Supplementary Materials

Molecular Mechanism Study on Stereo-Selectivity of α or β Hydroxysteroid Dehydrogenases

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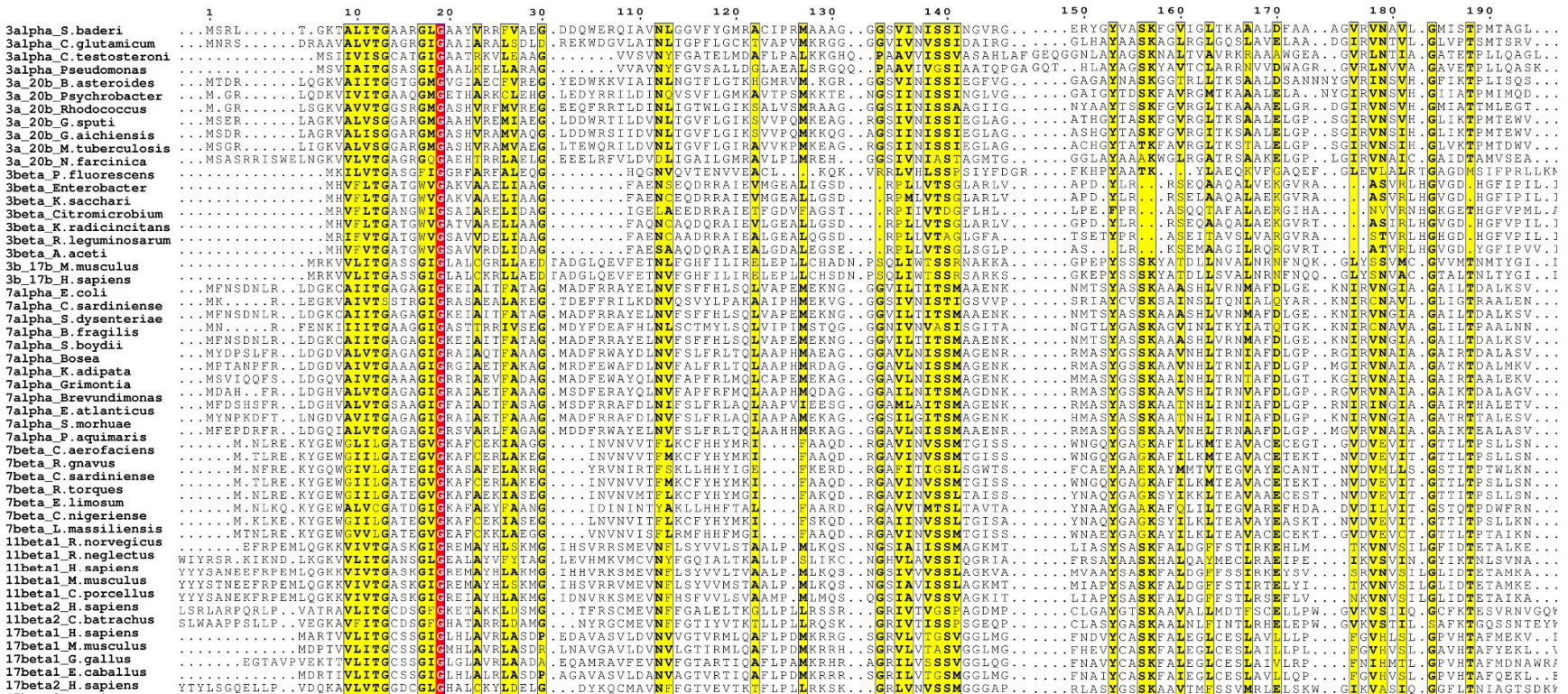

