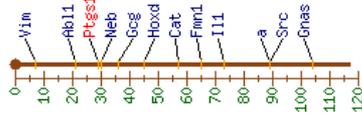
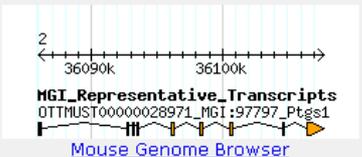


| protein_complexes [Compatibility Mode] | | |
|---|--------------------------|---|
| A | B | C |
| 1 Complex | EC | Subunits (transient subunits are highlighted) |
| 2 3-methylcrotonyl-CoA carboxylase | 6.4.1.4 | methylcrotonoyl-Coenzyme A carboxylase, α subunit |
| 3 | | methylcrotonoyl-Coenzyme A carboxylase, β subunit |
| 4 | | |
| 5 ADP-forming succinate-CoA ligase | 6.2.1.5 | succinate-CoA ligase, α subunit |
| 6 | | succinate-CoA ligase, ADP-forming, β subunit |
| 7 | | |
| 8 GDP-forming succinate-CoA ligase | 6.2.1.4 | succinate-CoA ligase, α subunit |
| 9 | | succinate-CoA ligase, GDP-forming, β subunit |
| 10 | | |
| 11 serine palmitoyltransferase | 2.3.1.50 | serine palmitoyltransferase, long chain base subunit 1 |
| 12 | | serine palmitoyltransferase, long chain base subunit 2 |
| 13 | | serine palmitoyltransferase, long chain base subunit 3 |
| 14 | | |
| 15 NADH dehydrogenase (ubiquinone) | 1.6.5.3 | mitochondrially encoded NADH dehydrogenase 1 |
| 16 | | mitochondrially encoded NADH dehydrogenase 2 |
| 17 | | mitochondrially encoded NADH dehydrogenase 3 |
| 18 | | mitochondrially encoded NADH dehydrogenase 4 |
| 19 | | mitochondrially encoded NADH dehydrogenase 4L |
| 20 | | mitochondrially encoded NADH dehydrogenase 5 |
| 21 | | mitochondrially encoded NADH dehydrogenase 6 |
| 22 | | NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, subunit 1 |
| 23 | | NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, subunit 2 |

PRO identifiers are being incorporated into MGI Gene Detail Pages

Ptgs1 Gene Detail Your Input Welcome

| | | |
|---------------------------|---|---|
| Symbol Name ID | Ptgs1 prostaglandin-endoperoxide synthase 1 MGI:97797 | Nomenclature History |
| Synonyms | Cox-1, Cox-3, COX1, cyclooxygenase 1, Pgbs1 | |
| Genetic Map | Chromosome 2 29.0 cM Detailed Genetic Map ± 1 cM Mapping data(13) |  |
| Sequence Map | Chr2:36085946-36107792 bp, + strand (From VEGA annotation of NCBI Build 37) VEGA ContigView Ensembl ContigView UCSC Browser NCBI Map Viewer |  |
| Mammalian homology | human; chimpanzee; cattle; dog, domestic; rat (Mammalian Orthology) Comparative Map (Mouse/Human Ptgs1 ± 2 cM) | |

