Supporting Information

Sjögren et al. 10.1073/pnas.1218504110

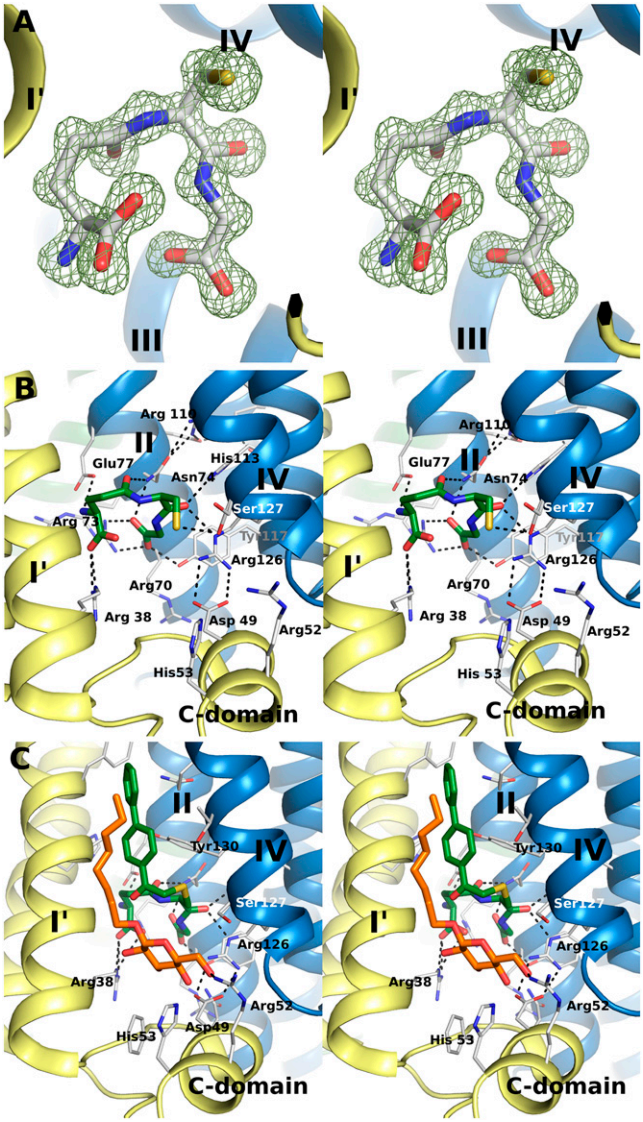

Fig. S1. Stereodiagrams of the structure of the active site in microsomal prostaglandin E synthase-1 (mPGES-1) at the monomer interface. (*A*) F_o-F_c electron density map for the glutathione (GSH) contoured at 4σ. (*B*) Interactions between mPGES-1 and GSH. The Arg38 side chain originates from the symmetry-related monomer. (*C*) mPGES-1 in complex with bis-phenyl-GSH. Bis-phenyl-GSH is shown in blue green representation. A β-octyl glucoside (orange stick representation) is bound to the active site. Distances between β-octyl glucoside and mPGES-1 shorter than 3.2 Å are indicated with dashed lines.

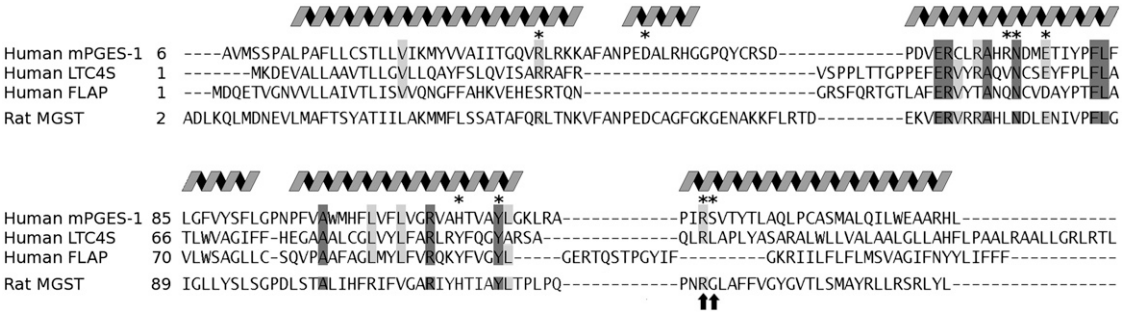

Fig. S2. Structure-based sequence alignment of membrane-associated proteins involved in eicosanoid and glutathione metabolism (MAPEG) family members with known X-ray structure. Structures included are human microsomal prostaglandin E synthase-1 (mPGES-1) [Protein Data Bank (PDB) ID code 4AL0, this work], human LTC4 synthase [PDB ID 2UUH (12)], and human 5-lipoxygenase activating protein [FLAP; PDB ID code 2Q7M (10)]. The low-resolution structure of rat microsomal glutathione transferase-1 [MGST1 (13)] could not be aligned to the others and is included as a sequence-based alignment. Residues involved in glutathione interactions in mPGES-1 are indicated with an asterisk. Ser127, Arg126, and Asp49, implicated in catalysis, are marked with arrows.

Table S1. Data collection and refinement statistics

	Native 2 high resolution	GSH analog* soak	Mersalyl acid soak
Data collection			
Space group	H3	H3	H3
Cell dimensions			
$a = b$, c (Å)	74.74	77.23	76.67
$\alpha = \beta$, γ (°)	123.40	123.39	123.23
Resolution (Å)	58.5–1.16 (1.23–1.16)†	30–1.95 (2.0–1.95)	20.5–1.80 (1.84–1.80)
R_{sym}	3.7 (51.3)	11.9 (48.8)	7.3 (27.7)
$I/\sigma I$	16.9 (1.9)	5.1(1.9)	16.6 (5.9)
Completeness (%)	96.9 (98.5)	100 (100)	99.9 (100.0)
Redundancy	3.1 (3.0)	3.0 (3.0)	3.8 (3.8)
Refinement			
Resolution (Å)	58.5–1.16	30–1.95	
No. reflections	89,826	19,681	25,046
R_{work}/R_{free}	12.2 (13.0)	16.3 (17.3)	
No. atoms			
Protein	1,271	1,176	
Ligand	75	102	
Water	88	83	
B factors			
Protein	16.9	16.5	
Ligand	32.6	33.1	
Water	32.9	36.0	
rmsd			
Bond lengths (Å)	0.012	0.012	
Bond angles (°)	1.26	1.12	

All datasets were collected from single crystals.
*1-(4-phenylphenyl)-2-(S-glutathionyl)-ethanone.
†Highest resolution shell is shown in parentheses.