Figure S1. Sequence alignment of HSDHs from SDR superfamily. The accession number are: 3α-HSDH from *Sphingobium baderi*, EQB00535.1; from *Corynebacterium glutamicum*, OKX78817.1; *Comamonas testosteroni*, P80702.2; *Pseudomonas* sp., Q59718; 3α,20β-HSDH from *Bifidobacterium asteroides*, AFU70844.1; from *Psychrobacter* sp., EGK15090.1; from *Rhodococcus* sp., EJI98359.1; from *Gordonia sputi*, GAB37211.1; from *Gordonia aichiensis*, GAC46751.1; from *Mycobacterium tuberculosis*, P9WGT1.1;

from *Nocardia farcinica*, PFX03567.1. 3β-HSDH from *Pseudomonas fluorescens*, AEV61354.1; from *Enterobacter* sp., AGN84589.1; from *Acetobacter aceti*, BCK76810.1; from *Kosakonia sacchari*, AIA25025.1; from *Citromicrobium* sp. ALG59463.1; from *Kosakonia radicincitans*, ARD60321.1; from *Rhizobium leguminosarum*, ASS56725.1. 3β,17β-HSDH from *Mus musculus*, O88736.1; from *Homo sapiens*, P56937.1. 7α-HSDH from *Escherichia coli*, P0AET8.1; from *Clostridium sardiniense*, G9FRD7.1; from *Shigella dysenteriae*, ABB61947.1; from *Bacteroides fragilis*, AAD49430.2; from *Shigella boydii*, ABB66134.1; from *Bosea sp.*, OYW60865.1; from *Kaistia adipate*, WP_029074103.1; from *Grimontia sp.*, WP_046304034.1; from *Brevundimonas*, WP_046653274.1; from *Erythrobacter atlanticus*, WP_048884278.1; from *Shewanella morhuae*, WP_076500293.1; from *Pseudoruegeria aquimaris*, WP_085868047.1.7β-HSDH from *Collinsella aerofaciens*, A4ECA9.1; from *Ruminococcus gnavus*, A7B4V1.1; from *Clostridium sardiniense*, AET80684.1; from *Ruminococcus torques*, CBL26204.1; from *Eubacterium limosum*, WP_038354045.1; from *Clostridium nigeriense*, WP_066892209.1; from *Libanicoccus massiliensis*, WP_073294202.1. 11β-HSD1 from *Rattus norvegicus*, AAN34655.1; from *Rhodnius neglectus*, JAI53896.1; from *Homo sapiens*, P28845.3; from *Mus musculus*, P50172.3; from *Cavia porcellus*, Q6QLL4.3. 11β-HSD2 from *Homo sapiens*, P80365.2; *Clarias batrachus*, AMH87641.1; 17β-HSD1 from *Homo sapiens*, P14061.3; from *Mus musculus*, NP_034605.1; from *Gallus gallus*, NP_990168.1; from *Equus caballus*, NP_001077067.1. 17β-HSD2 from *Homo sapiens*, P37059.1; from *Ovis aries*, NP_001254811.1; from *Macaca fascicularis*, NP_001272753.1. 17β-HSD3 from *Homo sapiens*, P37058.2; from *Mus musculus*, AAB06793.1; from *Danio rerio*, AAS58451.1. 17β-HSD4 from *Homo sapiens*, P51659.3; from *Danio rerio*, AAK27967.1. 17β-HSD6 from *Rattus norvegicus*, NP_775427.1; from *Mus musculus*, NP_001346306.1. 17β-HSD7 from *Oryctolagus cuniculus*, AAK20950.1; from *Mus musculus*, CAA75742.1. 17β-HSD8 from *Oreochromis niloticus*, NP_001266465.1. This figure was created by ESPript on line [1].

Table S1. HSDHs identified belonging to SDR superfamily.

Hydroxysteroid dehydrogenase	UniProtKB/Swiss-Prot/ GenBank	Organism	Length	Structure PDB ID	PubMed	Family
3α–HSDH	Q59718	*Pseudomonas* sp.	255 aa	2DKN	8344521	SDR
	P80702	*Comamonas testosteroni*	257 aa	1FK8	9812981; 8944761; 10833462; 11139589; 11007791	SDR
	OKX78817.1	*Corynebacterium glutamicum*	245 aa		28198668	SDR
	EQB00535.1	*Sphingobium baderi* LL03	245 aa		24051322	SDR
3α(20β)–HSDH	P9WGT1.1	*Mycobacterium tuberculosis* H37Rv	260 aa		9634230;21969609; 12524453	SDR
	PFX03567.1	*Nocardia farcinica*	249 aa			SDR
	AFU70844.1	*Bifidobacterium asteroides* PRL2011	246 aa		23028506	SDR
	EGK15090.1	*Psychrobacter* sp.	244 aa			SDR
	GAC46751.1	*Gordonia aichiensis* NBRC 108223	252 aa			SDR
	GAB37211.1	*Gordonia sputi* NBRC 100414	257 aa			SDR
	EJI98359.1	*Rhodococcus* sp. JVH1	245 aa		22965106	SDR
3β–HSDH	AEV61354.1	*Pseudomonas fluorescens* F113	330 aa		22328765	SDR
	AGN84589.1	*Enterobacter* sp. R4-368	293 aa		23908287	SDR

