Cytochrome P450 (E.C. 1.14.-.-)

Overview: The cytochrome P450 enzyme family (CYP450) were originally defined by their strong absorbance at 450 nm due to the reduced carbon monoxide-complexed heme component of the cytochromes. They are an extensive family of heme-containing monooxygenases with a huge range of both endogenous and exogenous substrates. Listed below are the human enzymes; their relationship with rodent CYP450 enzyme activities is obscure in that the species orthologue may not mediate metabolism of the same substrates. Although the majority of CYP450 enzyme activities are concentrated in the liver, the extrahepatic enzyme activities also contribute to patho/physiological processes. Genetic variation of CYP450 isoforms is widespread and likely underlies a significant proportion of the individual variation to drug administration.

CYP1 family (ENSFM00250000000349, EC 1.14.1.1)

Nomenclature	Other names	Ensembl ID	Comments
CYP1A1	Aryl hydrocarbon hydroxylase, CP11, CYP1, P1-450, P450-C, P450DX	ENSG00000140465	–
CYP1A2	Phenacetin O-deethylase, CP12, P3-450	ENSG00000140505	–
CYP1B1	CP1B, GLC3A	ENSG00000138061	Mutations have been associated with primary congenital glaucoma (Stoilov *et al.*, 1997). Inhibited by tetramethoxystilbene (Chun *et al.*, 2001)

CYP2 family (ENSFM00400000131704, ENSFM00400000131705, ENSFM00550000747662)

Nomenclature	Other names	Ensembl ID	EC	Comments
CYP2A6/2A7	Coumarin 7-hydroxylase, CPA6, CYP2A, CYP2A3, CYP2A, CYPIIA7, P450-IIA4	ENSG00000198077	1.14.14.1	Metabolises nicotine
CYP2A13	CYPIIA13	ENSG00000197838	1.14.14.1	–
CYP2B6	CYPIIB6, P450 IIB1	ENSG00000197408	1.14.14.1	–
CYP2C8	CYPIIC8, P450 form 1, P450 MP-12/MP-20, P450 IIC2, S-mephenytoin 4-hydroxylase	ENSG00000138115	1.14.14.1	–
CYP2C9	(R)-limonene 6-monooxygenase, (S)-limonene 6-monooxygenase, (S)-limonene 7-monooxygenase, CYPIIC9, P450 PB-1, P450 MP-4/MP-8, S-mephenytoin 4-hydroxylase, P-450MP	ENSG00000138109	1.14.13.80, 1.14.13.48, 1.14.13.49	–
CYP2C18	CYPIIC18, P450-6B/29C	ENSG00000108242	1.14.14.1	–
CYP2C19	(R)-limonene 6-monooxygenase, (S)-limonene 6-monooxygenase, (S)-limonene 7-monooxygenase, CYPIIC19, P450-11A, Mephenytoin 4-hydroxylase, CYPIIC17, P450-254C	ENSG00000165841	1.14.13.80, 1.14.13.48, 1.14.13.49	–
CYP2D6	Debrisoquine 4-hydroxylase, CYPIID6, P450-DB1	ENSG00000100197	1.14.14.1	–
CYP2E1	CYPIIE1, P450-J	ENSG00000130649	1.14.14.1	–
CYP2F1	CYPIIF1	ENSG00000197446	1.14.14.1	–
CYP2J2	Arachidonic acid epoxygenase, CYPIIJ2	ENSG00000134716	1.14.14.1	–
CYP2R1	Vitamin D 25-hydroxylase	ENSG00000186104	1.14.13.15	–
CYP2S1	CYPIIS1	ENSG00000167600	1.14.14.1	–
CYP2U1	–	ENSG00000155016	1.14.14.1	–
CYP2W1	CYPIIW1	ENSG00000073067	1.14.14.-	–

CYP2A7P1 (ENSG00000213908), CYP2D7P1 (ENSG00000205702), CYP2G1P (ENSG00000130612) and AC008537.5-2 (ENSG00000198251, fragment) are uncharacterized potential pseudogenes from the same families.

CYP3 family (ENSFM00310000088994)

Nomenclature	Other names	Ensembl ID	EC	Comments
CYP3A4	Quinine 3-monooxygenase, CYPIIIA4, Nifedipine oxidase, CYP4503A3, CYPIIIA3, HLp, taurochenodeoxycholate 6-α-hydroxylase, NF-25, P450-PCN1, albendazole monooxygenase, albendazole sulfoxidase	ENSG00000160868	1.14.13.67, 1.14.13.97, 1.14.13.32	Metabolises a vast range of xenobiotics, including antidepressants, benzodiazepines, calcium channel blockers, and chemotherapeutic agents and thus, arguably, the most significant enzyme in drug metabolism interactions
CYP3A5	CYPIIIA5, P450-PCN3, HLp2	ENSG00000106258	1.14.14.1	–
CYP3A7	CYPIIIA7, P450-HFLA	ENSG00000160870	1.14.14.1	–
CYP3A43	Cytochrome P450 3A43	ENSG00000021461	1.14.14.1	–

CYP4 family (ENSFM00400000131716, ENSFM00400000131707)

