

Gene Section

Mini Review

CYP2W1 (cytochrome P450, family 2, subfamily W, polypeptide 1)

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Identity

Other names: CYP2W1; FLJ20359; MGC34287

HGNC (Hugo): CYP2W1

Location: 7p22.3

Local order: ADAP1 (960811 - 904066 on minus strand); COX19 (981761 - 971012 on minus strand); CYP2W1; C7orf50 (1144360 - 1003168 on minus strand); LOC100130456 (1055992 - 1056381 on plus strand); GPR146 (1063667 - 1065423 on plus strand).

DNA/RNA

Description

The CYP2W1 gene has nine exons resulting in an open reading frame of 1473 bp.

Transcription

At this point five different CYP2W1 transcripts have been described in different databases. In particular two transcripts have gained interest. The first variant, corresponding to the reference sequence, consists of nine exons and has a typical cytochrome P450 family 2 structure, containing conserved features etc. The second variant has only eight exons although the eighth exon is longer in this transcript than in the nine-exon-transcript. The absence of a conserved cysteine indicates that this transcript can not result in a functional P450 enzyme (see figure below).

Pseudogene

No pseudogene is known to date for CYP2W1.

Protein

Note

CYP2W1 is a cytochrome P450 enzyme belonging to family 2. Other family 2 members are important for the metabolism of drugs and other xenobiotics. In mammals the P450 enzymes are membrane bound and mainly localized to the endoplasmic reticulum (ER) but also to the mitochondria.

Description

All cytochrome P450 enzymes have a similar fold although their sequence identity can be very low. Structurally, P450 enzymes have a conserved core consisting of a four-helix bundle, including helices D, E, I and L, and the two helices J and K. In addition there are two sets of conserved beta-sheets containing five and two strands respectively. All P450 enzymes contain a heme group and one of the few conserved residues is a conserved cysteine serving as the fifth heme iron ligand. A structural similarity of mammalian P450 enzymes is the hydrophobic NH₂-terminal part spanning the membrane and serving as membrane anchor.

Expression

CYP2W1 mRNA and/or protein are highly expressed in some cancer types including colon, adrenal gland, lung and gastric cancers. In addition high CYP2W1 expression has been detected in two human derived cell lines, Caco2-TC7 and HepG2. HepG2 is the cell line where CYP2W1 was first identified, however the expression levels in Caco2-TC7 exceeds the levels in HepG2 cells significantly.