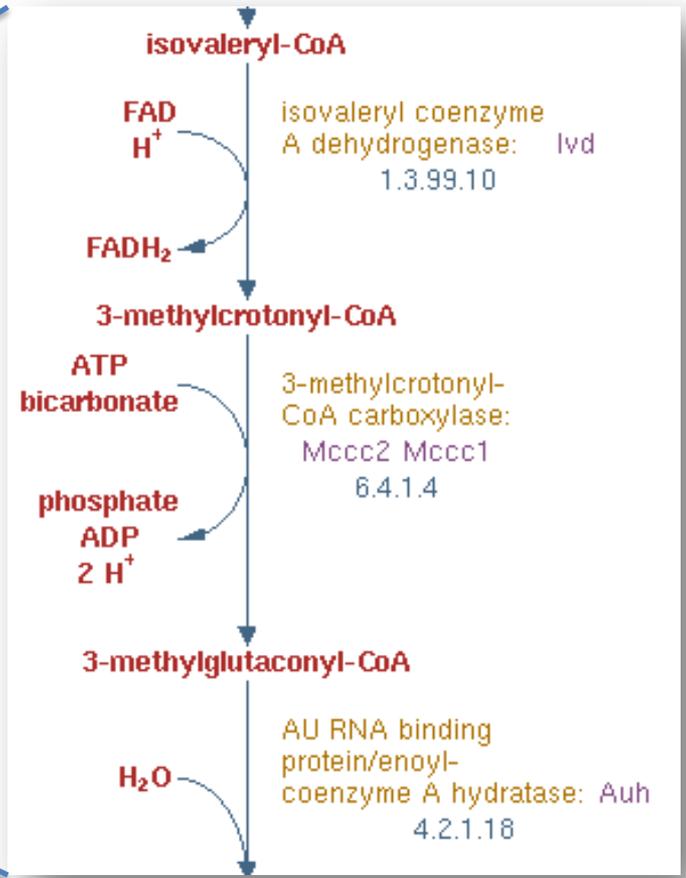
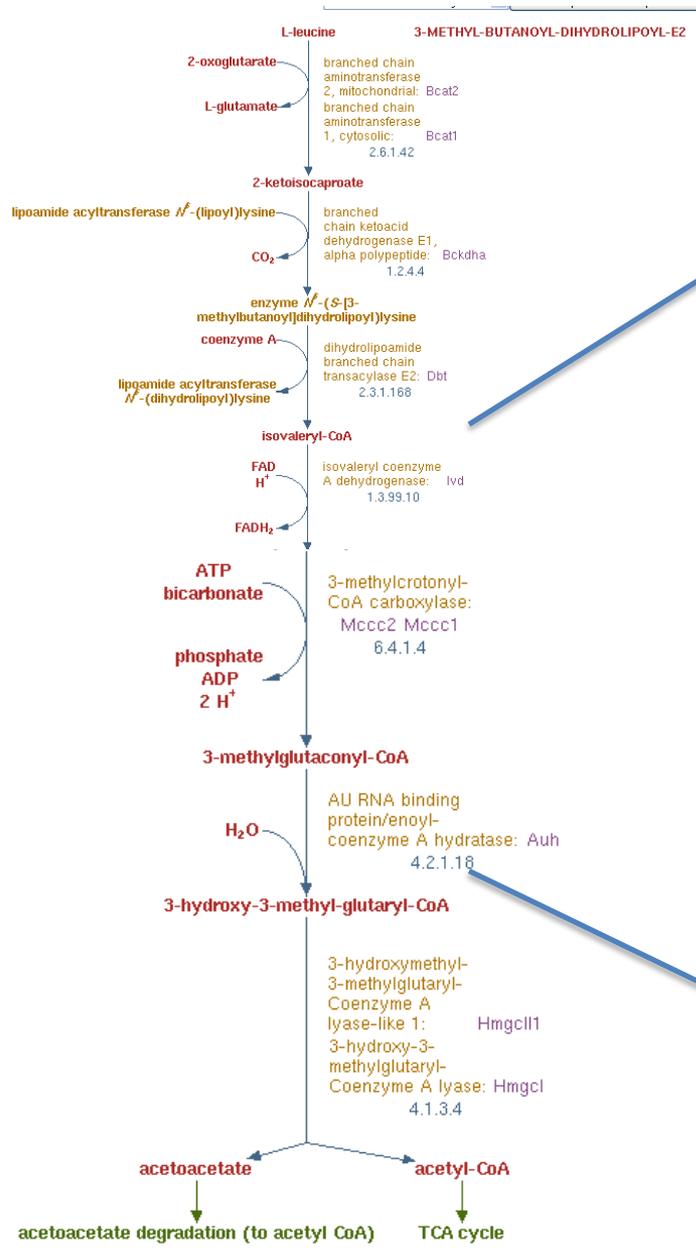
| Protein-related information | Resource | ID | Description |
|-----------------------------|------------------|-------------------------------|-----------------------------------|
| | InterPro | IPR000742 | EGF-like, type 3 |
| | InterPro | IPR002007 | Haem peroxidase, animal |
| | InterPro | IPR006210 | EGF-like |
| | InterPro | IPR010255 | Haem peroxidase |
| | InterPro | IPR019791 | Haem peroxidase, animal, subgroup |
| | Protein Ontology | PRO:000013427 | prostaglandin G/H synthase 1 |