	AIA25025.1	*Kosakonia sacchari* SP1	293 aa		23209221	SDR
	ALG59463.1	*Citromicrobium* sp. JL477	296 aa			SDR
	ARD60321.1	*Kosakonia radicincitans* DSM 16656	293 aa		22965092	SDR
	ASS56725.1	*Rhizobium leguminosarum* bv. Viciae	296 aa			SDR
	BCK76810.1	*Acetobacter aceti* NBRC 14818	287 aa		21081762	SDR
	EAQ78839.1	*Blastopirellula marina* DSM 3645	328 aa			SDR
	OBQ10510.1	*Anabaena* sp. LE011-02	333 aa			SDR
	QCS10811.1	*Streptomyces clavuligerus*	216 aa			SDR
3β(17β)–HSDH	P56937	*Homo sapiens (human)*	341 aa		10544267;12732193; 11165030	SDR
	O88736	*Mus musculus (house mouse)*	334 aa		18669642; 9658408; 12829805	SDR
7α–HSDH	P0AET8.1	*Escherichia coli*	255 aa	1FMC	2007545	SDR
	G9FRD7.1.	*Clostridium sardiniense*	262 aa	5EPO	26961171	SDR
	WP_048884278.1	*Erythrobacter atlanticus*	255 aa		[2]	SDR
	WP_076500293.1	*Shewanella morhuae*	255 aa		[2]	SDR
	OYW60865.1	*Bosea* sp. 12-68-7	255 aa		[2]	SDR
	WP_046653274.1	*Brevundimonas* sp.	253 aa		[2]	SDR
	WP_046304034.1	*Grimontia* sp. AD028	255 aa		[2]	SDR
	WP_029074103.1	*Kaistia adipata*	255 aa		[2]	SDR
	WP_085868047.1	*Pseudoruegeria aquimaris*	255 aa		[2]	SDR
	ABB61947	*Shigella dysenteriae* Sd197	255 aa		16275786	SDR
	AAD49430.2	*Bacteroides fragilis*	259 aa		14756531	SDR
	ABB66134.1	*Shigella boydii* Sb227	255 aa		16275786	SDR
7β–HSDH	A4ECA9.1	*Collinsella aerofaciens* ATCC 25986	263 aa	5FYD;5GT9	6954878; 21181147; 27006087; 28471355; 25131646	SDR
	AET80684.1	*Clostridium sardiniense* DSM599	261 aa		22198717; 6945134; 24810359; 26961171	SDR
	WP_066892209.1	*Clostridium nigeriense Marseille*	263 aa		[2]	SDR

	A7B4V1.1	*Ruminococcus gnavus* ATCC 29149	263 aa		23729502; [2]	SDR
	AGN52919.1	*Ruminococcus gnavus* N53	263 aa		23729502; [2]	SDR
	CBL26204	*Ruminococcus torques*	264 aa		[2]	SDR
	WP_073294202.1	Libanicoccus massiliensis	267 aa		10387002; 9735295; [2]	SDR
	WP_038354045.1	*Eubacterium limosum*	265 aa		10387002; 9735295; [2]	SDR
11β–HSD1	Q6QLL4.3	*Cavia porcellus (domestic guinea pig)*	300 aa	3LZ6	10699594;15542590; 19507261	SDR
	P28845.3	*Homo sapiens (human)*	292 aa	6NJ7	1885595	SDR
	P50172.3	*Mus musculus (house mouse)*	292 aa	5QIJ	7851387; 8973338; 15865440	SDR
	AAN34655.1	*Rattus norvegicus*	252 aa			SDR
	JAI53896.1	*Rhodnius neglectus*	304 aa		27129103	SDR
11β–HSD2	P80365.2	*Homo sapiens (human)*	405 aa		8611140; 8611186; 17314322	SDR
	AMH87641.1	*Clarias batrachus*	411 aa			SDR
12α–HSDH	P21215.1	*Clostridium* sp. ATCC 29733	29 aa, partial		2007406	SDR
	CDD59475	*Eggerthella* sp. CAG:298	266 aa		[3]	SDR
		Clostridium group P (strain C 48-50)			[4–9]	
		Acinetobacter calcoaceticus lwoffi			[10]	
		Eubacterwm lentum ATCC No. 25559			[11]	
		Clostridium leptum			[12]	
12β–HSDH		*Clostridium paraputrijiicum* (strain D 762-06)			[13]	
		Clostridium paraputrificum ATCC 25780			[14]	
17β–HSD1	P14061.3	*Homo sapiens (human)*	327 aa	6MNE	2547159; 19929851	SDR
	NP_034605.1	*Mus musculus*	344 aa		29371331; 29401623	SDR
	NP_990168.1	*Gallus gallus*	302 aa		10375623	SDR
	NP_001077067.1	*Equus caballus*	308 aa		26107351; 17242170	SDR