Nomenclature	Other names	Ensembl ID	EC
CYP4A11	CYPIVA11, lauric acid ω-hydroxylase, fatty acid ω-hydroxylase, P-450 HK ω, CYP4AII, P450-HL-ω, 20-hydroxyeicosatetraenoic acid synthase, 20-HETE synthase	ENSG00000187048	1.14.15.3
CYP4A22	CYPIVA22, lauric acid ω-hydroxylase, fatty acid ω-hydroxylase	ENSG00000162365	1.14.15.3
CYP4B1	CYPIVB1, P450-HP	ENSG00000142973	1.14.14.1
CYP4F2	Leukotriene B_4 20-monooxygenase 1, leukotriene B_4 ω-hydroxylase 1, CYPIVF2, cytochrome P450-LTB-ω	ENSG00000186115	1.14.13.30
CYP4F3	Leukotriene B_4 20-monooxygenase 2, leukotriene B_4 ω-hydroxylase 2, CYPIVF3, cytochrome P450-LTB-ω	ENSG00000186529	1.14.13.30
CYP4F8	CYPIVF8	ENSG00000186526	1.14.14.1
CYP4F11	CYPIVF11	ENSG00000171903	1.14.14.1
CYP4F12	CYPIVF12	ENSG00000186204	1.14.14.1
CYP4F22	–	ENSG00000171954	1.14.14.-
CYP4V2	–	ENSG00000145476	1.14.-.-
CYP4X1	CYPIVX1	ENSG00000186377	1.14.14.1
CYP4Z1	CYPIVZ1	ENSG00000186160	1.14.14.1

AC004597.1 (ENSG00000225607) is described as being highly similar to CYP4F12.

CYP5, CYP7 and CYP8 families (ENSFM00250000001362)

Nomenclature	Other names	Ensembl ID	EC	Comments
CYP5A1	TBXAS1, CYP5, THAS, TS, TXAS, TXS, Thromboxane-A synthase, TXA synthase, TXS	ENSG00000059377	5.3.99.5	Converts prostaglandin H_2 to thromboxane A_2. Inhibited by dazoxiben (Randall *et al.*, 1981) and camonagrel (Gryglewski *et al.*, 1995)
CYP7A1	Cholesterol 7-α-monooxygenase, cholesterol 7-α-hydroxylase, CYPVII	ENSG00000167910	1.14.13.17	–
CYP7B1	Oxysterol 7-α-hydroxylase, 25-hydroxycholesterol 7-α-hydroxylase	ENSG00000172817	1.14.13.100	–
CYP8A1	Prostaglandin I_2 synthase, PTGIS	ENSG00000124212	5.3.99.4	Inhibited by tranylcypromine (Gryglewski *et al.*, 1976).
CYP8B1	7-α-Hydroxycholest-4-en-3-one 12-α-hydroxylase, CYPVIIIB1, 7-α-hydroxy-4-cholesten-3-one 12-α-hydroxylase, sterol 12-α-hydroxylase	ENSG00000180432	1.14.13.95	–

CYP11 (ENSFM00500000269868), CYP17, CYP19, CYP20 and CYP21 families

Nomenclature	Other names	Ensembl ID	EC	Comments
CYP11A1	Cholesterol side-chain cleavage enzyme, cholesterol desmolase, CYPXIA1, $P450_{scc}$	ENSG00000140459	1.14.15.6	Converts cholesterol to pregnenolone.
CYP11B1	Steroid 11β-hydroxylase, CYPXIB1, P450C11, P-450c11	ENSG00000160882	1.14.15.4	Converts deoxycortisone and 11-deoxycortisol to cortisone and cortisol, respectively. Loss-of-function mutations are associated with familial adrenal hyperplasia and hypertension. Inhibited by metyrapone (Watanuki *et al.*, 1978).
CYP11B2	Aldosterone synthase, ALDOS, CYPXIB2, P-450Aldo, aldosterone-synthesizing enzyme, steroid 18-hydroxylase, P-450C18	ENSG00000179142	1.14.15.4, 1.14.15.5	Converts corticosterone to aldosterone.
CYP17A1	Steroid 17-α-hydroxylase/17,20 lyase, CYPXVII, P450-C17, P450c17, steroid 17-α-monooxygenase	ENSG00000148795	1.14.99.9	Converts pregnenolone and progesterone to 17α-hydroxypregnenolone and 17α-hydroxyprogesterone, respectively. Converts 17α-hydroxypregnenolone and 17α-hydroxyprogesterone to dehydroepiandrostandione and androstenedione, respectively. Converts corticosterone to cortisol.

CYP19A1	Aromatase, estrogen synthetase, P-450AROM, CYPXIX	ENSG00000137869	1.14.14.1	Converts androstenedione and testosterone to estrone and estradiol, respectively. Inhibited by anastrazole (Plourde *et al.*, 1994) and letrozole (Bhatnagar *et al.*, 1990).
CYP20A1	CYP-M	ENSG00000119004	1.14.-.-	–
CYP21A2	Steroid 21-hydroxylase, cytochrome P450 XXI, 21-OHase, P450-C21, P-450c21, P450-C21B	ENSG00000198457	1.14.99.10	Converts progesterone and 17α-hydroxyprogesterone to deoxycortisone and 11-deoxycortisone, respectively.