Examples of Protein Complex Representation in PRO

- methylcrotonoyl-CoA carboxylase complex, mitochondrial (mouse)
- Isocitrate dehydrogenase complex, mitochondrial (mouse)
- COX1 homodimer complex
- Mitochondrial cytochrome oxidase:
Respiratory chain complex IV (mouse)

Case 1: methylcrotonoyl-CoA carboxylase complex, mitochondrial (mouse)

- Complex composed of two subunits
 - None of the subunits have isoforms
- **Methylcrotonyl CoA carboxylase (MCC)**
 - biotin-requiring enzyme
 - located in the mitochondria
 - uses bicarbonate as a carboxyl group source to catalyze the carboxylation of a carbon adjacent to a carbonyl group performing the 4th step in processing leucine, an essential amino acid.
- Point mutations and deletion events in the genes, MCC1 and MCC2, lead to MCC deficiency, an inborn error of metabolism
 - vomiting, metabolic acidosis, very low plasma glucose concentration, and very low levels of carnitine in plasma.
 - 1 in 36,000 births (ranges in severity)



Mus musculus Enzyme: 3-methylcrotonyl-CoA carboxylase

Subunit composition of 3-methylcrotonyl-CoA carboxylase = [Mccc1][Mccc2]

[methylcrotonyl-Coenzyme A carboxylase 1 \(alpha\)](#) = Mccc1

[methylcrotonyl-Coenzyme A carboxylase 2 \(beta\)](#) = Mccc2

Gene-Reaction Schematic: 



MultiFun Terms: [UNCLASSIFIED](#)

Credits:

Created 10-Nov-2008 by [Evsikov A](#)

| <input type="checkbox"/> PRO ID | PRO Name | PRO Term Definition | Category | Parent | Matched Fields |
|--|--|---|---------------|-------------------------------|---|
| <input type="checkbox"/> PRO:000010233 | methylcrotonoyl-CoA carboxylase subunit alpha, mitochondrial | A protein that is a translation product of the MCCC1 gene or a 1:1 ortholog thereof. [PRO:DNx] | gene | PRO:000000001 | PRO Name=>methylcrotonoyl |
| <input type="checkbox"/> PRO:000010234 | methylcrotonoyl-CoA carboxylase beta chain, mitochondrial | A protein that is a translation product of the MCCC2 gene or a 1:1 ortholog thereof. [PRO:DNx] | gene | PRO:000000001 | PRO Name=>methylcrotonoyl |
| <input type="checkbox"/> PRO:000025354 | methylcrotonoyl-CoA carboxylase subunit alpha, mitochondrial (mouse) | A methylcrotonoyl-CoA carboxylase subunit alpha, mitochondrial that is encoded in the genome of mouse. [PRO:CB] | organism-gene | PRO:000010233 | PRO Name=>methylcrotonoyl; PRO Term Definition=>methylcrotonoyl |
| <input type="checkbox"/> PRO:000025357 | methylcrotonoyl-CoA carboxylase beta chain, mitochondrial (mouse) | A methylcrotonoyl-CoA carboxylase beta chain, mitochondrial that is encoded in the genome of mouse. [PRO:HJD] | organism-gene | PRO:000010234 | PRO Name=>methylcrotonoyl; PRO Term Definition=>methylcrotonoyl |

methylcrotonoyl-CoA carboxylase complex, mitochondrial : **subunit 1**

[Term]

id: **PRO:000025354**

name: methylcrotonoyl-CoA carboxylase subunit alpha, mitochondrial (mouse)

def: "A methylcrotonoyl-CoA carboxylase subunit alpha, mitochondrial that is encoded in the genome of mouse." [PRO:CB]

comment: Category=organism-gene.

