

# Oxalidaceace and Talarozole inhibitor of seven cytochrome P450 isoforms retinoic acid hydroxylase vitamin D degradation

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The Oxalidaceae herbaceous plants, shrubs and small trees where the genus Averrhoa with the species of starfruit, grapefruit, and carambola is a potent inhibitor of seven cytochrome P450 isoforms. These enzymes are significant in the first-pass elimination of medications and the consumption of these species in combination with certain prescription medications can significantly increase their effective dosage within the body. Cytochromes P450 (CYPs) are a superfamily of enzymes with heme as a cofactor monooxygenases present in most tissues of the body. They have an important roles in (1) hormone synthesis and (2) breakdown (i.e. estrogen and testosterone synthesis and metabolism), (3) cholesterol synthesis, and (4) vitamin D metabolism. Cytochrome P450 enzymes metabolize potentially (a) toxic compounds such as drugs and products of endogenous metabolism like bilirubin. At relatively high concentrations, starfruit juice inhibits CYP2A6 and other CYPs like Watercress-inhibitor of the cytochrome P450 CYP2E1. This can alter drug metabolism for individuals on certain medications like chlorzoxazone, Saint-John's wort, a common herbal remedy induces CYP3A4 and inhibits CYP1A1, CYP1B1. [1] [2][3] For Oxalidaceace and Talarozole and SMILE notation

CCC(CC)C(C1=CC=C(C=C1)

NC2=NC3=CC=CC=C3S2)N4C=NC=N4 presented in Figure 1. [2][3]

## 1 Abstract

Digestion system movement removes most of the oxygen is removed and carbon dioxide has increased. Low oxygen levels in the tissues,i.e. hypoxia can suppress some aspects of the immune response and induce and accentuate other important functions of the immune cells. Tumors have low oxygen levels and have resistance to EM wavelength ranges. For example, some bacteria like Facultative: grow in the presence or absence of oxygen and Microaerophilic: grow best at very low levels of oxygen. As water temperature increases, the amount of oxygen the water can hold decreases and the older adults typically have lower oxygen saturation levels than younger adults.

Human CYPs are primarily membrane-associated proteins located either in the inner membrane of mitochondria or in the endoplasmic reticulum of cells and metabolize thousands of endogenous and exogenous chemicals. Here CYP26 retinoic acid hydroxylase CYP2 drug and steroid metabolism CYP51 cholesterol biosynthesis and CYP24 vitamin D degradation. A Co-Expression Network CYP26A1 with CYP1A1, CYP1A2, CYP26A1, CYP26B1, CYP2A6, CYP2B6, CYP2E1, CYP2S1, CYP3A4, CYP3A5, CYP3A7 and CYP4A11 and for the expression network of CYP51A1 with CYP19A1, CYP1B1, CYP27A1, CYP1B1, CYP27A1, CYP2B6, CYP2C9, CYP2E1, CYP46A1 and CYP7A1 is presented.

Keywords: CYP26, retinoic acid hydroxylase, CYP2, drug and steroid metabolism, CYP51, cholesterol biosynthesis, and CYP24, vitamin D degradation

## 2 Introduction

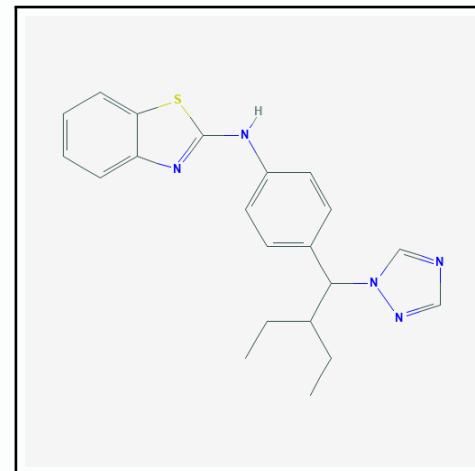


Figure 1: Talarozole CCC(CC)C(C1=CC=C(C=C1)  
NC2=NC3=CC=CC=C3S2)N4C=NC=N4

Figure 2 has the Co-Expression Network CYP51A1.

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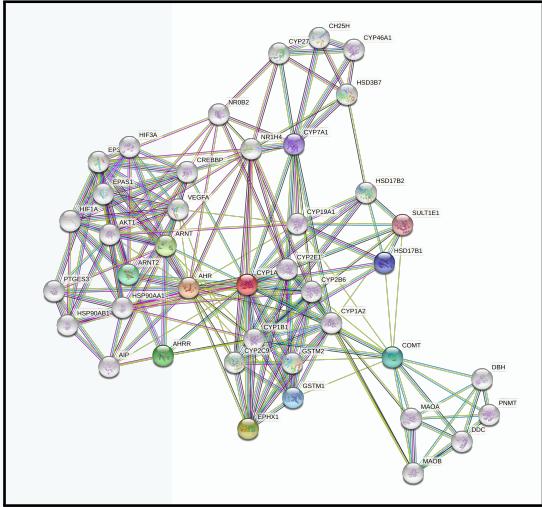


Figure 2: Co-Expression Network CYP51A1

Table 1 has the protein descriptions.[480]

Protein	Description
1 AHR	Aryl hydrocarbon receptor; Ligand-activated transcriptional activator. Binds to the XRE promoter region of genes it activates. Activates the expression of multiple phase I and II xenobiotic chemical metabolizing enzyme genes (such as the CYP1A1 gene). Mediates biochemical and toxic effects of halogenated aromatic hydrocarbons. Involved in cell-cycle regulation. An important role in the development and maturation of many tissues and regulates the circadian clock by inhibiting the basal and circadian expression of the core circadian component PER1. Inhibits PER1.
2 AHRR	Aryl hydrocarbon receptor repressor; Mediates dioxin toxicity and is involved in regulation of cell growth and differentiation. Represses the transcription activity of AHR by competing with this transcription factor for heterodimer formation with the ARNT and subsequently binding to the xenobiotic response element (XRE) sequence present in the promoter regulatory region of variety of genes. Represses CYP1A1 by binding the XRE sequence and recruiting ANKRA2, HDAC4 and/or HDAC5. Autoregulates its expression by associating with its own XRE site; Basic helix-loop-helix proteins
3 AIP	AH receptor-interacting protein; May play a positive role in AHR-mediated (aromatic hydrocarbon receptor) signaling, possibly by influencing its receptivity for ligand and/or its nuclear targeting; FKBp prolyl isomerases
4 AKT1	RAC-alpha serine/threonine-protein kinase; AKT1 is one of 3 closely related serine/threonine protein kinases (AKT1, AKT2 and AKT3) called the AKT kinase, and which regulates many processes including metabolism, proliferation, cell survival, growth and angiogenesis. This is mediated through serine and/or threonine phosphorylation of a range of downstream substrates. Over 100 substrate candidates have been reported so far, but for most of them, no isoform specificity has been reported.
5 ARNT	Aryl hydrocarbon receptor nuclear translocator; Required for activity of the Ah (dioxin) receptor. This protein is required for the ligand-binding subunit to translocate from the cytosol to the nucleus after ligand binding. The complex then initiates transcription of genes involved in the activation of PAH procarcinogens. The heterodimer with HIF1α or EPAS1/HIF2α functions as a transcriptional regulator of the adaptive response to hypoxia; Basic helix-loop-helix proteins
6 ARNT2	Aryl hydrocarbon receptor nuclear translocator 2; Transcription factor that plays a role in the development of the hypothalamo-pituitary axis, postnatal brain growth, and visual and renal function. Specifically recognizes the xenobiotic response element (XRE); Basic helix-loop-helix proteins
7 CH25H	Cholesterol 25-hydroxylase; Catalyzes the formation of 25-hydroxycholesterol from cholesterol, leading to repression of cholesterol biosynthetic enzymes. Plays a key role in cell positioning and movement in lymphoid tissues; 25-hydroxycholesterol is an intermediate in biosynthesis of 7-alpha,25-dihydroxycholesterol (7-alpha,25-OHC), an oxysterol that acts as a ligand for the G protein-coupled receptor GPR183/EBI2, a chemotactic receptor for a number of lymphoid cells.
8 COMT	Catechol O-methyltransferase; Catalyzes the O-methylation, and thereby the inactivation, of catecholamine neurotransmitters and catechol hormones. Also shortens the biological half-lives of certain neuroactive drugs, like L-DOPA, alpha-methyl DOPA and isoproterenol; Seven-beta-strand methyltransferase motif.
9 CREBBP	CREB-binding protein; Acetylates histones, giving a specific tag for transcriptional activation. Also acetylates non-histone proteins, like NCOA3 and FOXO1. Binds specifically to phosphorylated CREB and enhances its transcriptional activity toward cAMP-responsive genes. Acts as a coactivator of ALX1. Acts as a circadian transcriptional coactivator which enhances the activity of the circadian transcriptional activators: NPAS2-ARNTL/BMAL1 and CLOCK-ARNTL/BMAL1 heterodimers. Acetylates PCNA; acetylation promotes removal of chromatin-bound PCNA and its degradation.

