Cyclooxygenases and prostaglandin synthases

Overview: Prostaglandin (PG) G/H synthase, most commonly referred to as cyclooxygenase [COX, (5Z,8Z,11Z,14Z)-icosa-5,8,11,14-tetraenoate,hydrogen-donor : oxygen oxidoreductase] activity, catalyses the formation of PG G_2 from arachidonic acid. Hydroperoxidase activity inherent in the enzyme catalyses the formation of PGH_2 from PGG_2. COX-1 and -2 can be nonselectively inhibited by ibuprofen, ketoprofen, naproxen, indometacin and paracetamol (acetaminophen).

Subsequent to the formation of PGH_2, the cytochrome P450 activities (see page S215) thromboxane synthase (CYP5A1, EC 5.3.99.5, ENSG00000059377) and prostacyclin synthase (CYP8A1, EC 5.3.99.4, ENSG00000124212) generate thromboxane A_2 and prostacyclin (PGI_2), respectively. Additionally, multiple enzyme activities are able to generate prostaglandin E_2, prostaglandin D_2 and prostaglandin $F_{2\alpha}$ (see tables).

Nomenclature	COX-1	COX-2
Other names	Prostaglandin G_2/H_2 synthase-1	Prostaglandin G_2/H_2 synthase-2
Ensembl ID	ENSG00000095303	ENSG00000073756
EC	1.14.99.1	1.4.99.1
Substrates	Arachidonic acid	Arachidonic acid, docosahexaenoic acid (see Smith, 2008)
Selective inhibitors	FR122047 (7.5, Ochi *et al.*, 2000), valeroylsalicylate (Bhattacharyya *et al.*, 1995)	Diclofenac (6.7), celecoxib (5.1), rofecoxib (4.3), valdecoxib, parecoxib, etoricoxib, lumiracoxib

Nomenclature	mPGES1	mPGES2	cPGES	L-PGDS	H-PGDS
Other names	Prostaglandin E synthase, microsomal glutathione S-transferase 1-like 1, MGST1-L1, p53-induced gene 12 protein p53-induced gene 12; PIG12	Prostaglandin E synthase 2, microsomal prostaglandin E synthase 2, mPGES-2	Cytosolic prostaglandin E_2 synthase, prostaglandin E synthase 3, telomerase-binding protein p23, hsp90 co-chaperone, progesterone receptor complex p23	Lipocalin-type prostaglandin-D synthase, prostaglandin D_2 synthase, prostaglandin H_2 D-isomerase, glutathione-independent PGD synthetase, β-trace protein, cerebrin-28	Hematopoietic prostaglandin D synthase, glutathione-requiring prostaglandin D synthase, glutathione-dependent PGD synthetase, prostaglandin-H_2 D-isomerase
EC	5.3.99.3	5.3.99.3	5.3.99.3	5.3.99.2	5.3.99.2
Ensembl ID	ENSG00000148344	ENSG00000148334	ENSG00000110958	ENSG00000107317	ENSG00000163106

Prostaglandin D_2 can be metabolised to 9α,11β-prostaglandin $F_{2\alpha}$ through the multifunctional enzyme activity AKR1C3. Prostaglandin E_2 can be metabolised to 9α,11α-prostaglandin $F_{2\alpha}$ through the 9-ketoreductase activity of CBR1.

Nomenclature	AKR1C3	CBR1
Other names	Aldo-keto reductase family 1 member C3, prostaglandin F synthase, PGFS, *trans*-1,2-dihydrobenzene-1,2-diol dehydrogenase, 3α-hydroxysteroid dehydrogenase type 2, 3α-HSD type 2, testosterone 17β-dehydrogenase 5, 17β-hydroxysteroid dehydrogenase type 5, 17β-HSD 5, dihydrodiol dehydrogenase type I, dihydrodiol dehydrogenase 3, chlordecone reductase homolog HAKRb, HA1753	Carbonyl reductase [NADPH] 1, prostaglandin E_2 9-reductase, prostaglandin 9-ketoreductase, NADPH-dependent carbonyl reductase 1, 15-hydroxyprostaglandin dehydrogenase [NADP+]
EC	1.1.1.188, 1.3.1.20, 1.1.1.213, 1.1.1.63, 1.1.1.64	1.1.1.197, 1.1.1.184, 1.1.1.189
Ensembl ID	ENSG00000196139	ENSG00000159228
Inhibitors	Flufenamic acid, indometacin (Matsuura *et al.*, 1998), flavonoids (Skarydova *et al.*, 2009)	–

Abbreviations: FR122047, 1-([4,5-bis{methoxyphenyl}-2-thazoyl]carbonyl)-4-methyl)piperazine hydrochloride

Further Reading

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