xref: UniProtKB:Q99MR8

intersection_of: [PRO:000010233](#) ! methylcrotonoyl-CoA carboxylase subunit alpha, mitochondrial

intersection_of: only_in_taxon taxon:10090 ! Mus musculus

methylcrotonoyl-CoA carboxylase complex, mitochondrial : **subunit 2**

[Term]

id: **PRO:000025357**

name: methylcrotonoyl-CoA carboxylase beta chain, mitochondrial (mouse)

def: "A methylcrotonoyl-CoA carboxylase beta chain, mitochondrial that is encoded in the genome of mouse." [PRO:HJD]

comment: Category=organism-gene.

xref: UniProtKB:Q3ULD5

intersection_of: [PRO:000010234](#) ! methylcrotonoyl-CoA carboxylase beta chain, mitochondrial

intersection_of: only_in_taxon taxon:10090 ! Mus musculus

methylcrotonoyl-CoA carboxylase **complex**, mitochondrial (mouse)

[Term]

id: PRO:XXXXXXXX

name: methylcrotonoyl-CoA carboxylase complex, mitochondrial (mouse)

def: "A heterodimeric complex having 3-methylcrotonyl-CoA carboxylase activity. The alpha subunit has a covalently bound biotin essential for the ATP-dependent carboxylation. The beta subunit possess carboxyltransferase activity which presumably is essential for binding to 3-methylcrotonyl-CoA.[ref]"

xref: EC 6.4.1.4

relationship: is_a: GO:0002169! 3-methylcrotonyl-CoA carboxylase complex, mitochondrial

relationship: has_part: ! PRO:000025354 methylcrotonoyl-CoA carboxylase subunit alpha,
mitochondrial (mouse)

relationship: has_part: ! PRO:000025357 methylcrotonoyl-CoA carboxylase beta chain,
mitochondrial (mouse)

- Store the disease context in PAF file? Set up to do this? Do our query tools allow users to retrieve these annotations?
 - OMIM **#210200**
 - OMIM **#210210**

Case 2: Isocitrate dehydrogenase complex, mitochondrial (NAD+) (mouse)

- Part of the TCA cycle
- Complex composed of multiple subunits
 - Alpha (two isoforms)
 - [PRO:000008889](#) (generic)
 - [PRO:000025358](#) (mouse)
 - » [PRO:000025352](#) (isoform 1)
PRO:000025355 (isoform 1, mouse)
 - » [PRO:000025353](#) (isoform 2)
PRO:000025356 (isoform 2, mouse)
 - Beta
 - [PRO:000008890](#) (generic)
 - [PRO:000025359](#) (mouse)
 - Gamma
 - [PRO:000008891](#) (generic)
 - [PRO:000025360](#) (mouse)

Two other types:

1. Cytosolic complex: homodimer
2. Mitochondrial (NADP+): homodimer

Isocitrate dehydrogenase 3 complex, mitochondrial (mouse): **alpha subunit**

[Term]

id: PRO:000025358

name: isocitrate dehydrogenase 3 [NAD] subunit alpha, mitochondrial (mouse)

def: "An isocitrate dehydrogenase [NAD] subunit alpha, mitochondrial that is encoded in the genome of mouse." [PRO:HJD]

comment: Category=organism-gene.

xref: UniProtKB:Q9D6R2

intersection_of: PRO:000008889 ! isocitrate dehydrogenase 3 [NAD] subunit alpha, mitochondrial

intersection_of: only_in_taxon taxon:10090 ! Mus musculus

Isocitrate dehydrogenase, mitochondrial (mouse): beta subunit and

Isocitrate dehydrogenase, mitochondrial (mouse): gamma subunit

..... have similar stanzas

Isocitrate dehydrogenase 3 complex, mitochondrial

[Term]

id: PRO:000008889

name: isocitrate dehydrogenase 3 [NAD] subunit alpha, mitochondrial

def: "An isocitrate dehydrogenase [NAD] subunit alpha, mitochondrial that is encoded in the genome of mouse." [PRO:HJD]