Table 2 has the protein descriptions.[480]

Protein	Description
10 CYP19A1	Aromatase; Catalyzes the formation of aromatic C18 estrogens from C19 androgens; Cytochrome P450 family 19.
11 CYP1A1	Cytochrome P450 1A1; Cytochromes P450 are a group of heme-thiolate monooxygenases. In liver microsomes, this enzyme is involved in an NADPH-dependent electron transport pathway. It oxidizes a variety of structurally unrelated compounds, including steroids, fatty acids, and xenobiotics.
12 CYP1A2	Cytochrome P450 1A2; Cytochromes P450 are a group of heme-thiolate monooxygenases. In liver microsomes, this enzyme is involved in an NADPH-dependent electron transport pathway. It oxidizes a variety of structurally unrelated compounds, including steroids, fatty acids, and xenobiotics. Most active in catalyzing 2-hydroxylation. Caffeine is metabolized primarily by cytochrome CYP1A2 in the liver through an initial N3-demethylation. Also acts in the metabolism of aflatoxin B1 and acetaminophen.
13 CYP1B1	Cytochrome P450 1B1; Cytochromes P450 are a group of heme-thiolate monooxygenases. In liver microsomes, this enzyme is involved in an NADPH-dependent electron transport pathway. It oxidizes a variety of structurally unrelated compounds, including steroids, fatty acids, retinoid and xenobiotics. Preferentially oxidizes 17beta-estradiol to the carcinogenic 4-hydroxy derivative, and a variety of procarcinogenic compounds to their activated forms, including polycyclic aromatic hydrocarbons.
14 CYP27A1	Sterol 26-hydroxylase, mitochondrial; Catalyzes the first step in the oxidation of the side chain of sterol intermediates; the 27-hydroxylation of 5-beta-cholestane-3-alpha,7-alpha,12-alpha-triol. Has also a vitamin D3-25-hydroxylase activity; Belongs to the cytochrome P450 family.
15 CYP2B6	Cytochrome P450 2B6; Cytochromes P450 are a group of heme-thiolate monooxygenases. In liver microsomes, this enzyme is involved in an NADPH-dependent electron transport pathway. It oxidizes a variety of structurally unrelated compounds, including steroids, fatty acids, and xenobiotics. Acts as a 1,4-cineole 2-exo-monooxygenase.
16 CYP2C9	Cytochrome P450 2C9; Cytochromes P450 are a group of heme-thiolate monooxygenases. In liver microsomes, this enzyme is involved in an NADPH-dependent electron transport pathway. It oxidizes a variety of structurally unrelated compounds, including steroids, fatty acids, and xenobiotics. This enzyme contributes to the wide pharmacokinetics variability of the metabolism of drugs such as (1) S-warfarin, (2) diclofenac, (3) phenytoin, (4) tolbutamide and (5) losartan.
17 CYP2E1	Cytochrome P450 2E1; Metabolizes several precarcinogens, drugs, and solvents to reactive metabolites. Inactivates a number of drugs and xenobiotics and also bioactivates many xenobiotic substrates to their hepatotoxic or carcinogenic forms; Cytochrome P450 family 2.
18 CYP46A1	Cholesterol 24-hydroxylase; Involved in the turnover of cholesterol. It converts cholesterol into 24S-hydroxycholesterol and, to a lesser extent, 25-hydroxycholesterol. Has also activity with xenobiotic compounds, such as clotrimazole; Cytochrome P450 family 46.
19 CYP7A1	Cholesterol 7-alpha-monooxygenase; Catalyzes a rate-limiting step in cholesterol catabolism and bile acid biosynthesis by introducing a hydrophilic moiety at position 7 of cholesterol. Important for cholesterol homeostasis; Cytochrome P450 family 7.

Table 3 has the protein descriptions.[480]

