase
*g X86076
$$
*g U34332
```

$$ Cyp4e2 is overexpressed in the Raleigh DDT resistant strain. Cyp4e2 is inducible by phenobarbital.

$$
*x AMICHOT M., A. BRUN, A. CUANY, C. HELVIG, J. P. SALAUN, F. DURST,. and J. B. BERGE, 1994. Expression study of CYP genes in drosophila strains resistant or sensitive to insecticides. pp. 689-692 in *Cytochrome P450* edited by M. C. Lechner. John Libbey Eurotext, Paris.
*x Dunkov, B.C., R. Rodriguez-Arnaiz, B. Pittendrigh, R. H. ffrench-Constant and R. Feyereisen. Cytochrome P450 gene clusters in *Drosophila melanogaster*. (Unpublished).(ref for accession number and localization)

#
*a Cyt-P450-A1
$$ Cyp4g1
*e Cytochrome P450 A1
$$ Cyp4g1, a member of the cytochrome P450 superfamily. Its product is known under the trivial name "P450-A1".

$$
*c 1B
*g U34328
*x Dunkov, B.C., R. Rodriguez-Arnaiz, B. Pittendrigh, R. H. ffrench-Constant and R. Feyereisen. Cytochrome P450 gene clusters in *Drosophila melanogaster*. (Unpublished).(ref for accession number and localization)

*z FBgn0010019
*F unspecific monooxygenase == EC 1.14.14.1
$$ monooxygenase

*p Visualised as 59.3 kD band on electrophoresis.
*p Ubiquitous in all strains,irrespective of resistance to insecticides (Sundseth, Kennel and Waters, 1989). Monoclonal antibodies
*p raised by Sundseth, Kennel and Waters (1989).
$$ corresponds to the cytochrome P450 A1 cDNA of Waters et al. 1992
*s cDNA isolated by Waters, Ch'ang and Kennel (1990), by
*s screening lambdagt11 library with monoclonal antibody
*s 13-2e (see Waters, Zelhof, Shaw and Ch'ang (1992) for
*s cDNA restriction map).

$$ None of the following references can be claimed to refer specifically to Cyp4g1, but refer to presumed P450 bands on SDS-PAGE etc.. To prevent any confusion, these references ought to be deleted.

*x FBrf0042110 == Hallstrom and Blanck, 1985, Chem. Biol. Interact. 56: 157--172
*x FBrf0040374 == Hallstrom et al., 1984, Biochem. Pharmac. 33: 13--20

*x FBrf0042111 == Hallstrom, 1985, Chem. Biol. Interact. 56: 173--184
*x FBrf0035042 == Naquira et al., 1980, Gustafsson, Carstedt-Duke, Mode, Rafter, 1980: 105--108
*x FBrf0044840 == Waters and Nix, 1986, J. Cell. Biochem. 10: 93
*x FBrf0048878 == Waters and Nix, 1988, Pestic. Biochem. Physiol. 30: 214--227
*x FBrf0040381 == Waters et al., 1984, Biochem. biophys. Res. Commun. 123: 907--913
*x FBrf0041528 == Waters et al., 1984, Mutat. Res. 139: 51--55

$$ the following references are appropriate:
*x FBrf0050756 == ew579.m == Sundseth et al., 1989, Pestic. Biochem. Physiol. 33(2): 176--188
*x FBrf0052776 == Waters et al., 1990, Pestic. Sci. 30(4): 456--458
*x FBrf0066870 == Waters et al., 1991, Mullin, Scott, 1991: 41--52
*x FBrf0057534 == ma71.g == Waters et al., 1992, Proc. natn. Acad. Sci. USA. 89: 4855--4859
*f mitochondrion
$$ endoplasmic reticulum /microsomes

*E FBrf0050756 == ew579.m == Sundseth et al., 1989, Pestic. Biochem. Physiol. 33(2): 176--188
*i P450-A
#
*a Cyt-P450-B1
$$ Cyp6a2
*i CYP6A2
$$ delete
*e Cytochrome P450 B1
$$ Cyp6a2, a member of the cytochrome P450 superfamily. Its product is known under the trivial name "P450-B1".
*z FBgn0000473
*y FBgn0010312
*b 2-[56]
*c 42D