Human_9e	1	MALLI-N---LFLGLLGLGGLLCCSCQI--PSPA&RPPPGPEPLPLVGNLHLLRLSQQRSLMELSERVGPVFTVHLGRQ
Human_8e	1	MALLI-N---LFLGLLGLGGLLCCSCQI--PSPA&RPPPGPEPLPLVGNLHLLRLSQQRSLMELSERVGPVFTVHLGRQ
Chimpanzee_1	1	MALLI-N---LFLGLLGLGGLLCCSCQI--PSPA&RPPPGPEPLPLVGNLHLLRLSQQRSLMELSERVGPVFTVHLGRQ
Chimpanzee_2	1	MALLI-N---LFLGLLGLGGLLCCSCQI--PSPA&RPPPGPEPLPLVGNLHLLRLSQQRSLMELSERVGPVFTVHLGRQ
Chimpanzee_3	1	MALLI-N---LFLGLLGLGGLLCCSCQI--PSPA&RPPPGPEPLPLVGNLHLLRLSQQRSLMELSERVGPVFTVHLGRQ
Rat	1	MALLI-N---LFLGLLGLGGLLCCSCQI--PSPA&RPPPGPEPLPLVGNLHLLRLSQQRSLMELSERVGPVFTVHLGRQ
Mouse	1	MALLI-N---LFLGLLGLGGLLCCSCQI--PSPA&RPPPGPEPLPLVGNLHLLRLSQQRSLMELSERVGPVFTVHLGRQ
Dog	1	MALLI-N---LFLGLLGLGGLLCCSCQI--PSPA&RPPPGPEPLPLVGNLHLLRLSQQRSLMELSERVGPVFTVHLGRQ
Chicken	1	MALLI-N---LFLGLLGLGGLLCCSCQI--PSPA&RPPPGPEPLPLVGNLHLLRLSQQRSLMELSERVGPVFTVHLGRQ
Human_9e	75	KTVOILTGFSAVKEALAGPGQELADRPPIAIFQLIQRCGGIIFTS3G&RRA&RQFTVRAALHSLGCGREPQADKILQELKCI
Human_8e	75	KTVOILTGFSAVKEALAGPGQELADRPPIAIFQLIQRCGGIIFTS3G&RRA&RQFTVRAALHSLGCGREPQADKILQELKCI
Chimpanzee_1	75	KTVOILTGFSAVKEALAGPGQELADRPPIAIFQLIQRCGGIIFTS3G&RRA&RQFTVRAALHSLGCGREPQADKILQELKCI
Chimpanzee_2	75	KTVOILTGFSAVKEALAGPGQELADRPPIAIFQLIQRCGGIIFTS3G&RRA&RQFTVRAALHSLGCGREPQADKILQELKCI
Chimpanzee_3	75	KTVOILTGFSAVKEALAGPGQELADRPPIAIFQLIQRCGGIIFTS3G&RRA&RQFTVRAALHSLGCGREPQADKILQELKCI
Rat	78	KTVOILGAEVREALAGTGFELADRPPIAIFQLIQRCGGIIFTS3G&RRA&RQFTVRAALHSLGCGREPQADKILQELKCI
Mouse	78	KTVOILGAEVREALAGTGFELADRPPIAIFQLIQRCGGIIFTS3G&RRA&RQFTVRAALHSLGCGREPQADKILQELKCI
Dog	75	KTVOILGAEVREALAGTGFELADRPPIAIFQLIQRCGGIIFTS3G&RRA&RQFTVRAALHSLGCGREPQADKILQELKCI
Chicken	79	QVVOILGAEVREALAGTGFELADRPPIAIFQLIQRCGGIIFTS3G&RRA&RQFTVRAALHSLGCGREPQADKILQELKCI
Human_9e	155	SGQLDGYRGRFFPLALLGQSPNITFALLGRRFDYRDFQFVSLLGLIDEVMVLLGSPGLQLFNGVYFOLGALLQLHRFOL
Human_8e	155	SGQLDGYRGRFFPLALLGQSPNITFALLGRRFDYRDFQFVSLLGLIDEVMVLLGSPGLQLFNGVYFOLGALLQLHRFOL
Chimpanzee_1	155	SGQLDGYRGRFFPLALLGQSPNITFALLGRRFDYRDFQFVSLLGLIDEVMVLLGSPGLQLFNGVYFOLGALLQLHRFOL
Chimpanzee_2	155	SGQLDGYRGRFFPLALLGQSPNITFALLGRRFDYRDFQFVSLLGLIDEVMVLLGSPGLQLFNGVYFOLGALLQLHRFOL
Chimpanzee_3	155	SGQLDGYRGRFFPLALLGQSPNITFALLGRRFDYRDFQFVSLLGLIDEVMVLLGSPGLQLFNGVYFOLGALLQLHRFOL
Rat	158	KGQLDSKGGQFFPLALLGQSPNITFALLGRRFDYRDFQFVSLLGLIDEVMVLLGSPGLQLFNGVYFOLGALLQLHRFOL
Mouse	158	KGQLDSKGGQFFPLALLGQSPNITFALLGRRFDYRDFQFVSLLGLIDEVMVLLGSPGLQLFNGVYFOLGALLQLHRFOL
Dog	155	MGLDGYRGRFFPLALLGQSPNITFALLGRRFDYRDFQFVSLLGLIDEVMVLLGSPGLQLFNGVYFOLGALLQLHRFOL
Chicken	159	IELDKSKGGQFFPLALLGQSPNITFALLGRRFDYRDFQFVSLLGLIDEVMVLLGSPGLQLFNGVYFOLGALLQLHRFOL
Human_9e	235	RKIEEVRSAILETLLARRPHVCPGDPQCSYVDALIQQGQDDEPC-LFA&R&V&ACTLIGQ&ACTETT&ATLQ&S&ALIG
Human_8e	235	RKIEEVRSAILETLLARRPHVCPGDPQCSYVDALIQQGQDDEPC-LFA&R&V&ACTLIGQ&ACTETT&ATLQ&S&ALIG
Chimpanzee_1	235	RKIEEVRSAILETLLARRPHVCPGDPQCSYVDALIQQGQDDEPC-LFA&R&V&ACTLIGQ&ACTETT&ATLQ&S&ALIG