	Protein	Description
20	DBH	Dopamine beta-hydroxylase; Conversion of dopamine to noreadrenaline.
21	DDC	Aromatic-L-amino-acid decarboxylase; Catalyzes the decarboxylation of L-3,4-dihydroxyphenylalanine (DOPA) to dopamine, L-5-hydroxytryptophan to serotonin and L-tryptophan to tryptamine
22	EP300	Histone acetyltransferase p300; Functions as histone acetyltransferase and regulates transcription via chromatin remodeling. Acetylates all four core histones in nucleosomes. Histone acetylation gives an epigenetic tag for transcriptional activation. Mediates cAMP-gene regulation by binding specifically to phosphorylated CREB protein. Mediates acetylation of histone H3 at 'Lys-122' (H3K122ac), a modification that localizes at the surface of the histone octamer and stimulates transcription, possibly by promoting nucleosome instability.
23	EPAS1	Endothelial PAS domain-containing protein 1; Transcription factor involved in the induction of oxygen regulated genes. Binds to core DNA sequence 5'-[AG]CGTG-3' within the hypoxia response element (HRE) of target gene promoters. Regulates the vascular endothelial growth factor (VEGF) expression and seems to be implicated in the development of blood vessels and the tubular system of lung. May also play a role in the formation of the endothelium that gives rise to the blood brain barrier.
24	EPHX1	Epoxide hydrolase 1; Biotransformation enzyme that catalyzes the hydrolysis of arene and aliphatic epoxides to less reactive and more water soluble dihydrodiols by the trans addition of water (By similarity). May play a role in the metabolism of endogenous lipids such as epoxide-containing fatty acids
25	GSTM1	Glutathione S-transferase Mu 1; Conjugation of reduced glutathione to a wide number of exogenous and endogenous hydrophobic electrophiles;
26	GSTM2	Glutathione S-transferase Mu 2; Conjugation of reduced glutathione to a wide number of exogenous and endogenous hydrophobic electrophiles; Belongs to the GST superfamily. Mu family
27	HIF1A	Hypoxia-inducible factor 1-alpha; Functions as a master transcriptional regulator of the adaptive response to hypoxia. Under hypoxic conditions and activates the transcription of over 40 genes such as (a) erythropoietin, (b) glucose transporters, (c) glycolytic enzymes, (d) vascular endothelial growth factor, (e) HILPDA, and other genes whose protein products increase oxygen delivery or facilitate metabolic adaptation to hypoxia and plays an essential role in (1) embryonic vascularization, (2) tumor angiogenesis and (3) pathophysiology of ischemic disease.
28	HIF3A	Hypoxia-inducible factor 3-alpha; Isoform 5: Attenuates the ability of transcription factor HIF1A to bind to hypoxia-responsive elements (HRE) located within the enhancer/promoter of hypoxia-inducible target genes and hence inhibits HRE-driven transcriptional activation; Basic helix-loop-helix proteins
29	HSD17B1	Estradiol 17-beta-dehydrogenase 1; Favors the reduction of estrogens and androgens. Also has 20-alpha-HSD activity. Uses preferentially NADH; Short chain dehydrogenase/reductase superfamily
30	HSD17B2	Estradiol 17-beta-dehydrogenase 2; Capable of catalyzing the interconversion of testosterone and androstenedione, as well as estradiol and estrone. Also has 20-alpha-HSD activity. Uses NADH while EDH17B3 uses NADPH; Short chain dehydrogenase/reductase superfamily
31	HSD3B7	3 beta-hydroxysteroid dehydrogenase type 7; The 3-beta-HSD enzymatic system plays a crucial role in the biosynthesis of all classes of hormonal steroids. HSD VII is active against four 7-alpha-hydroxylated sterols. Does not metabolize several different C(19/21) sterols as substrates. Involved in bile acid synthesis. Plays a key role in cell positioning and movement in lymphoid tissues by mediating degradation of 7-alpha,25-dihydroxycholesterol (7-alpha,25-OHC);
32	HSP90AA1	Heat shock protein HSP 90-alpha; Molecular chaperone that promotes the maturation, structural maintenance and proper regulation of specific target proteins involved for instance in cell cycle control and signal transduction. Undergoes a functional cycle that is linked to its ATPase activity which is essential for its chaperone activity. This cycle probably induces conformational changes in the client proteins and causes their activation with dynamical interactions of various co-chaperones that modulate its substrate recognition, ATPase cycle and chaperone function.
33	HSP90AB1	Heat shock protein HSP 90-beta; Molecular chaperone that promotes the maturation, structural maintenance and proper regulation of specific target proteins involved for instance in cell cycle control and signal transduction. Undergoes a functional cycle that is linked to its ATPase activity. This cycle probably induces conformational changes in the client protein and causes their activation. Interacts dynamically with various co-chaperones that modulate its substrate recognition, ATPase cycle and chaperone function.
34	MAOA	Amine oxidase flavin-containing A and catalyzes the oxidative deamination of biogenic and xenobiotic amines and has important functions in the metabolism of neuroactive and vasoactive amines in the central nervous system and peripheral tissues. MAOA preferentially oxidizes biogenic amines such as (1) 5-hydroxytryptamine (5-HT), (2) norepinephrine and (3) epinephrine; Belongs to the flavin monooxygenase oxidase family.
35	MAOB	Amine oxidase flavin-containing B that catalyzes the oxidative deamination of biogenic and xenobiotic amines and has important functions in the metabolism of neuroactive and vasoactive amines in the central nervous system and peripheral tissues. MAOB preferentially degrades benzylamine and phenylethylamine.
36	NR0B2	Nuclear receptor subfamily 0 group B member 2; Acts as a transcriptional regulator. Acts as a negative regulator of receptor-dependent signaling pathways. Specifically inhibits transactivation of the nuclear receptor with whom it interacts. Inhibits transcriptional activity of NEUROD1 on E-box-containing promoter by interfering with the coactivation function of the p300/CBP-mediated transcription complex for NEUROD1; Nuclear hormone receptors.
37	NR1H4	Bile acid receptor; Isoform 4: Promotes transcriptional activation of target genes ABCB11/BSEP (inducible by unconjugated CDCA, ACA and DCA), NR0B2/SHP (inducible by unconjugated CDCA, ACA and DCA), SLC51B/OSTB (inducible by unconjugated CDCA and DCA) and FABP6/BIPAP; most efficient isoform compared to isoforms 1 to 3; not inducible by tauroine- and glycine-amidated CDCA; Belongs to the nuclear hormone receptor family. NR1 subfamily.
38	PNMT	Phenylethanolamine N-methyltransferase; Converts noreadrenaline to adrenaline; Belongs to the class I-like SAM-binding methyltransferase superfamily and NN-MT/PNMT/TEMT family
39	PTGES3	Prostaglandin E synthase 3; Cytosolic prostaglandin synthase that catalyzes the oxidation/reduction of prostaglandin endoperoxide H2 (PGH2) to prostaglandin E2 (PGE2). Molecular chaperone that localizes to genomic response elements in a hormone-dependent manner and disrupts receptor-mediated transcriptional activation, by promoting disassembly of transcriptional regulatory complexes. Facilitates HIF alpha protein hydroxylation via interaction with EGLN1/PHD2, leading to recruit EGLN1/PHD2 to the HSP90 pathway.
40	SULT1E1	Estrogen sulfotransferase; Sulfotransferase that utilizes 3'-phospho-5'-adenylyl sulfate (PAPS) as sulfate donor to catalyze the sulfate conjugation of estradiol and estrone and has a role in the regulation of estrogen receptor activity by metabolizing free estradiol. Maximally sulfates beta-estradiol and estrone at concentrations of 20 nM. Also sulfates (1) dehydroepiandrosterone, (2) pregnenolone, (3) ethynodiol, (4) equilenin, (5) diethylstilbestrol and (6) 1-naphthol, at significantly higher concentrations; however, cortisol, testosterone and dopamine are not sulfated.
41	VEGFA	Vascular endothelial growth factor A; Growth factor active in angiogenesis, vasculogenesis and endothelial cell growth and induces (1) endothelial cell proliferation, (2) promotes cell migration, (3) inhibits apoptosis and induces permeabilization of blood vessels. Binds to the FLT1/VEGFR1 and KDR/VEGFR2 receptors, heparan sulfate and heparin. RP1/Neuropilin-1 binds isoforms VEGF-165 and VEGF-145. Isoform VEGF165B binds to KDR and does not activate downstream signaling pathways, does not activate angiogenesis and inhibits tumor growth.

Table 4 has Protein, Stability Index, Binding Potential, Aliphatic, f.1 with

CpH5, CpH7 and CpH9 for a collection and for the expression network of CYP51A1 with CYP1A1, CYP1B1, CYP27A1, CYP1B1, CYP27A1, CYP2B6, CYP2C9, CYP2E1, CYP46A1 and CYP7A1. [1001]

Protein	Stability Index	Binding Potential	Aliphatic	f.1	CpH5	CpH7	CpH9	
1	AHR	10.61	0.4013	15.03	-0.117740	17.685	-9.504	-31.933
2	AHRR	10.59	0.3176	12.00	-0.078103	47.436	24.549	-0.888
3	AIP	2.72	0.1417	6.24	-0.035881	9.491	-4.345	-14.945
4	AKT1	3.87	0.2257	7.81	-0.062648	9.177	-8.052	-18.887
5	ARNT	10.10	0.4155	11.71	-0.118388	15.145	-4.539	-20.604
6	ARNT2	10.78	0.3381	10.44	-0.095536	17.495	-2.977	-17.715
7	CH25H	3.65	0.0217	5.79	0.017845	21.633	2.474	-11.131
8	COMT	1.97	0.0445	6.72	0.009387	0.942	-8.321	-17.578
9	CREBBP	65.91	1.8490	60.95	-0.690336	110.540	44.961	-12.504
10	CYP1A1	4.39	0.1355	11.34	-0.000388	18.431	2.869	-9.285
11	CYP1A1	4.78	0.1576	10.81	-0.009835	24.175	8.341	-3.846
12	CYP1A2	4.80	0.1700	10.67	-0.018063	27.237	12.923	2.856
13	CYP1B1	4.71	0.1993	10.99	-0.016724	28.134	12.375	1.344
14	CYP27A1	6.04	0.1637	11.01	-0.022559	28.552	12.401	1.230
15	CYP2B6	4.18	0.1504	10.41	-0.011040	25.646	7.188	-3.019
16	CYP2C9	5.03	0.1371	10.56	-0.008170	19.789	5.502	-8.989
17	CYP2E1	3.78	0.1614	10.23	-0.022364	25.790	7.095	-5.522
18	CYP46A1	5.95	0.1793	10.03	-0.024179	23.249	11.730	2.676
19	CYP7A1	5.13	0.1628	10.21	-0.024110	26.560	8.759	-5.866
20	DBH	7.81	0.1839	12.38	-0.027748	14.590	-7.394	-26.326
21	DDC	4.50	0.1389	9.66	-0.004882	18.852	1.497	-13.121
22	EP300	65.52	1.8235	58.39	-0.708866	113.866	45.125	-14.271
23	EPAS1	11.00	0.3851	14.78	-0.106951	18.038	-12.128	-37.754
24	EPHX1	3.88	0.1379	8.56	-0.026801	18.708	1.733	-7.708
25	GSTM1	1.87	0.0732	4.01	-0.018131	5.926	-0.924	-6.936
26	GSTM2	2.14	0.0810	3.78	-0.021646	3.838	-1.376	-6.152
27	HIF1A	12.19	0.4434	15.95	-0.120625	-2.029	-30.126	-50.212
28	HIF3A	8.72	0.2833	12.86	-0.059763	9.868	-11.759	-27.082
29	HSD17B1	2.93	0.0858	6.81	0.004192	2.644	-6.490	-13.840
30	HSD17B2	3.52	0.0537	8.26	0.016411	15.659	8.823	-3.403
31	HSD3B7	2.27	0.0894	7.64	-0.000111	18.722	5.936	-3.528
32	HSP90AA1	10.11	0.4801	16.55	-0.148040	-7.828	-34.589	-49.631
33	HSP90AB1	7.34	0.3986	14.15	-0.118077	-12.875	-36.955	-48.177
34	MAOA	4.27	0.1742	10.42	-0.033693	20.802	4.866	-7.952
35	MAOB	4.19	0.1670	10.59	-0.028093	18.804	2.869	-9.697
36	NR0B2	3.59	0.0490	5.80	0.007348	9.773	3.828	-7.078
37	NR1H4	6.11	0.2085	8.11	-0.055321	14.917	-1.371	-19.437
38	PNMT	3.42	0.0891	5.26	-0.012495	3.895	-3.740	-10.959
39	PTGES3	1.92	0.1077	1.84	-0.036504	-13.503	-19.421	-24.857
40	SULT1E1	2.11	0.1158	4.67	-0.035817	9.181	-1.952	-9.301
41	VEGFA	5.51	0.2300	5.00	-0.074396	35.542	20.531	1.155