$$ we (Dunkov et al.) found it at 43A1-2; Dr. Ganguly and coworkers will recheck this unpublished localization.
*d cytochrome P450
*J PS00086 == Cytochrome P450 cysteine heme-iron ligand signature.
*j CYP6A1 [Musca domestica] 49% aa similarity
*F unspecific monooxygenase == EC 1.14.14.1
$$ monooxygenase
*g S51248
*g M88009
*m PIR/A45378
*m SWP/P33270
*m PIR/A47198

$$ the following comments are an oversimplification of the situation. All that is known for sure is that Cyp6a2 is overexpressed in some resistant strains (e.g. the 91R strain). The ACTIVITY of the enzyme CYP6A2 is unknown. Furthermore there has been no thorough linkage analysis of Cyp6a2 overexpression and resistance. I suggest replacing this statement by: "Cyp6a2 expression varies considerably between diffeent strains. For instance, higher RNA levels are found in the 91R strain (insecticide resistant) when compared to the 91C strain (susceptible)(Waters, Zelhof, Shaw and Ch'ang, 1992)".

*p Different strains differ with respect to presence or
*p absence of this activity. Associated with insecticide
*p resistance. The activity
*p of cytochrome P450-B correlates with phenylurea
*p resistance (Waters and Nix, 1988) and with malathion
*p and DDT resistance (Sundseth, Kennel and Waters,
*p 1989). The 56 kD and 54 kD bands associated with
*p p-nitroanisole demethylase and biphenyl-3-hydroxylase
*p activity by Hallstrom, Blanck and Atuma (1984) and
cytochrome P450-III of Naquira, White and Agosine
*p (1980) are
*p probably also due to P-450-B1.

$$ the following comments are factual and appropriate:

*p Monoclonal antibodies to cytochrome P450-B1 raised by
*p Sundseth, Kennel and Waters (1989) and these reveal
*p protein even in insecticide-susceptible strains in
*p which activity cannot be seen otherwise.
*s cDNAs isolated by screening a lambdagt11 library with
*s monoclonal antibody 8-1d (Waters, Ch'ang and Kennel,
*s 1990; Waters, Zelhof, Shaw and Ch'ang, 1992). An
*s intronless gene that encodes a 507 amino acid protein,
*s MW 58,835 daltons; 49% similar in sequence to CYP6A1
*s of Musca domestica. mRNA is 20-30 times more abundant
*s in 91R (insecticide resistant) than in the susceptible
*s 91C strain. The Cyt-P450-B1 gene of the 91C strain
*s differs from that of 91R by a 17.6 element LTR
*s insertion (513bp) in the 3' untranslated region.
*s 560bp 3' to the translated region of the gene a 96bp
*s insert characterises 91R. This sequence has about 70%
*s similarity with U1b small nuclear RNA sequences in
*s U1snRNA82Ea and U1snRNA82Eb (Lo and Mount, 1990). It
*s is suggested by Waters, Zelhof, Shaw and Ch'ang (1992)
*s that the 17.6 insertion down regulates Cyt-P450-B1 in
*s 91C by reducing mRNA stability.

$$ the following references and comments are confusing and not appropriate. There is little evidence that these papers directly or indirectly refered to Cyp6a2.

*u Relationship of Cyt-P450-B1 to Rst(2)mth (Houpt,
*u Pursey and Morton, 1988) is unclear.
*x FBrf0068133 == Dombrowski et al., 1994, A. Conf. Dros. Res. 35 : 224
*x FBrf0058754 == Ganguly et al., 1993, Int. Congr. Genet. 17 Abstr. 17: 170

*x FBrf0042110 == Hallstrom and Blanck, 1985, Chem. Biol. Interact. 56: 157--172
*x FBrf0040374 == Hallstrom et al., 1984, Biochem. Pharmac. 33: 13--20