Chimpanzee_2	235	RKIEEVRSAILETLLARRPHVCPGDPQCSYVDALIQQGQDDEPC-LFA&R&V&ACTLIGQ&ACTETT&ATLQ&S&ALIG
Chimpanzee_3	235	RKIEEVRSAILETLLARRPHVCPGDPQCSYVDALIQQGQDDEPC-LFA&R&V&ACTLIGQ&ACTETT&ATLQ&S&ALIG
Rat	238	SKIEEVRSAILETLLARRPHVCPGDPQCSYVDALIQQGQDDEPC-LFA&R&V&ACTLIGQ&ACTETT&ATLQ&S&ALIG
Mouse	238	SKIEEVRSAILETLLARRPHVCPGDPQCSYVDALIQQGQDDEPC-LFA&R&V&ACTLIGQ&ACTETT&ATLQ&S&ALIG
Dog	235	RKIEEVRSAILETLLARRPHVCPGDPQCSYVDALIQQGQDDEPC-LFA&R&V&ACTLIGQ&ACTETT&ATLQ&S&ALIG
Chicken	239	RKIEEVRSAILETLLARRPHVCPGDPQCSYVDALIQQGQDDEPC-LFA&R&V&ACTLIGQ&ACTETT&ATLQ&S&ALIG
Human_9e	314	RHEDVQGRQVEELDRVLGPGRTPLRDQQLPPTS&VLHEVQRFITLLPH&PRCT&A&DTQLCG&LLPXGTPVWPLLT&SVL
Human_8e	314	RHEDVQGRQVEELDRVLGPGRTPLRDQQLPPTS&VLHEVQRFITLLPH&PRCT&A&DTQLCG&LLPXGTPVWPLLT&SVL
Chimpanzee_1	314	RHEDVQGRQVEELDRVLGPGRTPLRDQQLPPTS&VLHEVQRFITLLPH&PRCT&A&DTQLCG&LLPXGTPVWPLLT&SVL
Chimpanzee_2	314	RHEDVQGRQVEELDRVLGPGRTPLRDQQLPPTS&VLHEVQRFITLLPH&PRCT&A&DTQLCG&LLPXGTPVWPLLT&SVL
Chimpanzee_3	314	RHEDVQGRQVEELDRVLGPGRTPLRDQQLPPTS&VLHEVQRFITLLPH&PRCT&A&DTQLCG&LLPXGTPVWPLLT&SVL
Rat	316	RHEDVQGRQVEELDRVLGPGRTPLRDQQLPPTS&VLHEVQRFITLLPH&PRCT&A&DTQLCG&LLPXGTPVWPLLT&SVL
Mouse	317	RHEDVQGRQVEELDRVLGPGRTPLRDQQLPPTS&VLHEVQRFITLLPH&PRCT&A&DTQLCG&LLPXGTPVWPLLT&SVL
Dog	314	RHEDVQGRQVEELDRVLGPGRTPLRDQQLPPTS&VLHEVQRFITLLPH&PRCT&A&DTQLCG&LLPXGTPVWPLLT&SVL
Chicken	317	RHEDVQGRQVEELDRVLGPGRTPLRDQQLPPTS&VLHEVQRFITLLPH&PRCT&A&DTQLCG&LLPXGTPVWPLLT&SVL
Human_9e	394	LDETQQQTPGQFNP&HFLD&NGHF&KRE&FLPFS&AGRE&CQG---DS&R&E&L&F&L&F&L&L&Q&R&E---LLPPFG---
Human_8e	394	LDETQQQTPGQFNP&HFLD&NGHF&KRE&FLPFS&AGRE&CQG---DS&R&E&L&F&L&F&L&L&Q&R&E---LLPPFG---
Chimpanzee_1	394	LDETQQQTPGQFNP&HFLD&NGHF&KRE&FLPFS&AGRE&CQG---DS&R&E&L&F&L&F&L&L&Q&R&E---LLPPFG---
Chimpanzee_2	394	LDETQQQTPGQFNP&HFLD&NGHF&KRE&FLPFS&AGRE&CQG---DS&R&E&L&F&L&F&L&L&Q&R&E---LLPPFG---
Chimpanzee_3	394	LDETQQQTPGQFNP&HFLD&NGHF&KRE&FLPFS&AGRE&CQG---DS&R&E&L&F&L&F&L&L&Q&R&E---LLPPFG---
Rat	396	LDETQQQTPGQFNP&HFLD&NGHF&KRE&FLPFS&AGRE&CQG---DS&R&E&L&F&L&F&L&L&Q&R&E---LLPPFG---
Mouse	397	LDETQQQTPGQFNP&HFLD&NGHF&KRE&FLPFS&AGRE&CQG---DS&R&E&L&F&L&F&L&L&Q&R&E---LLPPFG---
Dog	394	LDETQQQTPGQFNP&HFLD&NGHF&KRE&FLPFS&AGRE&CQG---DS&R&E&L&F&L&F&L&L&Q&R&E---LLPPFG---
Chicken	397	LDETQQQTPGQFNP&HFLD&NGHF&KRE&FLPFS&AGRE&CQG---DS&R&E&L&F&L&F&L&L&Q&R&E---LLPPFG---
Human_9e	462	---G---PS&L&D&T&P&E&F&T&M&R&E&S&Q&L&C&V&E&R---E---
Human_8e	446	---G---P&Q&L&R---L&E&P---D&H&E---P&P&I---E---F---
Chimpanzee_1	468	A&A&V&G&S&A&M&P&P&S&S&C&L&L&A&S&R&G&T&A&C&P&R&L&A&S&V&R&P---Q&T&E&R&P&P&G&L---L---E---
Chimpanzee_2	446	---G---P&Q&L&R---L&E&P---D&H&E---P&P&I---E---F---
Chimpanzee_3	462	---G---PS&L&D&T&P&E&F&T&M&R&E&S&Q&L&C&V&E&R---E---
Rat	464	---G---PS&L&D&T&P&E&F&T&M&R&E&S&Q&L&C&V&E&R---E---
Mouse	465	---G---PS&L&D&T&P&E&F&T&M&R&E&S&Q&L&C&V&E&R---E---
Dog	462	---G---PS&L&D&T&P&E&F&T&M&R&E&S&Q&L&C&V&E&R---E---
Chicken	465	---G---PS&L&D&T&P&E&F&T&M&R&E&S&Q&L&C&V&E&R---E---