CYP24, CYP26 and CYP27 families (ENSFM00500000269772, ENSFM00250000002048)

Nomenclature	Other names	Ensembl ID	EC	Comments
CYP24A1	1,25-Dihydroxyvitamin D_3 24-hydroxylase, vitamin D_3 24-hydroxylase, 24-OHase, P450-CC24	ENSG00000019186	1.14.13.n4	–
CYP26A1	Retinoic acid-metabolizing cytochrome, P450 retinoic acid-inactivating 1, P450RAI, retinoic acid 4-hydroxylase	ENSG00000095596	1.14.-.-	Inhibited by liarozole.
CYP26B1	Retinoic acid-metabolizing cytochrome, P450 retinoic acid-inactivating 2, P450RAI-2, P450 26A2	ENSG00000003137	1.14.-.-	–
CYP26C1	–	ENSG00000187553	1.14.-.-	–
CYP27A1	Sterol 26-hydroxylase, cytochrome P-450C27/25, sterol 27-hydroxylase, vitamin D_3 25-hydroxylase, 5-β-cholestane-3-α,7-α,12-α-triol 27-hydroxylase	ENSG00000135929	1.14.13.15	–
CYP27B1	25-hydroxyvitamin D-1 α hydroxylase, cytochrome P450 subfamily XXVIIB polypeptide 1, calcidiol 1-monooxygenase, 25-OHD-1 α-hydroxylase, 25-hydroxyvitamin D_3 1-α-hydroxylase, VD3 1A hydroxylase, P450C1 α, P450VD1-α	ENSG00000111012	1.14.13.13	–
CYP27C1	–	ENSG00000186684	1.14.-.-	–

CYP39, CYP46 and CYP51 families

Nomenclature	Other names	Ensembl ID	EC
CYP39A1	Oxysterol 7-α-hydroxylase, 24-hydroxycholesterol 7-α-hydroxylase	ENSG00000146233	1.14.13.99
CYP46A1	Cholesterol 24-hydroxylase, CH24H	ENSG00000036530	1.14.13.98
CYP51A1	Lanosterol 14-α-demethylase, leucine-rich repeat and death domain-containing protein LOC401387, CP51, CYP51, CYPL1, LDM, P450-14DM, P450L1	ENSG00000001630	–

Further Reading

Cipollone F, Cicolini G, Bucci M (2008). Cyclooxygenase and prostaglandin synthases in atherosclerosis: recent insights and future perspectives. *Pharmacol Ther*, **118**: 161–180.

Fleming I (2008). Vascular cytochrome P450 enzymes: physiology and pathophysiology. *Trends Cardiovasc Med* **18**: 20–25.

Haining RL, Nichols-Haining M (2007). Cytochrome P450-catalyzed pathways in human brain: metabolism meets pharmacology or old drugs with new mechanism of action? *Pharmacol Ther* **113**: 537–545.

Ingelman-Sundberg M, Sim SC, Gomez A, Rodriguez-Antona C (2007). Influence of cytochrome P450 polymorphisms on drug therapies: pharmacogenetic, pharmacoepigenetic and clinical aspects. *Pharmacol Ther* **116**: 496–526.

Johnson WW (2008). Cytochrome P450 inactivation by pharmaceuticals and phytochemicals: therapeutic relevance. *Drug Metab Rev* **40**: 101–147.

Kirchheiner J, Seeringer A (2007). Clinical implications of pharmacogenetics of cytochrome P450 drug metabolizing enzymes. *Biochim Biophys Acta* **1770**: 489–494.

Pelkonen O, Turpeinen M, Hakkola J, Honkakoski P, Hukkanen J, Raunio H (2008). Inhibition and induction of human cytochrome P450 enzymes: current status. *Arch Toxicol* **82**: 667–715.

Rezen T, Contreras JA, Rozman D (2007). Functional genomics approaches to studies of the cytochrome P450 superfamily. *Drug Metab Rev* **39**: 389–399.

Wijnen PA, Op den Buijsch RA, Drent M, Kuijpers PM, Neef C, Bast A, Bekers O, Koek GH (2007). The prevalence and clinical relevance of cytochrome P450 polymorphisms. *Aliment Pharmacol Ther* **26** (Suppl. 2): 211–219.

References

Bhatnagar AS *et al.* (1990). *J Steroid Biochem Mol Biol* **37**: 1021–1027.

Chun YJ *et al.* (2001). *Cancer Res* **61**: 8164–8170.

Gryglewski RJ *et al.* (1976). *Prostaglandins* **12**: 685–713.

Gryglewski RJ *et al.* (1995). *Wien Klin Wochenschr* **107**: 283–289.

Plourde PV *et al.* (1994). *Breast Cancer Res Treat* **30**: 103–111.

Randall MJ *et al.* (1981). *Thromb Res* **23**: 145–162.

Stoilov I *et al.* (1997). *Hum Mol Genet* **6**: 641–647.

Watanuki M *et al.* (1978). *Biochemistry* **17**: 127–130.