Table 1: A protein whose instability index is smaller than 40 is predicted as stable, a value above 40 predicts that the protein may be unstable. A protein have high binding potential if the index value is higher than 2.48. The relative volume occupied by aliphatic side chains (Alanine, Valine, Isoleucine, and Leucine) a positive factor for the increase of thermostability of globular proteins. net charge of a protein sequence based on the Henderson-Hasselbalch equation for pH levels of 7 and 9. f.1 is the crosscovariance based on one of the sequence S at lag 1 is given by f.1 with property1 = Hydrophobicity based on the KyteDoolittle Scale and property2 =Hydrophobicity based on the Eisenberg scale.

Figure 3 has the Co-expression network CYP26A1 with a collection [480]

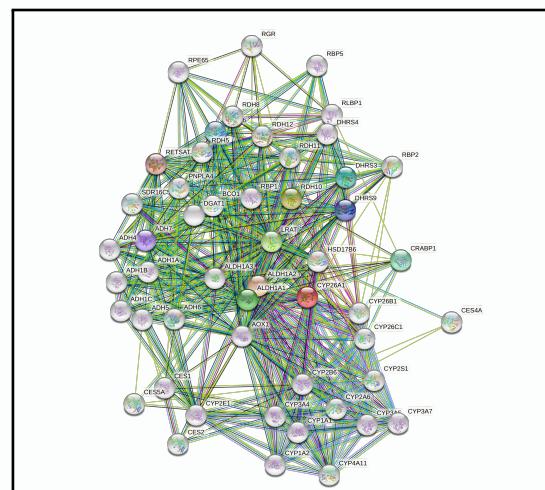


Figure 3: Co-expression network CYP26A1

Table 5 Co-Expression Network ADH1A ADH1B ADH1C ADH4 ADH5

ADH6 ADH7 ALDH1A1 ALDH1A2 ALDH1A3 AOX1 BCO1 CES1 CES2 CES4A CES5A [480]

Protein	Description
1 ADH1A	Alcohol dehydrogenase 1A, alpha polypeptide; Belongs to the zinc-containing alcohol dehydrogenase family
2 ADH1B	Alcohol dehydrogenase 1B, beta polypeptide; Belongs to the zinc-containing alcohol dehydrogenase family
3 ADH1C	Alcohol dehydrogenase 1C, gamma polypeptide
4 ADH4	Alcohol dehydrogenase 4, pi polypeptide
5 ADH5	Alcohol dehydrogenase class-3; Class-III ADH is remarkably ineffective in oxidizing ethanol, but it readily catalyzes the oxidation of long-chain primary alcohols and the oxidation of S-(hydroxymethyl) glutathione; Belongs to the zinc-containing alcohol dehydrogenase family, Class-III subfamily
6 ADH6	Alcohol dehydrogenase 6
7 ADH7	Alcohol dehydrogenase class 4 mu/sigma chain; Could function in retinol oxidation for the synthesis of retinoic acid, a hormone important for cellular differentiation. Medium-chain (octanol) and aromatic (m-nitrobenzaldehyde) compounds are the best substrates. Ethanol is not a good substrate but at the high ethanol concentrations reached in the digestive tract and has a role in the ethanol oxidation and contributes to the first pass ethanol metabolism; Alcohol dehydrogenases
8 ALDH1A1	Retinal dehydrogenase 1; Can convert/oxidize retinaldehyde to retinoic acid. Binds free retinal and cellular retinol-binding protein-bound retinal (By similarity). May have a broader specificity and oxidize other aldehydes <i>in vivo</i> .
9 ALDH1A2	Retinal dehydrogenase 2; Recognizes as substrates free retinal and cellular retinol-binding protein-bound retinal. Does metabolize octanal and decanal but does not metabolize citral, benzaldehyde, acetaldehyde and propenal efficiently (By similarity) and belongs to the aldehyde dehydrogenase family.
10 ALDH1A3	Aldehyde dehydrogenase family 1 member A3; NAD-dependent aldehyde dehydrogenase that catalyzes the formation of retinoic acid and has high activity with all-trans retinal, and has much lower <i>in vitro</i> activity with acetaldehyde. Required for the biosynthesis of normal levels of retinoic acid in the embryonic ocular and nasal regions; retinoic acid is required for normal embryonic development of the eye and the nasal region.
11 AOX1	Aldehyde oxidase; Oxidase with broad substrate specificity, (a) oxidizing aromatic azaheterocycles, such as (1) N1-methylnicotinamide, (2) N- methylphthalazinium and (3) phthalazine, as well as (b) aldehydes, such as (1) benzaldehyde, (2) retinal, (3) pyridoxal, and (4) vanillin and has a key role in the metabolism of xenobiotics and drugs containing aromatic azaheterocyclic substituents that participates in the bioactivation of prodrugs such as famciclovir that catalyzes the oxidation step from 6-deoxyciclovir to penciclovir-potent antiviral agent. Possibly involved in the regulation of reactive oxygen species.
12 BCO1	Beta,beta-carotene 15,15'-dioxigenase; Symmetrically cleaves beta-carotene into two molecules of retinal using a dioxygenase mechanism and belongs to the carotenoid oxygenase family.
13 CES1	Liver carboxylesterase 1; Involved in the detoxification of xenobiotics and in the activation of ester and amide prodrugs and hydrolyzes aromatic and aliphatic esters with no catalytic activity toward amides or a fatty acyl-CoA ester. Hydrolyzes the methyl ester group of cocaine to form benzoylecgonine and catalyzes the transesterification of cocaine to form cocaine. Displays fatty acid ethyl ester synthase activity, catalyzing the ethyl esterification of oleic acid to ethyleate.
14 CES2	Cocaine esterase; Involved in the detoxification of xenobiotics and in the activation of ester and amide prodrugs with a high catalytic efficiency for hydrolysis of cocaine, 4-methylumbelliferyl acetate, heroin and 6-monacetylmorphine that belongs to the type-B carboxylesterase/Ilipase family
15 CES4A	Carboxylesterase 4A; Probable carboxylesterase; Carboxylesterases
16 CES5A	Carboxylesterase 5A; Involved in the detoxification of xenobiotics and in the activation of ester and amide prodrugs; Carboxylesterases