	NP_001306375.1	*Macaca fascicularis*	320 aa			SDR
	ABU49886.1	*Sus scrofa*	321 aa			SDR
	NP_001040597.1	*Macaca mulatta*	320 aa		25319552	SDR
17β–HSD2	P37059.1	*Homo sapiens (human)*	387 aa		8099587; 7546291	SDR
	NP_001272753.1	*Macaca fascicularis*	387 aa			SDR
	NP_001254811.1	*Ovis aries (sheep)*	388 aa		23096084	SDR
	NP_001161121.1	*Sus scrofa (pig)*	388 aa		14681463	SDR
	XP_005020223.2	*Anas platyrhynchos (mallard)*	390 aa			SDR
	NP_001069194.1	*Bos taurus (cattle)*	388 aa			SDR
17β–HSD3	P37058.2	*Homo sapiens (human)*	310 aa		8075637; 16216911	SDR
	AAB06793	*Mus musculus (house mouse)*	305 aa			SDR
	AAS58451.1	*Danio rerio (zebrafish)*	307 aa		16216911	SDR
17β–HSD4	AAK27967.1	*Danio rerio (zebrafish)*	725 aa			SDR
	P51659.3	*Homo sapiens (human)*	327 aa	1ZBQ		SDR
17β–HSD6	NP_001346306.1	*Mus musculus (house mouse)*	317 aa		10537158	SDR
	NP_775427.1	*Rattus norvegicus (Norway rat)*	327 aa		9188497	SDR
17β–HSD7	CAA75742.1	*Mus musculus (house mouse)*	334 aa		9658408	SDR
	AAK20950.1	*Oryctolagus cuniculus (rabbit)*	309 aa		11165026	SDR
17β–HSD8	NP_001266465.1	*Oreochromis niloticus (Nile tilapia)*	256 aa		16087725	SDR

Table S2. HSDHs identified belonging to AKR superfamily.

Hydroxysteroid dehydrogenases	UniProtKB/Swiss-Prot/ GenBank	Organism	Length	Structure PDB ID	Pubmed	Family
3*α*–HSDH	P17516	Homo sapiens	323 aa	2FVL	8274401; 10634139; 8172617	AKR1C4
	P23457	Rattus norvegicus – liver	322 aa	1RAL	1840601; 7515872; 8146147; 8718859	AKR1C9