Alignment of the deduced CYP2W1 amino acid sequences from human, chimpanzee, rat, mouse, dog and chicken. Human 9e corresponds to the CYP2W1 reference sequence consisting of nine exons, whereas human 8e corresponds to the eight-exon-transcript mentioned above. For chimpanzee three transcripts are known, here numbered 1-3. All animal sequences correspond to the CYP2W1 homologous genes listed below. The conserved cysteine serving as the fifth heme iron ligand (mentioned below) is indicated with a red box.

Some scientists have also reported CYP2W1 mRNA expression in various adult human tissues as well as in keratinocytes and MCF10A cells, however so far no protein has been identified in these tissues/cells, which might be an indication of low expression levels. For non-human tissues high CYP2W1 mRNA expression levels are found in whole mouse embryo and in rat fetal colon. The expression in fetal rat colon increased by fetal age, whereas the opposite was seen in adult rat colon where the expression levels decreased again after birth.

Localisation

Cytochrome P450 family 2 members are usually located in the ER membrane, however CYP2W1 have been detected both in microsomes (i.e. ER) and in mitochondria.

Function

Cytochrome P450 enzymes are monooxidases and as mentioned other family 2 enzymes are involved in the metabolism of many drugs. The knowledge about CYP2W1 substrates are today limited. The substrates identified are arachidonic acid, benzphetamine and indole. In addition, CYP2W1 has been reported to activate a number of procarcinogens, e.g. PAHs, aflatoxin B1, sterigmatocystin etc. (for a more detailed list see Wu et al., 2006).

Based on the high CYP2W1 expression in fetal rat colon and mouse embryo it is possible that CYP2W1 has some yet unknown function during embryogenesis/differentiation.

Homology

- CYP2W1 (Pan troglodytes)
 - Cyp2w1 (Mus musculus)
 - Cyp2w1 (Rattus norvegicus)
- Denoted as similar to CYP2W1:
- LOC416454 (Gallus gallus)
 - LOC491601 (Canis lupus familiaris)

Mutations

Note

Several SNPs have been detected in the CYP2W1 gene, both synonymous and non-synonymous. For an updated overview of CYP2W1 polymorphisms and CYP2W1 alleles

see <http://www.cypalleles.ki.se/cyp2w1.htm>.

Implicated in

Various cancer

Note

CYP2W1 mRNA and/or protein are highly expressed in some cancer types, in particular colorectal cancer, but also adrenal gland, lung and gastric cancers. In addition CYP2W1 mRNA and protein expression has been detected in two human derived cancer cell lines,

Caco2-TC7 (colorectal adenocarcinoma) and HepG2 (hepatocellular carcinoma).

Disease

A recent pilot study shows that CYP2W1 is a prognostic marker for overall survival in colon cancer. In addition high tumoral CYP2W1 protein expression was associated with a worse clinical outcome. Previously it has been shown that the overexpression of CYP2W1 in cancer tissue could be associated with a decreased CpG methylation within the CYP2W1 gene. At this point there is no further data regarding CYP2W1 and its role in carcinogenesis and/or cancer treatment.

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