A xenobiotic is a chemical substance in an organism not naturally produced or expected to be present within the organism or substances present in much higher concentrations than are usual. Hepatic enzymes are responsible for the metabolism of xenobiotics by first activating them by (a) oxidation, (b) reduction, (c) hydrolysis and/or (d) hydration of the xenobiotic and conjugates the active secondary metabolite with (1) glucuronic acid, (2) sulfuric acid, or (3) glutathione, followed by excretion in bile or urine. Hepatic microsomal cytochrome P450 metabolize xenobiotics are very important for the pharmaceutical industry because their ability to breakdown of medications. [1] [2][3]

The smooth endoplasmic reticulum of the liver cell is the organ of drug metabolism chemicals are absorbed, and very high concentrations of most drug-metabolizing enzyme systems relative to other organs. If a drug is taken into the gastrointestinal tract, it enters hepatic circulation through the portal vein becomes well-metabolized with the first pass effect. Drug metabolism include epithelial cells of the gastrointestinal tract, lungs, kidneys, and the skin and these sites usually responsible for localized toxicity reactions. [1] [2][3]

The metabolism of xenobiotics is often divided into three phases: (1) modification, (2) conjugation, and (3) excretion. These reactions act in concert to detoxify xenobiotics and remove them from cells. Phase I non-synthetic reactions may occur by (a) oxidation, (b) reduction, (c) hydrolysis, (d) cyclization, (e) decyclization, and (f) addition of oxygen or removal of hydrogen, carried out by mixed function oxidases, often in the liver. These oxidative reactions typically involve a cytochrome P450 monooxygenase (CYP), NADPH and oxygen. In subsequent phase II reactions, these activated xenobiotic metabolites are conjugated with charged species such as (1) glutathione (GSH), (2) sulfate, (3) glycine, or (4) glucuronic acid with the sites of drugs have conjugation reactions like (a) carboxy (-COOH), (b) hydroxy (-OH), (c) amino (NH<sub>2</sub>), and (d) thiol (-SH) groups. Products of conjugation reactions have increased molecular weight and

tend to be less active than their substrates, unlike Phase I reactions which often produce active metabolites. [1] [2][3]

After phase II reactions, the xenobiotic conjugates may be further metabolized such as in processing of (1) glutathione conjugates to acetylcysteine (mercapturic acid) conjugates where gamma-glutamate and glycine residues in the glutathione molecule are removed by Gamma-glutamyl transpeptidase and dipeptidases and the cysteine residue in the conjugate is acetylated. These conjugates and their metabolites can be excreted from cells in phase III of their metabolism where anionic groups act as affinity tags for a variety of membrane transporters of the multidrug resistance protein (MRP) family. [1] [2][3]

The next three Tables, 6,7 and 8 have the proteins and their descriptions. Table 1 has CRABP1 CYP1A1 CYP1A2 CYP26A1 CYP26B1 CYP26C1 CYP2A6 CYP2B6 CYP2E1 CYP2S1 CYP3A4 CYP3A5 CYP3A7 CYP4A11 [480]

Protein	Description
17 CRABP1	Cellular retinoic acid-binding protein 1; Cytosolic CRABPs may regulate the access of retinoic acid to the nuclear retinoic acid receptors; Belongs to the calycin superfamily. Fatty-acid binding protein (FABP) family
18 CYP1A1	Cytochrome P450 1A1; Cytochromes P450 are a group of heme-thiolate monooxygenases. In liver microsomes, this enzyme is involved in an NADPH-dependent electron transport pathway. It oxidizes a variety of structurally unrelated compounds, including steroids, fatty acids, and xenobiotics.
19 CYP1A2	Cytochrome P450 1A2; Cytochromes P450 are a group of heme-thiolate monooxygenases. In liver microsomes, this enzyme is involved in an NADPH-dependent electron transport pathway. It oxidizes a variety of structurally unrelated compounds, including steroids, fatty acids, and xenobiotics.
20 CYP26A1	Cytochrome P450 26A1; Plays a key role in retinoic acid metabolism. Acts on retinoids, including all-trans-retinoic acid (RA) and its stereoisomer 9-cis-RA. Capable of both 4-hydroxylation and 18-hydroxylation. Responsible for generation of several hydroxylated forms of RA, including 4-OH-RA, 4-oxo-RA and 18-OH-RA; Belongs to the cytochrome P450 family
21 CYP26B1	Cytochrome P450 26B1; Involved in the metabolism of retinoic acid (RA), rendering this classical morphogen inactive through oxidation. Involved in the specific inactivation of all-trans-retinoic acid (all-trans-RA), with a preference for the following substrates: all-trans-RA > 9-cis-RA > 13-cis-RA. Generates several hydroxylated forms of RA, including 4-OH-RA, 4-oxo-RA, and 18-OH- RA. Essential for postnatal survival. Plays a central role in germ cell development: acts by degrading RA in the developing testis, preventing STRA8 expression, thereby leading to delay of meiosis.
22 CYP26C1	Cytochrome P450 26C1; Plays a role in retinoic acid metabolism. Acts on retinoids, including all-trans-retinoic acid (RA) and its stereoisomer 9-cis-RA (preferred substrate); Belongs to the cytochrome P450 family
23 CYP2A6	Cytochrome P450 2A6; Exhibits a high coumarin 7-hydroxylase activity. Can act in the hydroxylation of the anti-cancer drugs cyclophosphamide and ifosfamide. Competent in the metabolic activation of aflatoxin B1. Constitutes the major nicotine O-dealkylase. Acts as a 1,4-cineole 2-oxoxygenase. Possesses low phenacetin O-deethylation activity. Cytochrome P450 family 2
24 CYP2B6	Cytochrome P450 2B6; Cytochromes P450 are a group of heme-thiolate monooxygenases. In liver microsomes, this enzyme is involved in an NADPH-dependent electron transport pathway. It oxidizes a variety of structurally unrelated compounds, including steroids, fatty acids, and xenobiotics. Acts as a 1,4-cineole 2-exo-monooxygenase
25 CYP2E1	Cytochrome P450 2E1; Metabolizes several precarcinogens, drugs, and solvents to reactive metabolites. Inactivates a number of drugs and xenobiotics and also biotransforms many xenobiotic substrates to their hepatotoxic or carcinogenic forms; Cytochrome P450 family 2
26 CYP2S1	Cytochrome P450 2S1; Has a potential importance for extrahepatic xenobiotic metabolism; Cytochrome P450 family 2
27 CYP3A4	Cytochrome P450 3A4; Cytochromes P450 are a group of heme-thiolate monooxygenases. In liver microsomes, this enzyme is involved in an NADPH-dependent electron transport pathway. It performs a variety of oxidation reactions (e.g. caffeine 8-oxidation, omeprazole sulphoxidation, midazolam 1'-hydroxylation and midazolam 4- hydroxylation) of structurally unrelated compounds, including steroids, fatty acids, and xenobiotics. Acts as a 1,8-cineole 2-exo-monooxygenase. The enzyme also hydroxylates etoposide. Catalyzes 4-beta-hydroxylation of cholesterol. May catalyze 25-hydroxylation
28 CYP3A5	Cytochrome P450 3A5; Cytochromes P450 are a group of heme-thiolate monooxygenases. In liver microsomes, this enzyme is involved in an NADPH-dependent electron transport pathway. It oxidizes a variety of structurally unrelated compounds, such as (1) steroids, (2) fatty acids, and (3) xenobiotics
29 CYP3A7	Cytochrome P450 3A7; Cytochromes P450 are a group of heme-thiolate monooxygenases. In liver microsomes, this enzyme is involved in an NADPH-dependent electron transport pathway. It oxidizes a variety of structurally unrelated compounds, such as (1) steroids, (2) fatty acids, and (3) xenobiotics
30 CYP4A11	Cytochrome P450 4A11; Catalyzes the omega- and (omega-1)-hydroxylation of various fatty acids such as laurate, myristate and palmitate. Has little activity toward prostaglandins A1 and E1. Oxidizes arachidonic acid to 20-hydroxyicosatetraenoic acid (20-HETE); Cytochrome P450 family 4

