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Gene Section
Mini Review

PTGS2 (prostaglandin-endoperoxide synthase 2 (prostaglandin G/H synthase and cyclooxygenase))

Panagiotis A Konstantinopoulos, Michalis V Karamouzis, Athanasios G Papavassiliou

Department of Biological Chemistry, Medical School, University of Athens, GR-11527 Goudi-Athens, Greece

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Identity

Hugo: PTGS2
Other names: COX2 (Cyclooxygenase 2); COX-2; PGG/HS; PGHS-2; PHS-2; hCox-2
Location: 1q31.1

DNA/RNA

Description

8633 bases, 10 exons.

Transcription

One transcript (chr1:184907546-184916179). COX2 promoter is regulated via the interplay between two opposite beta isoforms of the CCAAT/enhancer binding protein and the p300 coactivator.

Protein

Description

COX2 is an enzyme that belongs to the prostaglandin G/H synthase family. It consists of 604 amino acids and has a molecular weight of 68996 Da.
COX2 possesses two catalytic activities and respective active sites:
- a cyclooxygenase (COX) that converts arachidonic acid to a prostaglandin endoperoxide, prostaglandin G2 (PGG2), and;
- a peroxidase (POX) that reduces PGG2 to PGH2.
COX2 functions as homodimer although each subunit has both a POX and a COX active site.
Each subunit binds one heme B (iron-protoporphyrin IX) group.

Expression

Wide expression in alimentary system (esophagus, pharynx), male reproductive system (prostate, seminal vesicles, ejaculatory duct), female reproductive system (cervix, uterus), hematopoietic system (bone marrow, monocytes).

Localisation

Intracellular, cytoplasm, microsome, microsomal membrane.

Function

Enzyme that functions both as a dioxygenase and as a peroxidase. COX-2 catalyzes the transformation of arachidonic acid to prostaglandin H2, which is the rate-limiting step in the formation of prostaglandins (PGs) and thromboxane A2 (TXA2). COX-2 is a potent mediator of inflammation and is implicated in prostanoid signaling in activity dependent plasticity. It is an inducible enzyme that plays an important role in several pathophysiological processes, including inflammation, angiogenesis, and tumorigenesis.

Mutations

Note: Five heterozygous mutations (1 missense/nonsense, 1 splicing, 3 regulatory) have been identified. Two were associated with diabetes mellitus type 2, one with bladder cancer risk, one with increased risk of colorectal cancer and one with decreased risk of colorectal cancer.

Implicated in

Colorectal cancers

Disease

COX2 is involved in regulation of apoptosis, proliferation and invasiveness of colorectal tumor cells and promotes angiogenesis in several animal colon cancer models. It is also implicated in several premalignant lesions including adenomatous polyps. COX2 stimulates colon cancer cell growth through its heterotrimeric guanine nucleotide-binding protein (G protein)-coupled receptor, EP2.

Gastric cancer

Disease

Expression of COX2 is elevated in gastric adenocarcinomas, which correlates with several clinicopathological parameters, including depth of invasion and lymph node metastasis.

Non small cell lung cancer

Disease

Non-small-cell lung cancer (NSCLC),
especially adenocarcinomas, overexpress COX2, which contributes to the progression of malignancy by several mechanisms.

Cholangiocarcinoma

Disease

COX2 has been implicated in cholangiocarcinogenesis. Selective COX-2 inhibitors have been shown to inhibit cholangiocarcinoma cell growth in vitro and in animal models.

Uterine carcinosarcoma

Disease

COX2 is overexpressed in one-third of uterine carcinosarcomas. COX-2 expression is a strong indicator of unfavorable prognosis.

Head and Neck squamous cell cancer

Disease

COX2 is overexpressed in a variety of premalignant and malignant conditions, including oral leukoplakia and squamous cell carcinoma of the head and neck.

Ovarian cancer

Disease

COX-2 is increased in epithelial ovarian cancer and PGE2-synthesis and signalling are important for malignant transformation and progression.

Pancreatic cancer

Disease

Mounting evidence suggests that COX2 is implicated in pancreatic cancer.

Immunohistochemical, RT-PCR, and Western blotting studies have shown that COX2, is upregulated in human pancreatic cancer cell lines as well as human pancreatic cancer tissues compared with normal ductal cells and normal pancreas specimens. COX2 inhibitors significantly inhibit pancreatic cancer growth both in vitro and in vivo while simultaneously induce apoptosis.

Other malignant diseases

Disease

Similar to above tumors, COX2 is implicated in carcinogenesis of multiple tumors including transitional cell bladder cancer, prostate cancer, uterine cancer, cervical cancer, angiosarcoma, hepatocellular cancer, melanoma, multiple myeloma, chronic lymphocytic leukemia, thyroid cancer, Wilms tumor.

Primary dysmenorrhea

Disease

In vivo studies have demonstrated that selective COX-2 inhibitors are effective in treatment of primary dysmenorrhea in women.

Inflammatory conditions

Disease

COX2 occupies an important in several inflammatory diseases such as osteoarthritis and rheumatoid arthritis.

Neurolomuscular disorders

Disease

COX2 is implicated in encephalitis, cerebral infarction, polyneuropathy and muscular dystrophies.

Cardiovascular toxicity and thromboembolic disorders

Note: Selective inhibition of COX2 (without concomitant inhibition of COX1) is associated with significant cardiovascular risk and thromboembolic phenomena.

Retinopathy

Disease

COX2 plays an important role in ischemic proliferative retinopathy, as in the case of diabetic retinopathy.

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