Isocitrate dehydrogenase, mitochondrial (mouse): beta subunit and

Isocitrate dehydrogenase, mitochondrial (mouse): gamma subunit

..... have similar stanzas

Isocitrate dehydrogenase 3 complex, mitochondrial (mouse): alpha subunit, **isoform 1**

[Term]
Id:PRO:000025355
name: isocitrate dehydrogenase 3 (NAD+) alpha, isoform 1 (mouse)
xref: UniProtKB:Q9D6R2-1
def: “ “
intersection_of: PRO:00002532! isocitrate dehydrogenase [NAD] subunit alpha, mitochondrial, isoform 1
intersection_of: only_in_taxon taxon:10090 ! Mus musculus

Isocitrate dehydrogenase 3 complex, mitochondrial (mouse): alpha subunit, **isoform 2**

[Term]
Id:PRO:000025356
name: isocitrate dehydrogenase 3 (NAD+) alpha, isoform 2 (mouse)
xref: UniProtKB:Q9D6R2-2
def: “ “
intersection_of: PRO:000025353! isocitrate dehydrogenase [NAD] subunit alpha, mitochondrial, isoform 2
intersection_of: only_in_taxon taxon:10090 ! Mus musculus

PRO:xxxxxx IDH3 [NAD]Complex

[PRO:000008889](#) (generic alpha)

[PRO:000008890](#) (generic beta)

[PRO:000008891](#) (generic gamma)

PRO:uuuuuu IDH3 [NAD]Complex 1 (mouse)

[PRO:000025359](#) (beta)

[PRO:000025360](#) (gamma)

[PRO:000025358](#) (alpha)

PRO:yyyyyy IDH3 [NAD]Complex 2 (mouse)

[PRO:000025359](#) (beta)

[PRO:000025360](#) (gamma)

[PRO:000025355](#) (alpha isoform 1)

PRO:zzzzzz IDH3 [NAD]Complex 3 (mouse)

[PRO:000025359](#) (beta)

[PRO:000025360](#) (gamma)

[PRO:000025356](#) (alpha isoform 2)

Isocitrate dehydrogenase complex, mitochondrial
the generic complex

[Term]

id: PRO:xxxxxxxxx

name: isocitrate dehydrogenase [NAD] complex, mitochondrial

xref:

def: “ “

is_a: GO:0005962! mitochondrial isocitrate dehydrogenase complex (NAD+)

has_part: PRO:000008889! isocitrate dehydrogenase [NAD] subunit alpha,
mitochondrial

has_part: PRO:000008890! isocitrate dehydrogenase [NAD] subunit beta,
mitochondrial

has_part: PRO:000008891! isocitrate dehydrogenase [NAD] subunit gamma,
mitochondrial

Isocitrate dehydrogenase 3 complex 2, mitochondrial (mouse)
the complex with isoform 1 of the alpha subunit

[Term]

id: PRO:yyyyyyy

name: isocitrate dehydrogenase 3 [NAD] complex 2, mitochondrial (mouse)

def: “ “

~~is_a: GO:0005962! mitochondrial isocitrate dehydrogenase complex (NAD+)~~

is_a: PRO:xxxxxx! isocitrate dehydrogenase 3 [NAD] complex, mitochondrial

has_part: PRO:000025359! isocitrate dehydrogenase 3 [NAD] subunit beta,
mitochondrial (mouse)

has_part: PRO:000025360! isocitrate dehydrogenase 3 [NAD] subunit gamma,
mitochondrial (mouse)

has_part: PRO:000025355! isocitrate dehydrogenase 3 (NAD+) alpha, isoform 1
(mouse)

Names and symbols for complexes—

- Who is the authority?
- Are there existing nomenclature standards?

Where to indicate tissue, cell type, developmental context, etc. in the PAF file?