Table 7 has DGAT1 DHRS3 DHRS4 DHRS9 HSD17B6 LRAT PNPLA4 [480]

	Protein	Description
31	DGAT1	Diacylglycerol O-acyltransferase 1; Catalyzes the terminal and only committed step in triacylglycerol synthesis by using diacylglycerol and fatty acyl CoA as substrates. In contrast to DGAT2 it is not essential for survival. May be involved in VLDL (very low density lipoprotein) assembly. In liver, plays a role in esterifying exogenous fatty acids to glycerol. Functions as the major acyl-CoA retinol acyltransferase (ARAT) in the skin, where it acts to maintain retinoid homeostasis and prevent retinoid toxicity leading to skin and hair disorders;
32	DHRS3	Short-chain dehydrogenase/reductase 3; Catalyzes the reduction of all-trans-retinol to all-trans-retinol in the presence of NADPH; Short chain dehydrogenase/reductase superfamily
33	DHRS4	Dehydrogenase/reductase SDR family member 4; Reduces all-trans-retinal and 9-cis-retinal. Can also catalyze the oxidation of all-trans-retinol with NADP as co-factor, but with much lower efficiency. Reduces alkyl phenyl ketones and alpha-dicarbonyl compounds with aromatic rings, such as pyrimidine-4-aldehyde, 3-benzoylpyridine, 4-benzoylpyridine, menadione and 4-hexanoylpyridine. Has no activity towards aliphatic aldehydes and ketones (By similarity); Belongs to the short-chain dehydrogenases/reductases (SDR) family
34	DHRS9	Dehydrogenase/reductase SDR family member 9; 3-alpha-hydroxy steroid dehydrogenase that converts 3- alpha-tetrahydroprogesterone (allo pregnanolone) to dihydroprogesterone and 3-alpha-androstanediol to dihydroxyprogesterone. May play a role in the biosynthesis of retinoic acid from retinaldehyde, but seems to have low activity with retinoids. Can utilize both NADH and NADPH; Belongs to the short-chain dehydrogenases/reductases (SDR) family
35	HSD17B6	17-beta-hydroxysteroid dehydrogenase type 6; NAD-dependent oxidoreductase with broad substrate specificity that shows both oxidative and reductive activity (in vitro). Has 17-beta-hydroxysteroid dehydrogenase activity towards various steroids (in vitro). Converts 5-alpha-androstan-3- alpha,17-beta-diol to androsterone and estradiol to estrone (in vitro). Has 3-alpha-hydroxysteroid dehydrogenase activity towards androsterone (in vitro). Has retinol dehydrogenase activity towards all-trans-retinol (in vitro). Can convert androsterone to epi-androsterone.
36	LRAT	Lecithin retinol acyltransferase; Transfers the acyl group from the sn-1 position of phosphatidylcholine to all-trans-retinol, producing all-trans-retinyl esters. Retinyl esters are storage forms of vitamin A. LRAT plays a critical role in vision. It provides the all-trans retinyl ester substrates for the isomerohydrolase which processes the esters into 11-cis-retinol in the retinal pigment epithelium; due to a membrane-associated alcohol dehydrogenase, 11-cis-retinol is oxidized and converted into 11-cis-retinaldehyde which is the chromophore for rhodopsin and the cone photopigments;
37	PNPLA4	Patatin-like phospholipase domain-containing protein 4; Lipid hydrolase; Patatin like phospholipase domain containing

Table 8 has descriptions for RBP1 RBP2 RBP5 RDH10 RDH11 RDH12 RDH16 RDH5 RDH8 RETSAT RGR RLBP1 RPE65 SDR16C5 [480]

	Protein	Description
38	RBP1	Retinol-binding protein 1; Cytoplasmic retinol-binding protein. Accepts retinol from the transport protein STRA6, and thereby contributes to retinol uptake, storage and retinol homeostasis; Belongs to the calycin superfamily. Fatty-acid binding protein (FABP) family
39	RBP2	Retinol-binding protein 2; Intracellular transport of retinol; Belongs to the calycin superfamily. Fatty-acid binding protein (FABP) family
40	RBP5	Retinol-binding protein 5; Intracellular transport of retinol; Fatty acid binding protein family
41	RDH10	Retinol dehydrogenase 10; Retinol dehydrogenase with a clear preference for NADP. Converts all-trans-retinol to all-trans-retinal. Has no detectable activity towards 11-cis-retinol, 9-cis-retinol and 13-cis-retinol; Short chain dehydrogenase/reductase superfamily.
42	RDH11	Retinol dehydrogenase 11; Exhibits an oxidoreductive catalytic activity towards retinoids. Most efficient as an NADPH-dependent retinal reductase. Displays high activity towards 9-cis and all-trans-retinol. Also involved in the metabolism of short-chain aldehydes. No sterol dehydrogenase activity detected.
43	RDH12	Retinol dehydrogenase 12; Exhibits an oxidoreductive catalytic activity towards retinoids. Most efficient as an NADPH-dependent retinal reductase. Displays high activity toward 9-cis and all-trans-retinol. Also involved in the metabolism of short-chain aldehydes. No sterol dehydrogenase activity detected. Might be the key enzyme in the formation of 11-cis-retinol from 11-cis-retinol during regeneration of the cone visual pigments.
44	RDH16	Retinol dehydrogenase 16; Oxidoreductase with a preference for NAD. Oxidizes all-trans-retinol and 13-cis-retinol to the corresponding aldehydes. Has higher activity towards CRBP-bound retinol than with free retinol. Oxidizes 3-alpha-hydroxysteroids. Oxidizes androstanediol and androsterone to dihydrotestosterone and androstanedione. Can also catalyze the reverse reaction; Short chain dehydrogenase/reductase superfamily.
45	RDH5	11-cis retinol dehydrogenase; Stereospecific 11-cis retinol dehydrogenase, which catalyzes the final step in the biosynthesis of 11-cis-retinaldehyde, the universal chromophore of visual pigments. Also able to oxidize 9-cis-retinol and 13-cis-retinol, but not all-trans-retinol. Active in the presence of NAD as cofactor but not in the presence of NADP; Short chain dehydrogenase/reductase superfamily.
46	RDH8	Retinol dehydrogenase 8; Retinol dehydrogenase with a clear preference for NADP. Converts all-trans-retinol to all-trans-retinol. May play a role in the regeneration of visual pigment at high light intensity (By similarity); Belongs to the short-chain dehydrogenases/reductases (SDR) family.
47	RETSAT	All-trans-retinol 13,14-reductase; Catalyzes the saturation of all-trans-retinol to all-trans-13,14-dihydroretinol. Does not exhibit any activity toward all-trans-retinoic acid, nor 9-cis, 11-cis or 13-cis-retinol isomers. May play a role in the metabolism of vitamin A. Independently of retinol conversion, may regulate liver metabolism upstream of MLXIP1/CHREBP. May play a role in adipocyte differentiation; Belongs to the carotenoid/retinol oxidoreductase family. C150 subfamily.
48	RGR	RPE-retinal G protein-coupled receptor Receptor for all-trans- and 11-cis-retinal. Binds preferentially to the former and may catalyze the isomerization of the chromophore by a retinochrome-like mechanism; Opsin receptors.
49	RLBP1	Retinaldehyde-binding protein 1; Soluble retinoid carrier essential the proper function of both rod and cone photoreceptors. Participates in the regeneration of active 11-cis-retinol and 11-cis-retinaldehyde, from the inactive 11-trans products of the rhodopsin photocycle and in the de novo synthesis of these retinoids from 11-trans metabolic precursors. The cycling of retinoids between photoreceptor and adjacent pigment epithelium cells is known as the 'visual cycle'
50	RPE65	Retinol isomerohydrolase; Critical isomerohydrolase in the retinoid cycle involved in regeneration of 11-cis-retinol, the chromophore of rod and cone opsins. Catalyzes the cleavage and isomerization of all-trans- retinyl fatty acid esters to 11-cis-retinol which is further oxidized by 11-cis retinol dehydrogenase to 11-cis-retinal for use as visual chromophore. Essential for the production of 11-cis retinol for both rod and cone photoreceptors. Also capable of catalyzing the isomerization of lutene to meso-xanthin an eye-specific carotenoid. The soluble form binds vitamin A.
51	SDR16C5	Epidemal retinol dehydrogenase 2; Oxidoreductase with strong preference for NAD. Active in both the oxidative and reductive directions. Oxidizes all-trans-retinol in all-trans-retinaldehyde. No activity was detected with 11-cis-retinol or 11-cis-retinaldehyde as substrates with either NAD(+)NADH or NADP(+)NADPH; Belongs to the short-chain dehydrogenases/reductases (SDR) family.