*x FBrf0042111 == Hallstrom, 1985, Chem. Biol. Interact. 56: 173--184
*x FBrf0052749 == Lo and Mount, 1990, Nucleic Acids Res. 18: 6971--6979
*x FBrf0035042 == Naquira et al., 1980, Gustafsson, Carstedt-Duke, Mode, Rafter, 1980: 105--108
*x FBrf0050756 == ew579.m == Sundseth et al., 1989, Pestic. Biochem. Physiol. 33(2): 176--188
*x FBrf0044840 == Waters and Nix, 1986, J. Cell. Biochem. 10: 93
*x FBrf0048878 == Waters and Nix, 1988, Pestic. Biochem. Physiol. 30: 214--227
*x FBrf0037524 == Waters et al., 1982, Biochem. biophys. Res. Commun. 106(3): 779--785
*x FBrf0039026 == Waters et al., 1983, Chem. Biol. Interact. 46: 55--66
*x FBrf0040381 == Waters et al., 1984, Biochem. biophys. Res. Commun. 123: 907--913
*x FBrf0041528 == Waters et al., 1984, Mutat. Res. 139: 51--55

$$ the following references are appropriate:

*x FBrf0052776 == Waters et al., 1990, Pestic. Sci. 30(4): 456--458
*x FBrf0066870 == Waters et al., 1991, Mullin, Scott, 1991: 41--52
*x FBrf0057513 == Waters et al., 1992, Proc. natn. Acad. Sci. USA. 89: 12209
*x FBrf0057534 == ma71.g == Waters et al., 1992, Proc. natn. Acad. Sci. USA. 89: 4855--4859

*x FBrf0059271 == 977.mUCLA-X == Delpuech et al., 1993, Proc. natn. Acad. Sci. USA. 90(12): 5643--5647
*x FBrf0078953 == ew2187 == Maitra et al., 1995, A. Conf. Dros. Res. 36: 277B
*f mitochondrion
$$ endoplasmic reticulum /microsomes

*E FBrf0057534 == ma71.g == Waters et al., 1992, Proc. natn. Acad. Sci. USA. 89: 4855--4859
*s Putative heme binding site near cysteine at aa 452.
*s has 17.6 element LTR insertion (513bp) in the 3'
*s untranslated region.
*Z 6.3
*T 1.69
*S 507 aa
*S 58.835 kD
*p The level of cytochrome P450-B1 monooxygenase is much higher in strains
*p resistant to DDT. In a susceptible strain a solitary 17.6 element LTR
*p is present in the 3' untranslated end of the gene; this is absent from
*p a resistant strain.
*E FBrf0050756 == ew579.m == Sundseth et al., 1989, Pestic. Biochem. Physiol. 33(2): 176--188
*i P450-B
*p Monoclonal antibody studies demonstrate that Cyt-P450-B1 expression
*p is regulated by resistance genes on the second and third chromosomes,
*p and is correlated with the resistance to phenylurea, DDT and malathion.
*E FBrf0059271 == 977.mUCLA-X == Delpuech et al., 1993, Proc. natn. Acad. Sci. USA. 90(12): 5643--5647
*p Presence or absence of a long terminal repeat of 17.6 is uncorrelated
*p with resistance or susceptibility to DDT in 31 strains of D. melanogaster
*p and D. simulans from around the world.
*E FBrf0078953 == ew2187 == Maitra et al., 1995, A. Conf. Dros. Res. 36: 277B
*i CYP6A2
*A Cyt-P450-B1[91C]
$$ Cyp6a2[91C] but see discussion above re: alleles
*z FBal0002207
*k characteristic of insecticide susceptible strains
*x FBrf0057534 == ma71.g == Waters et al., 1992, Proc. natn. Acad. Sci. USA. 89: 4855--4859
*x FBrf0050756 == ew579.m == Sundseth et al., 1989, Pestic. Biochem. Physiol. 33(2): 176--188
*E FBrf0057534 == ma71.g == Waters et al., 1992, Proc. natn. Acad. Sci. USA. 89: 4855--4859
*P 17.6{}Cyt-P450-B1[91C]
*A Cyt-P450-B1[91R]
$$ Cyp6a2[91R] but see discussion above re: alleles
*z FBal0002208
*k Selected on basis of resistance to DDT: ten times more resistant to malathion