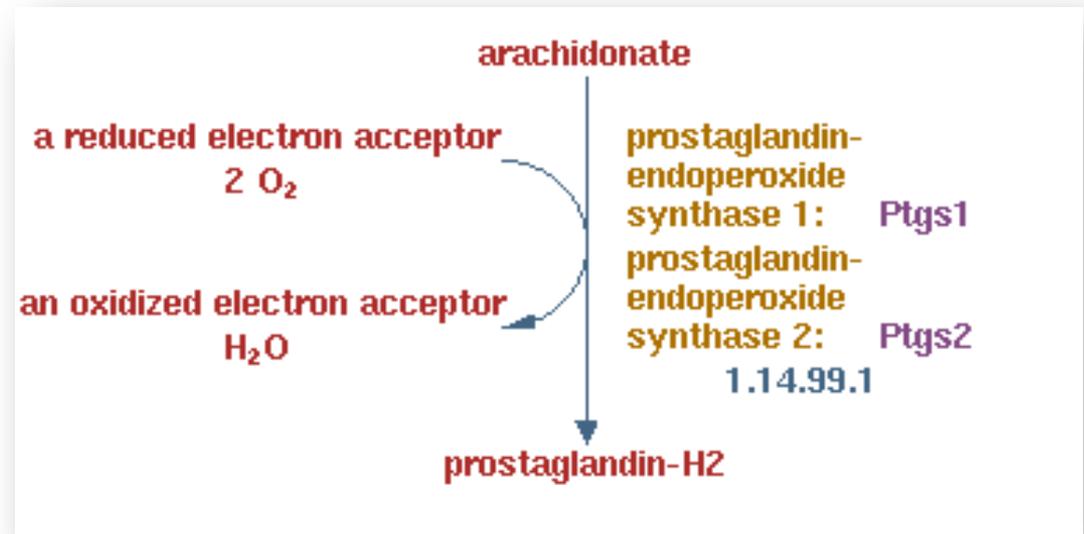
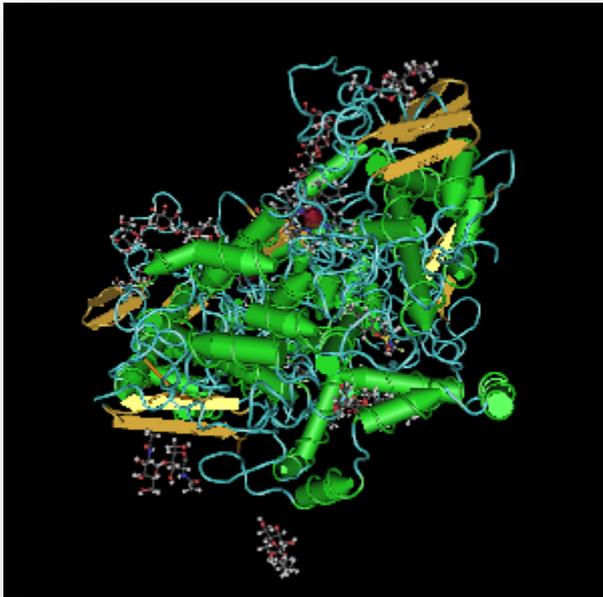
Case 3: Homodimers

Prostaglandin biosynthesis

Ptgs1 (aka, Cox1) and Ptgs2 (aka, Cox2)

[PRO:000013427](#)

[PRO:000013428](#)



Cox1 homodimer complex complexed with aspirin

<http://www.ncbi.nlm.nih.gov/Structure/mmdb/mmdbsrv.cgi?Dopt=s&uid=78790>

Proc Natl Acad Sci U S A. 2010 Jan 5;107(1):28-33. Epub 2009 Dec 1.

Coxibs interfere with the action of aspirin by binding tightly to one monomer of cyclooxygenase-1.

Rimon G, Sidhu RS, Lauver DA, Lee JY, Sharma NP, Yuan C, Frieler RA, Trievel RC, Lucchesi BR, Smith WL.

Department of Biological Chemistry, University of Michigan, Ann Arbor, MI 4810, USA.