3α(17α)–HSDH	P52895	Homo sapiens	323 aa	4JQ1; 4XO7; 4XO6; 4L1X;	15929998; 11514561; 11513593	AKR1C2
	NP_084177	Mus musculus	323 aa	3FJN;2P5N	19237748; 20124700	AKR1C21
3α(17β)–HSDH	NP_003730	Homo sapiens	323 aa	1RYO	8718859	AKR1C3
	BAM37088.1	Oryctolagus cuniculus (rabbit)	323 aa		23228597	AKR1C27
	BAM37089.1	Oryctolagus cuniculus (rabbit)	323 aa		23228597	AKR1C28
3α(20α)–HSDH	NP_001344	Homo sapiens	323 aa	3C3U	7626489	AKR1C1
	BAB63209.2	Macaca fuscata (Japanese macaque)	323 aa		15618685	AKR1C25
3α/17β/20α–HSDH	BAN84251.1	Oryctolagus cuniculus (rabbit)	323 aa		24510382	AKR1C31
	BAN84252.1	Oryctolagus cuniculus (rabbit)	323 aa		24510382	AKR1C32
	BAN84253.1	Oryctolagus cuniculus (rabbit)	323 aa		24510382	AKR1C33
3β(17β)–HSDH	BAP76083	Mesocricetus auratus (golden hamster)	323 aa			AKR1C35
17β–HSDH	BAN84250.1	Oryctolagus cuniculus (rabbit)	323 aa		24510382	AKR1C30
	P42330.4	Homo sapiens (human)	323 aa	7C7H	11165022	AKR1C3
20α–HSDH	P80508	Oryctolagus cuniculus (rabbit)	323 aa	1Q13	8446108; 8529651; 15123423	AKR1C5
	P51652	Rattus norvegicus (Norway rat)	323 aa		8172618	AKR1C8
	NP_001333464	Mus musculus	297 aa		14967952;15222881; 15471942	AKR1C18
	AAY16444	Equus caballus (horse)	322 aa		16720716	AKR1C23
	Q04828	Homo sapiens	323 aa	6IJX	7626489; 11013348	AKR1C1

Table S3. Functions of HSDHs and their related metabolic pathways.

HSDHs	Classis	Natural Substrates (corresponding Profucts)	Pathways (KEGG and MetaCyc)	Disease
3β–HSDH (type1, type2)	EC 1.1.1.145; SDR	5-pregnen-3β-ol-2-one(progesterone); androstenone (5α-androst-16-en-3β-ol β-androstenol); Δ5-androstenediol (testosterone); epiandrosterone(5α-androstan-3,17-dione), pregnenolone(pregn-5-en-3,20-dione), etc.	Steroid degradation, Steroid hormone biosynthesis; androgen biosynthesis, androstenedione degradation, cholesterol degradation to androstenedione II (cholesterol dehydrogenase), progesterone biosynthesis, sitosterol degradation to androstenedione	3(or 17)β–HSDH deficiency; Abortion, Spontaneous; Adrenal Hyperplasia, Congenital; Adrenogenital Syndrome; Choriocarcinoma
3α–HSDH	EC 1.1.1.50; SDR	Androsterone (5α-androstan-3,17-dione; androstanedione); 5α-pregnan-3,20-dione(3α-hydroxy-5α-pregnan-20-one), etc.	Primary bile acid biosynthesis; Steroid hormone biosynthesis; Degradation of testosterone and androsterone to androstendione	Adenoma; Adrenal Hyperplasia, Congenital; Astrocytoma; Breast Neoplasms; Carcinogenesis; Carcinoma
7α–HSDH	EC 1.1.1.159; SDR	7-keto-lithocholic acid (chenodeoxycholic acid); cholate (3α,12α-dihydroxy-7-oxo-5β-cholanate)	Secondary bile acid biosynthesis	
7β–HSDH	EC 1.1.1.201; SDR	7-keto-lithocholic acid（ursodeoxycholic acid）	Secondary bile acid biosynthesis; glycocholate metabolism and ursodeoxycholate biosynthesis (bacteria)	
11β–HSDH (type1, type2)	EC 1.1.1.146; SDR	corticosterone(11-dehydrocorticosterone); androstenedione(testosterone); cortisol (cortisone); oracin (dihydrooracin), etc.	Metabolism of xenobiotics by cytochrome P450, Steroid hormone biosynthesis	11β–HSDH deficiency; Acidosis; Acromegaly; ACTH Syndrome, Ectopic; Acute Lung Injury