*k than the unselected Cyt-P450-B1[91C] (Sundseth et al., 1989).

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*x FBrf0050756 == ew579.m == Sundseth et al., 1989, Pestic.
Biochem. Physiol. 33(2): 176--188
*x FBrf0057534 == Waters et al., 1992, Proc. natn. Acad. Sci.
USA. 89: 4855--4859
*E FBrf0057534 == Waters et al., 1992, Proc. natn. Acad. Sci.
USA. 89: 4855--4859
*s 96bp insert 560bp 3' to the translated region of the
*s gene has about 70% similarity with U1b small nuclear RNA
*s sequences in U1snRNA82Ea and U1snRNA82Eb.
*V Microsomes (whole body); essentially absent in susceptible
91-C strain.

#
$$ delete this entry. see Cyp4d2 entry
*a Cyt-P450-D2
*e Cytochrome P450 D2
*z FBgn0010384
*b 1-
*F unspecific monooxygenase == EC 1.14.14.1
*g X75955
*m PIR/S41192
*x FBrf0073110 == Frolov and Alatortsev, 1994, DNA Cell Biol.
13(6): 663--668
*f mitochondrion

#
*a Cyt-P450-rAF4
$$ Cyp6a9
*d cytochrome P450
*F unspecific monooxygenase == EC 1.14.14.1
$$ monooxygenase
*x FBrf0078953 == ew2187 == Maitra et al., 1995, A. Conf.
Dros. Res. 36: 277B
*E FBrf0078953 == ew2187 == Maitra et al., 1995, A. Conf.
Dros. Res. 36: 277B
*e cytochrome P450 related AF4
$$ Cyp6a9, a member of the cytochrome P450 superfamily.
*b 2-
*c 51C (determined by in situ hybridisation)
*u Isolated in a cDNA library under low stringency using
@Cyt-P450-B1@
*u cDNA as a probe.
$$ the clone was called AF4.

#
*a Cyt-P450-rAF5
$$ Cyp6a8
*d cytochromeP450
*F unspecific monooxygenase == EC 1.14.14.1
$$ monooxygenase
*x FBrf0078953 == ew2187 == Maitra et al., 1995, A. Conf.
Dros. Res. 36: 277B
*E FBrf0078953 == ew2187 == Maitra et al., 1995, A. Conf.
Dros. Res. 36: 277B
```

```
*e cytochrome P450 related AF5
$$ Cyp6a8, a member of the cytochrome P450 superfamily
*b 2-
*c 51C (determined by in situ hybridisation)
*u Isolated in a cDNA library under low stringency using
@Cyt-P450-B1@
*u cDNA as a probe.
$$ the clone was called AF5

#
$$ this entry is for a P450 gene fragment that has not been
named yet. I don't think it is useful to quote genes by their
preliminary lab notebook names. It only makes a mess later
on. Why not wait until even a partial sequence is deposited
and named ?
*a Cyt-P450-rBF6-2
*d cytochrome-P450
*F unspecific monooxygenase == EC 1.14.14.1
*x FBrf0078953 == ew2187 == Maitra et al., 1995, A. Conf.
Dros. Res. 36: 277B
*E FBrf0078953 == ew2187 == Maitra et al., 1995, A. Conf.
Dros. Res. 36: 277B
*e cytochrome P450 related BF6-2
*u Isolated in a cDNA library under low stringency using
@Cyt-P450-B1@
*u cDNA as a probe.

#
$$ delete this entry; see Cyp4d2 entry
*a Cyt-P450-X
*e Cytochrome P450 on X
*z FBgn0010219
*b 1-
*d cytochrome-P450
*F unspecific monooxygenase == EC 1.14.14.1
*g Z23005
*x FBrf0073110 == Frolov and Alatortsev, 1994, DNA Cell Biol.
13(6): 663--668
*f mitochondrion
*m PIR/S34291
#

$$ new entries:

*a Cyp4e1
*e Cyp4e1, a member of the cytochrome P450 superfamily
*c 44D
*d cytochrome P450
*F monooxygenase
*g K00045
*x This P450 fragment was discovered by D. Nero and by T.
Holton in GenBank. see discussion in:
NELSON, D. R., T. KAMATAKI, D. J. WAXMAN, F. P. GUENGERICH,
R. W. ESTABROOK, R. FEYEREISEN, F. J. GONZALEZ, M. J. COON,
```