Abstract

Pain associated with inflammation involves prostaglandins synthesized from arachidonic acid (AA) through cyclooxygenase-2 (COX-2) pathways while thromboxane A₂ formed by platelets from AA via cyclooxygenase-1 (COX-1) mediates thrombosis. COX-1 and COX-2 are both targets of nonselective nonsteroidal antiinflammatory drugs (nsNSAIDs) including aspirin whereas COX-2 activity is preferentially blocked by COX-2 inhibitors called coxibs. COXs are homodimers composed of identical subunits, but we have shown that only one subunit is active at a time during catalysis; moreover, many nsNSAIDs bind to a single subunit of a COX dimer to inhibit the COX activity of the entire dimer. Here, we report the surprising observation that celecoxib and other coxibs bind tightly to a subunit of COX-1. Although celecoxib binding to one monomer of COX-1 does not affect the normal catalytic processing of AA by the second, partner subunit, celecoxib does interfere with the inhibition of COX-1 by aspirin *in vitro*. X-ray crystallographic results obtained with a celecoxib/COX-1 complex show how celecoxib can bind to one of the two available COX sites of the COX-1 dimer. Finally, we find that administration of celecoxib to dogs interferes with the ability of a low dose of aspirin to inhibit AA-induced *ex vivo* platelet aggregation. COX-2 inhibitors such as celecoxib are widely used for pain relief. Because coxibs exhibit cardiovascular side effects, they are often prescribed in combination with low-dose aspirin to prevent thrombosis. Our studies predict that the cardioprotective effect of low-dose aspirin on COX-1 may be blunted when taken with coxibs.

“Coxs are homodimers composed of identical subunits, but we have shown that only one subunit is active during catalysis; moreover, many nsAIDS bind to a single subunit of a COX dimer to inhibit the COX activity of the entire dimer.”

[Term]

id: PRO:XXXXXXXX

name: COX1 homodimer complex

def: ""

relationship: has_part: PRO: aaaaaaa! prostaglandin G/H synthase 1

Composition not part of
stanza...how to indicate this info is
in annotation file?



[Term]

id: PRO:XXXXXXXX

name: COX1 homodimer complex

def: ""

xref: EC 1.14.99.1

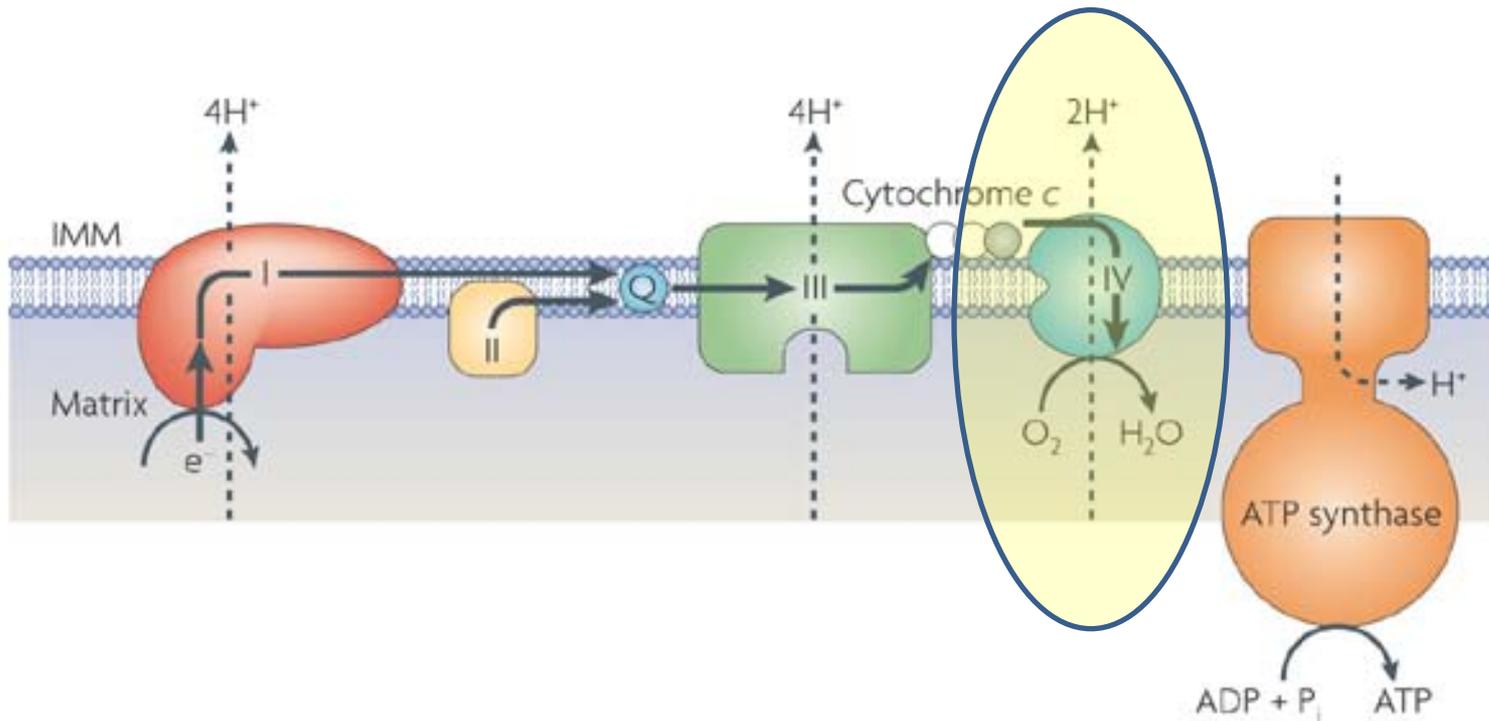
relationship: has_part: PRO: aaaaaaaa! prostaglandin G/H synthase 1 active