Table 9 has A protein whose instability index is smaller than 40 is predicted as stable, a value above 40 predicts that the protein may be unstable. A protein have high binding potential if the index value is higher than 2.48. The relative volume occupied by aliphatic side chains (Alanine, Valine, Isoleucine, and Leucine) a positive factor for the increase of thermostability of globular proteins. net charge of a protein sequence based on the Henderson-Hasselbalch equation for pH levels of 5 7 and 9. f.1 is the crosscovariance based on one of the sequence S at lag 1 is given by f.1 with property1 = Hydrophobicity based on the KyteDoolittle Scale and property2 =Hydrophobicity based on the Eisenberg scale. [1001]

	Protein	Stability Index	Binding Potential	Aliphatic	f.1	CpH5	CpH7	CpH9
1	ADH1A	4.038	0.1213	15.21	0.028900	15.275	5.44	-9.6420
2	ADH1B	3.377	0.1295	14.91	0.022382	17.163	7.47	-7.0298
3	ADH1C	4.218	0.1359	15.08	0.023381	16.375	7.99	-5.9048
4	ADH4	4.085	0.1234	15.30	0.027613	13.222	4.95	-9.7372
5	ADH5	4.955	0.1201	14.86	0.025673	11.756	2.23	-12.1062
6	ADH6	4.687	0.0974	15.97	0.042807	12.296	4.65	-11.2440
7	ADH7	5.298	0.1761	15.23	0.014110	15.758	5.47	-8.9574
8	ALDH1A1	6.818	0.2818	19.72	-0.037471	10.281	-1.40	-13.8223
9	ALDH1A2	10.401	0.3077	20.25	-0.031650	5.712	-4.02	-13.2247
10	ALDH1A3	7.511	0.3297	19.84	-0.049076	11.976	1.04	-12.6257
11	AOX1	43.265	1.2461	88.33	-0.122720	46.940	3.17	-41.7566
12	BCO1	10.994	0.4374	20.75	-0.094317	15.891	-3.17	-17.1873
13	CES1	10.131	0.2615	23.83	-0.028510	12.467	-3.01	-12.1005
14	CES2	15.381	0.3821	25.32	-0.056259	14.356	-5.65	-17.9376
15	CES4A	10.606	0.2155	19.12	-0.002264	24.888	13.40	3.0541
16	CESSA	12.892	0.2730	26.79	0.007529	14.971	-3.97	-18.2448
17	CRABP1	1.783	0.1157	3.99	-0.026703	0.130	-3.62	-7.3520
18	CYP1A1	9.665	0.3184	21.83	-0.019871	24.175	8.34	-3.8457
19	CYP1A2	9.706	0.3439	21.57	-0.036528	27.237	12.92	2.8561
20	CYP26A1	11.465	0.3054	21.70	-0.018498	29.657	13.95	-1.6224
21	CYP26B1	8.303	0.3234	23.29	-0.018808	25.778	8.65	-2.2389
22	CYP26C1	11.598	0.3115	23.61	0.004271	34.208	15.25	1.1389
23	CYP2A6	9.138	0.3667	18.30	-0.053208	22.920	11.09	4.7465
24	CYP2B6	8.408	0.3024	20.93	-0.022197	25.646	7.19	-3.0186
25	CYP2E1	7.600	0.3246	20.58	-0.044984	25.790	7.10	-5.5224
26	CYP2S1	7.548	0.2588	21.74	-0.005663	20.127	6.78	-0.6966
27	CYP3A4	9.534	0.2667	22.10	-0.009250	16.170	4.72	-4.7849
28	CYP3A5	7.461	0.2904	22.18	-0.026679	18.082	8.30	0.6232
29	CYP3A7	8.018	0.2960	24.20	-0.011864	25.139	12.93	2.3213
30	CYP4A11	10.528	0.3293	23.69	-0.044738	35.635	13.53	-0.0736
31	DGAT1	9.709	0.2018	21.23	0.034781	28.893	16.63	5.5284
32	DHRS3	5.239	0.1306	12.90	0.016891	16.496	8.47	0.3566
33	DHRS4	5.696	0.1422	11.06	0.009383	10.586	4.81	-0.8877
34	DHRS9	7.106	0.1557	16.85	-0.001393	22.140	11.19	1.7436
35	HSD17B6	4.097	0.1614	12.93	-0.001187	15.494	7.49	-0.5063
36	LRAT	3.138	0.0940	10.16	0.018152	8.004	1.31	-4.4992
37	PNPLA4	4.952	0.1197	10.11	-0.000867	15.042	8.31	2.4652
38	RBP1	3.302	0.1481	5.97	-0.038524	3.517	-2.92	-8.1500
39	RBP2	0.482	0.1338	3.37	-0.042250	0.193	-2.86	-6.5061
40	RBP5	1.767	0.1129	4.56	-0.025266	3.921	-1.14	-5.4623
41	RDH10	5.698	0.1488	13.82	0.019957	13.332	2.04	-10.7491
42	RDH11	5.546	0.1336	13.60	0.010941	25.035	10.63	0.3057
43	RDH12	5.012	0.1805	13.01	0.002542	30.226	19.39	9.3646
44	RDH16	5.526	0.1593	13.06	0.004239	13.030	6.74	-1.4271
45	RDH5	5.854	0.1199	14.40	0.026460	16.777	10.25	3.1565
46	RDH8	5.855	0.1533	14.29	0.020640	11.480	4.92	-4.1411
47	RETSAT	12.703	0.2632	28.09	0.008858	24.914	9.01	-6.0649
48	RGR	5.011	0.0473	12.62	0.048845	12.342	5.39	-4.4841
49	RLBP1	7.462	0.2550	10.54	-0.054599	-4.173	-12.90	-18.7141
50	RPE65	9.451	0.3309	20.59	-0.058843	12.589	-4.78	-21.1565
51	SDR16C5	3.772	0.0637	13.06	0.037643	13.666	6.92	-2.6535

Table 2: A protein whose instability index is smaller than 40 is predicted as stable, a value above 40 predicts that the protein may be unstable. A protein have high binding potential if the index value is higher than 2.48. The relative volume occupied by aliphatic side chains (Alanine, Valine, Isoleucine, and Leucine) a positive factor for the increase of thermostability of globular proteins. net charge of a protein sequence based on the Henderson-Hasselbalch equation for pH levels of 5 7 and 9. f.1 is the crosscovariance based on one of the sequence S at lag 1 is given by f.1 with property1 = Hydrophobicity based on the KyteDoolittle Scale and property2 =Hydrophobicity based on the Eisenberg scale.