I. C. GUNSALUS, O. GOTOH, K. OKUDA and D. W. NEBERT, 1993 The P450 superfamily: Update on new sequences, gene mapping, accession numbers, early trivial names of enzymes, and nomenclature. DNA and Cell Biology 12: 1-51.

The original reference for the sequence accession is : SNYDER, M. and N. DAVIDSON, 1983 Two gene families clustered in a small region of the *Drosophila* genome. J. Mol. Biol. 166: 101-118.

*f endoplasmic reticulum / microsomes
#
*a Cyp4d8
*e Cyp4d8, a member of the cytochrome P450 superfamily
*c 2E
*d cytochrome P450
*F monooxygenase
*g U34329
*x Dunkov, B.C., R. Rodriguez-Arnaiz, B. Pittendrigh, R. H. ffrench-Constant and R. Feyereisen. Cytochrome P450 gene clusters in *Drosophila melanogaster*. (Unpublished).
*f endoplasmic reticulum / microsomes

#
*a Cyp4e4
*e Cyp4e4, a member of the cytochrome P450 superfamily
*c 2E1-2
*d cytochrome P450
*F monooxygenase
*g U34331
*x Dunkov, B.C., R. Rodriguez-Arnaiz, B. Pittendrigh, R. H. ffrench-Constant and R. Feyereisen. Cytochrome P450 gene clusters in *Drosophila melanogaster*. (Unpublished).
*f endoplasmic reticulum / microsomes

#
*a Cyp4e3
*e Cyp4e3, a member of the cytochrome P450 superfamily
*c 30C5-7
*d cytochrome P450
*F monooxygenase
*g U34325
*x Dunkov, B.C., R. Rodriguez-Arnaiz, B. Pittendrigh, R. H. ffrench-Constant and R. Feyereisen. Cytochrome P450 gene clusters in *Drosophila melanogaster*. (Unpublished).
*f endoplasmic reticulum / microsomes

#
*a Cyp9b2
*e Cyp9b2, a member of the cytochrome P450 superfamily
*c 242D1-2
*d cytochrome P450
*F monooxygenase
*g U34325

*x Dunkov, B.C., R. Rodriguez-Arnaiz, B. Pittendrigh, R. H. ffrench-Constant and R. Feyereisen. Cytochrome P450 gene clusters in *Drosophila melanogaster*. (Unpublished).
*f endoplasmic reticulum / microsomes

#
*a Cyp9b1
*e Cyp9b1, a member of the cytochrome P450 superfamily
*c 43A1-2
*d cytochrome P450
*F monooxygenase
*g U34324
*x Dunkov, B.C., R. Rodriguez-Arnaiz, B. Pittendrigh, R. H. ffrench-Constant and R. Feyereisen. Cytochrome P450 gene clusters in *Drosophila melanogaster*. (Unpublished).
*f endoplasmic reticulum / microsomes

#
*a Cyp4p1
*e Cyp4p1, a member of the cytochrome P450 superfamily
*c 45C1-2
*d cytochrome P450
*F monooxygenase
*g U34327
*x Dunkov, B.C., R. Rodriguez-Arnaiz, B. Pittendrigh, R. H. ffrench-Constant and R. Feyereisen. Cytochrome P450 gene clusters in *Drosophila melanogaster*. (Unpublished).
*f endoplasmic reticulum / microsomes

#
*a Cyp9c1
*e Cyp9c1, a member of the cytochrome P450 superfamily
*c 60D13-16
*d cytochrome P450
*F monooxygenase
*g U34326
*x Dunkov, B.C., R. Rodriguez-Arnaiz, B. Pittendrigh, R. H. ffrench-Constant and R. Feyereisen. Cytochrome P450 gene clusters in *Drosophila melanogaster*. (Unpublished).
*f endoplasmic reticulum / microsomes