12α–HSDH	EC 1.1.1.176	12-ketochenodeoxycholic acid (cholic acid); cholate (α,7α-dihydroxy-12-oxo-5β-cholanate)	Secondary bile acid biosynthesis	
3(17)α–HSDH	EC 1.1.1.209	21-hydroxy-5β-pregnane-3,20-dione(21-hydroxy-5β-pregnane-20α-ol-3-one); 5β-pregnane-3α,20α-diol(5β-pregnane-20α-ol-3-one); androstenedione (androsterone)	testosterone and androsterone degradation to androstendione	Neoplasms
3α(17β)–HSDH	EC 1.1.1.239	5α-dihydrotestosterone (androstandione); androstandiol(androsterone); daunorubicin(daunorubicinol); testosterone (androst-4-ene-3,17-dione; androstenedione), etc.	Steroid hormone biosynthesis	3α(17β)–HSDH (nad+) deficiency; Acne Vulgaris; Breast Neoplasms; Carcinogenesis; Carcinoma Et al
3(17)β–HSDH	EC 1.1.1.51; SDR?	4-androstene-3,17-dione (testosterone); 5-androstenedione (5α-dihydrotestosterone); androstenedione(testosterone); estrone(estradiol); zymosterone(zymosterol), etc.	Microbial metabolism in diverse environments, Steroid degradation, Steroid hormone biosynthesis; testosterone and androsterone degradation to androstendione	3(or 17)β–HSDH deficiency; Acne Vulgaris; Adenocarcinoma; Adenoma; Adenomyosis
3α (20β)–HSDH	EC 1.1.1.53；	17α-hydroxyprogesterone(17α,20β-dihydroxy-4-pregnene-3-one); progesterone(20β-hydroxy-pregn-4-ene-3-one), etc.	Steroid hormone biosynthesis	3α(or 20β)–HSDH deficiency；
17β–HSDH type 5; prostaglandin-F synthase	EC 1.1.1.188; AKR	(5Z,13E)-(15S)-9α,11α,15-trihydroxyprosta-5,13-dienoate((5Z,13E)-(15S)-9α,15-dihydroxy-11-oxoprosta-5,13-dienoate); prostaglandin D2(9α,11α-prostaglandin F2α); prostaglandin H2(prostaglandin F2α), etc.	arachidonic acid metabolism	Asthma; Callosities; Carcinoma, Squamous Cell; Fatty Liver; Hematologic Neoplasms; Hypertriglyceridemia

17β-HSDH type 5; 3α–HSDH type 2	EC 1.1.1.213; AKR	17β-hydroxy-5α-androstan-3-one(3α,17β-dihydroxy-5α-androstan); tibolone (3α-hydroxytibolone, 3β-hydroxytibolone); 3-ketosteroids(3-hydroxysteroids); acetophenone (1-phenylethanol; 5α-androstane-3,17-dione; androstanedione), etc.	Folate biosynthesis, Steroid hormone biosynthesis; allopregnanolone biosynthesis, bile acid biosynthesis, neutral pathway, testosterone and androsterone degradation to androstendione	Breast Neoplasms; Carcinoma; Carcinoma, Hepatocellular; Carcinoma, Non-Small-Cell Lung
17β–HSDH type 10;	EC 1.1.1.178; SDR	2-methyl-3-hydroxybutyryl-CoA(2-methylacetoacetyl-CoA)	Biosynthesis of secondary metabolites, Valine, leucine and isoleucine degradation	3-hydroxy-2-methylbutyryl-coa dehydrogenase deficiency
20α–HSDH; aldose reductase	EC 1.1.1.21	4-hydroxy-trans-2-nonenal (1,4-dihydroxynonane); 4-hydroxynonena(4-hydroxynonanol); aldose(alditol), etc.	Folate biosynthesis, Fructose and mannose metabolism, Galactose metabolism, Glycerolipid metabolism, Pentose and glucuronate interconversions	Acute Kidney Injury; Adenocarcinoma; Adenocarcinoma of Lung; Adenoma; Albuminuria
20α–HSDH; prostaglandin-E2 9-reductase	EC 1.1.1.189	(5Z,13E) -(15S)-9α,11α,15-trihydroxyprosta-5,13-dienoate((5Z,13E) -(15S)-11α,15-dihydroxy-9-oxoprosta-5,13-dienoate); prostaglandin E2(prostaglandin F2α); prostaglandin H2(prostaglandin F2α; prostaglandin E2)	arachidonic acid metabolism	Essential Hypertension; Placenta, Retained

Table S4. Residues that interact with NAD(P)(H) in AKR superfamily and their conformation differences of coenzyme.