### 3 Results

Figures 4 and 5 has the Atom Frequency for Talarozole Tanimoto Similarities and Atom Frequency for Cisplatin Tanimoto Similarities. [1]

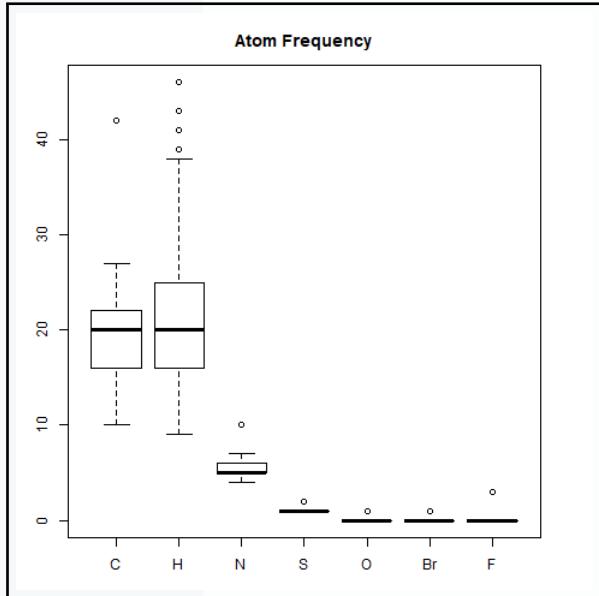


Figure 4: Atom Frequency for Talarozole Tanimoto Similarities

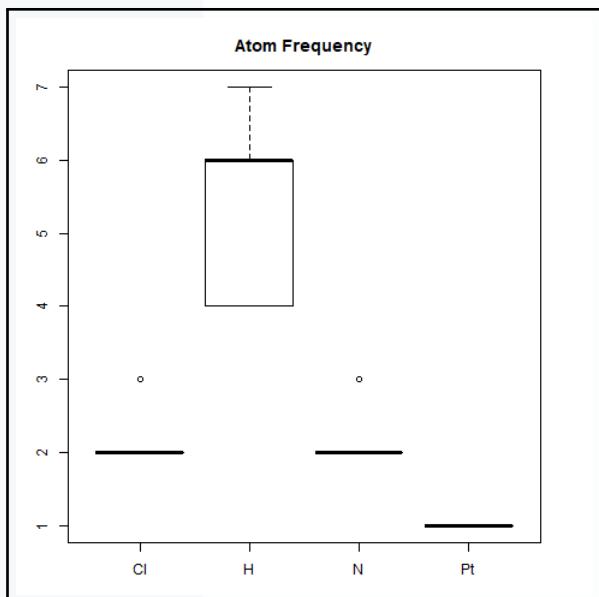


Figure 5: Atom Frequency for Cisplatin Tanimoto Similarities

Correlations with Cisplatin [R][Pt+2]([R])[ClH-] and CYP51A1, CYP26A1, CYP26B1, CYP26C1, CYP1A2, CYP2E1, CYP2S1, CYP51P1, CYP51P2 expression levels with NCI-60 were developed. Table 10 has the correlations and the p and q values for the hypothesis testing of significant positive or negative or zero collection. For the CYP51A1, CYP26A1, CYP26B1, CYP26C1, CYP1A2, CYP2E1, CYP2S1, CYP51P1, CYP51P2 the following results from cisplatin are given. [1006]

	COR	PVAL	QVAL
CYP2S1	-0.26	0.05	0.44
CYP2E1	0.14	0.28	0.50
CYP51A1	-0.15	0.27	0.50
CYP51P1	-0.15	0.25	0.50
CYP1A2	-0.20	0.13	0.50
CYP26C1	-0.06	0.65	0.73
CYP51P2	-0.07	0.62	0.73
CYP26B1	-0.07	0.57	0.73
CYP26A1	-0.01	0.96	0.96

Table 11 has DGAT1 DHRS3 DHRS4 DHRS9 HSD17B6 LRAT PNPLA4 Correlations with Cisplatin [R][Pt+2]([R])[ClH-][ClH-]. [1006]

	COR	PVAL	QVAL
PNPLA4	-0.36	0.01	0.04
LRAT	-0.19	0.15	0.35
DGAT1	-0.21	0.11	0.35
DHRS4	0.10	0.43	0.61
DHRS3	-0.11	0.42	0.61
DHRS9	-0.08	0.53	0.61
HSD17B6	0.00	1.00	1.00

Table 12 has RBP1 RBP2 RBP5 RDH10 RDH11 RDH12 RDH16 RDH5 RDH8 RETSAT RGR RLBP1 RPE65 SDR16C5 Correlations with Cisplatin [R][Pt+2]([R])[ClH-][ClH-]. [1006]

	COR	PVAL	QVAL
RPE65	0.14	0.28	0.71
RDH10	-0.13	0.31	0.71
RDH16	-0.15	0.25	0.71
RETSAT	-0.17	0.19	0.71
SDR16C5	-0.20	0.13	0.71
RBP2	-0.24	0.06	0.71
RDH8	0.07	0.62	0.82
RLBP1	-0.06	0.64	0.82
RGR	-0.07	0.61	0.82
RBP5	-0.07	0.60	0.82
RDH11	-0.08	0.55	0.82
RBP1	0.04	0.75	0.88
RDH12	0.02	0.87	0.92
RDH5	0.01	0.92	0.92

Table 13 has CRABP1 CYP1A1 CYP1A2 CYP26A1 Correlations with Cisplatin [R][Pt+2]([R])[ClH-][ClH-]. [1006]

	COR	PVAL	QVAL
CRABP1	0.18	0.16	0.30
CYP1A1	-0.16	0.22	0.30
CYP1A2	-0.20	0.13	0.30
CYP26A1	-0.01	0.96	0.96

Figure 6 has the Cell Line Expressions for CRABP1 CYP1A1 CYP1A2 CYP26A1. [1006]

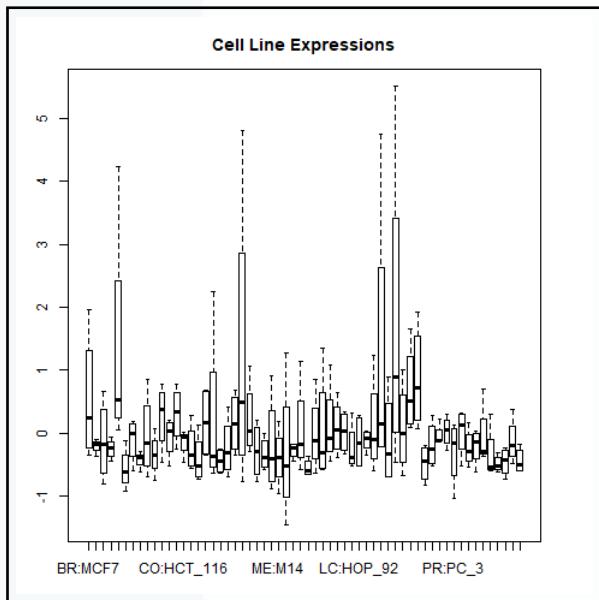


Figure 6: Cell Line Expressions for CRABP1 CYP1A1 CYP1A2 CYP26A1

## 4 Conclusions

In the Co-Expression Network CYP26A1 with CYP1A1, CYP1A2, CYP26A1, CYP26B1, CYP2A6, CYP2B6, CYP2E1, CYP2S1, CYP3A4, CYP3A5, CYP3A7 and CYP4A11 and for the expression network of CYP51A1 with CYP19A1, CYP1B1, CYP27A1, CYP1B1, CYP27A1, CYP2B6, CYP2C9, CYP2E1, CYP46A1 and CYP7A1, several molecular properties Protein, Stability Index, Binding Potential, Aliphatic, f.1 and CpH5, CpH7 and CpH9 with Correlations with Cisplatin [R][Pt+2][([R])[ClH-]][ClH-] and CYP51A1 ,CYP26A1, CYP26B1, CYP26C1,CYP1A2, CYP2E1, CYP2S1, CYP51P1, CYP51P2 expression levels with NCI-60 were presented.

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