#
*a Cyp4c3
*e Cyp4c3, a member of the cytochrome P450 superfamily
*c 100B1-2
*d cytochrome P450
*F monooxygenase
*g U34323
*x Dunkov, B.C., R. Rodriguez-Arnaiz, B. Pittendrigh, R. H. ffrench-Constant and R. Feyereisen. Cytochrome P450 gene clusters in *Drosophila melanogaster*. (Unpublished).
*f endoplasmic reticulum / microsomes

From [redacted] **Thu Nov 2 10:42:34 1995**
From: Michael Ashburner (Genetics) [redacted]
To: [redacted]
Cc: [redacted]
Subject: Re: cytochrome P450s in FlyBase
Date: Thu, 2 Nov 95 10:37:38 GMT

Dear Rene

Many thanks.

The only problems I see are:

*a Cyt-P450-rBF6-2
..

you say as yet un-named ! But we cannot have unnamed genes in FlyBase !

what about
*a CyprBF6-2
until such time it is properly characterised ?
with a note that it is not yet characterised ?
>
*u Not yet fully characterised and, therefore, not yet named systematically.

#

yr text says
*a Cyp9b2
*c 242D1-2
I take this to be 42D1-2

Otherwise I have made all of the very helpful changes and additions.

btw Gerry Rubin has a new P450 in region 35. Since he will come across
others in his sequencing project I suggest you send him a copy
of the naming document ! (G.M. Rubin, HHMI, Life Sciences Annex,
U. of California, Berkeley, CA94720).

Again - I wish others would do as good a job with groups of genes, it
would make our lives easier !

Michael

From [redacted] **Thu Nov 2 18:14:17 1995**
From: Michael Ashburner (Genetics) [redacted]
To: [redacted]
Subject: Re: cytochrome P450s in FlyBase
Date: Thu, 2 Nov 95 18:09:29 GMT

----- Begin Included Message -----

>From [redacted] Thu Nov 2 18:12:53 1995
Date: Thu, 02 Nov 1995 10:35:36 -0700 (MST)
Date-Warning: Date header was inserted by Arizona.EDU
From: [redacted] (Rene' Feyereisen)
Subject: Re: cytochrome P450s in FlyBase
To: [redacted]
Mime-Version: 1.0
Content-Type: text/plain; charset=us-ascii
Content-Transfer-Encoding: 7BIT
Content-Length: 1676

Dear Michael:
Quick answer to your queries:

>*a Cyt-P450-rBF6-2
>..
>
>you say as yet un-named ! But we cannot have unnamed genes in FlyBase !
>
>what about
>*a CyprBF6-2 $$$ I prefer to keep Cyt-P450-rBF6-2, with your *u note. Let's
>keep the Cyp prefix for P450 genes that have gone through David Nelson's
>baptismal procedure $$$
>until such time it is properly characterised ?
>with a note that it is not yet characterised ?
>>
>*u Not yet fully characterised and, therefore, not yet named systematically.
>
>#
>
>yr text says
>*a Cyp9b2
>*c 242D1-2
>I take this to be 42D1-2
>$$ yes, you are correct, sorry. this was a typo $$
>
>Otherwise I have made all of the very helpful changes and additions.
>
>btw Gerry Rubin has a new P450 in region 35. Since he will come across
>others in his sequencing project I suggest you send him a copy
>of the naming document ! (G.M. Rubin, HHMI, Life Sciences Annex,
>U. of California, Berkeley, CA94720).
>
$$$this sounds like a really good idea. I haven't had time to browse through the Drosophila ESTs. David Nelson looked at the human ESTs and got 1,400 entries that matched the query P450. Nobody I know has yet bothered to see how many of these are resamplings of the 50 or so known human P450 genes and how many represent previously unreported genes! In the next couple of days I should send you a manuscript for Molecular and Gencral Genetics on our attempts to probe systematically for P450 genes in Drosophila. This is the Dunkov et al. data with all the new P450 genes$$$.

Rene

.Rene' Feyereisen
.Department of Entomology
.Forbes 410
.University of Arizona
.Tucson AZ 85721

.fax [redacted]
.phone [redacted]

----- End Included Message -----