		Interaction between NADP(H)/NAD(H) and HSDHs			Distance/Å	A	B	C
		Adenosine ring	Pyrophosphate	Nicotinamide ring		A	B	C
3α–HSDH	1J96	Leu 219, **Ala253**, **Lys270**, Ser271, **Tyr272**, Ser 273, **Arg276**, Gln279	**Ser217**, **Ala218**, **Leu219**, Gly220, **Ser221**, His222, **Leu268**, Lys270,	**Thr23**, **Tyr24**, **Asp50**, Tyr55, **Ser166**, **Asn167**, **Gln190**, **Tyr216**,	17.0	134.8	–26.3	64.7

	1IHI	**Lys270**, **Tyr272**, **Arg276**, Gln 279, Asn280	**Ser217**, **Leu219**, **Ser221**, His222, Lys270,	**Thr23**, **Tyr24**, **Asn50**, **Ser166**, **Asn167**, **Tyr216**	17.0	133.9	15.7	70.5
	2FVL	Gln222, Thr251, **Ala253**, **Lys270**, Ser271, **Tyr272**, **Arg276**, Glu279, Asn280,	**Thr221**, His216, **Ser217**, **Ala218**, **Leu219**, Gly220, **Leu268**, Ala269,	**Thr23**, **Tyr24**, **Asp50**, **Ser166**, **Asn167**, **Gln190**	17.1	130.5	37.8	65.5
3(17) α–HSDH	2P5N	Thr251, **Ala253**, Leu272, Lys273, **Arg276**, Glu279, Asn280,	Tyr216, Gly217, Val218, **Leu219**, **Thr221**, Gln222, Tyr224, **Leu268**, Asn269,	**Thr23**, **Ala24**, **Asp50**, His117, Tyr118, **Ser166**, **Asn167**, **Gln190**,	17.3	136.1	–109.2	78.6
3α(17β)–HSDH	4L1X	**Ala253**, **Lys270**, Ser271, **Tyr272**, **Arg276**,	**Ser217**, **Ala218**, **Leu219**, Gly220, His222, **Leu268**, Ala269,	**Thr23**, **Asp50**, **Ser166**, **Asn167**, **Gln190**, **Tyr216**,	17.3	140.8	–33.8	64.6
	4XO7	**Lys270**, Ser271, **Tyr272**, **Ala253**, **Arg276**,	Tyr24, **Ser217**, **Ala218**, **Leu219**, **Ser221**, **Leu268**	**Thr23**, **Asp50**, **Ser166**, **Gln190**, **Tyr216**, His222,	17.1	135.6	–27.8	79.9
17β–HSDH	1XF0	**Ala253**, **Lys270**, Ser271, **Tyr272**, **Arg276**, Asn280,	**Ser217**, **Ala218**, **Leu219**, **Ser221**, Gln222, **Leu268**	**Tyr24**, **Asp50**, **Ser166**, **Tyr216**,	17.1	137.7	–47.1	67.9
	1ZQ5	**Ala253**, Ser271, **Tyr272**, **Lys270**, **Arg276**, Gln279, Asn280,	**Ser217**, **Ala218**, **Leu219**, Gly220, **Ser221**, Gln222, **Leu268**, Lys270	**Thr23**, **Tyr24**, **Asp50**, Ser118, **Ser166**, **Asn167**, **Gln190**, **Tyr216**,	17.0	137.1	–50.8	64.4
20α–HSDH	1MRQ	**Ala253**, Ser271, **Lys270**, **Tyr272**, **Arg276**, Gln279, Asn280,	**Ser217**, **Ala218**, **Leu219**, **Ser221**, His222, **Leu268**,	**Thr23**, **Tyr24**, **Asp50**, Tyr55, His117, **Ser166**, **Asn167**, **Gln190**, **Tyr216**,	17.1	136.7	–31.4	67.4
	1Q5M	**Ala253**, Ser271, Phe272, Thr273, **Arg276**, Glu279, Asn280,	**Ser217**, **Ala218**, **Leu219**, Gly220, **Ser221**, His222, **Leu268**, Ala269, Lys270,	Gly22, **Thr23**, **Tyr24**, **Asn50**, Tyr55, His117, **Ser166**, **Gln190**	17.0	129.5	–22	65.2

Dihedral angles A, B and C represents C4B-C2B-C1B-N9A (adenosine ring), PA-O3-PN-O5D (pyrophosphate group) and C4D-C2D-C2N-C5N (nicotinamide ring). Residues with bold font are conserved in these crystals.

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