Relationship: has_part: PRO:bbbbbbb! prostaglandin G/H synthase 1 inactive

Make a PRO entry for both an
active and inactive subunit?

Case 4: A more complex complex

Mitochondrial cytochrome oxidase: Respiratory chain complex IV



Nature Reviews | Molecular Cell Biology

Respiratory chain complex IV

The respiratory chain complex IV has 13 parts.

Many of those parts (proteins) are encoded by a single gene.

But some of those parts can be encoded by multiple genes depending on the cell/tissue type.

- Mitochondrial encoded parts
 - COX I (mt-Co1) **PRO:000025364**
 - COX II (mt-Co2) **PRO:000025366**
 - COX III (mt-Co3) **PRO:000025367**
- Nuclear encoded mitochondrial parts
 - COX IV (Cox4i1, Cox4i2) (**PRO:000025368, PRO:000025369**)
 - COX Va (Cox5a) (**PRO:000025370**)
 - COXVb (Cox5b) (**PRO:000025371**)
 - COXVIa (Cox6a1, Cox6a2, Cox6a-ps) (**PRO:000025372, PRO:000025373**)
 - COXVIb (Cox6b1, Cox6b2) (**PRO:000025374, PRO:000025375**)
 - COX Vic (Cox6c) (**PRO:000025376**)
 - COX VIIa (Cox7a1, Cox7a2, Cox7a2l) (**PRO:000025377, PRO:000025378, PRO:000025379**)
 - COXVIIb (Cox7c) (**PRO:000025383**)
 - COXIII (Cox8a, Cox8b, Cox8c) (**PRO:000025380, PRO:000025381, PRO:000025382**)

A further complication....these entities can be
“Fuzzy” Complexes....

We know the complex exists...we
don't always know what specific
parts the complex contains

[Term]

id: PRO:XXXXXXXX

name: respiratory chain complex IV

def: ""

xref:

relationship: has_part: PRO:000025364 cox 1, mitochondrial

relationship: has_part: PRO:000025366 cox 2, mitochondrial

relationship: has_part: PRO:000025367 cox 3, mitochondrial

relationship: has_part: PRO:000025370 cox 5a, mitochondrial

relationship: has_part: PRO:000025371 cox 5b, mitochondrial

relationship: has_part: PRO:000025376 cox 6c, mitochondrial

relationship: has_part: PRO:000025383 cox 7c, mitochondrial

relationship: has_one_of: (PRO:000025368 cox4i1, PRO:000025369 cox4i2)

relationship: has_one_of : (PRO:000025377 cox7a1, PRO:000025378 cox7a2,
PRO:000025379 cox7a2l)

Etc.....



How to represent component
uncertainty in a complex in
PRO?