A.

PTGIS
NP_000952.1
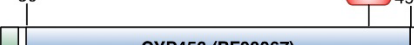[500 aa]

30   C441   494

CYP450 (PF00067)

24

Metal Binding: Heme Iron: C441

CG3466
NP_525043.1
[501 aa]

31   C449   495

CYP450 (PF00067)

18

Predicted Metal Binding: Heme Iron: C449

B.

```
                                   α1                                        α2
CG3466/1-501    ϙϙϙϙϙϙϙϙϙϙϙϙϙϙϙϙϙϙϙϙϙϙϙϙϙϙϙ                      ϙϙϙϙ.ϙ        ϙϙ
                1       10        20        30        40        50
CG3466/1-501    MLGVVGVLLLVAFATLLLWDFLWRRRGN...GILPG.PRPLPF.LGNLLMY.RGLDPEQI
2IAG/23-504     .......................RT..RRPGEPPLDL..GSIPWLGYALDFGK.....DA


                   α3         β1          β2       α4          β3   α5   η1
CG3466/1-501    ϙϙϙϙϙϙϙϙϙϙϙ.ϙ    →          →      ϙϙϙϙϙϙϙϙϙ       →   ϙϙϙϙ ϙϙϙ
                60        70        80        90        100
CG3466/1-501    MDEVKKNQRK.YGRLYRVWILHQLAVFSIDPRDIEFVLSSQQ...HITKNNLY.KLL.NC
2IAG/23-504     ASELTRMK.EKHGDIFTIIVGGRYVTVLLDPHSYDAVV.WEPRTRLDFHA.YAIF.LMER


                                       α6                           α7
CG3466/1-501                    ϙϙϙ.ϙϙϙϙϙϙϙϙϙϙ ϙϙϙϙϙϙϙϙϙϙϙϙϙϙϙϙϙ ϙϙϙϙ..ϙ....ϙ
                110       120       130       140       150
CG3466/1-501    ..WLGD..GLLMSTGRK.WHGRRKILTPTFHFKILEQFVEIFDQQSA.VMVE..Q....L
2IAG/23-504     IFDVQLPH........YSPSDEKARMKILLHRELQALTEAMYTNLHAVL.LGDATEAG.


                              β4           α8
CG3466/1-501    ϙ              →     ϙϙϙϙϙϙϙϙϙϙϙϙϙϙϙϙϙϙ            TT        ϙϙ
                160       170       180              190
CG3466/1-501    QS..RADGMIPINIFPVICLIALDIIAETAMGT............KIN..AQKNPN..LP
2IAG/23-504     .SGWH....E.MGLLDFSYSFLLRAGYLTLYGIEALPRTHESQAQD.RVHS...ADVFHT


                     α9              α10   α11                       α12
CG3466/1-501    ϙϙϙϙϙϙϙϙϙϙϙϙ.ϙϙϙϙϙ    ϙϙϙ..ϙϙ ϙϙϙϙ    ϙϙϙϙϙϙϙϙ.ϙϙϙϙ.ϙϙϙϙϙϙϙϙϙϙ
                200       210       220       230       240       250
CG3466/1-501    YVQAVNDVTN.ILIKR.FIHAW..QRVDWIFRLTQPTEAKRQDK.AIKV.MHDFTENIIR
2IAG/23-504     FRQLDRL.LPKLA..RG....SLS.........V..GDKDHM.CSVK.SRLWKLLS..PA


                                 α13          α14
CG3466/1-501    ϙϙϙϙϙ.ϙϙ        ϙϙϙϙϙϙ       ϙ.ϙϙϙϙϙϙϙϙϙϙ          ϙϙϙϙ.ϙϙϙϙϙ
                260       270       280       290       300
CG3466/1-501    ERRET.LVNNSKETTPEEEVNFLGQKRRMA.LLDVLLQSTIDGAPLSD..EDIR.EEVDT
2IAG/23-504     RLA.RR........A............HRSKWLESYLHLE..EMGVSEEM.QARA.LVL


                     α15                  α16
CG3466/1-501    ϙϙϙϙϙϙϙϙϙϙϙϙϙϙϙϙϙϙϙϙϙϙϙ ϙϙϙϙϙϙϙϙϙϙϙϙϙϙϙϙ        TT      ϙϙϙ
                310       320       330       340       350
CG3466/1-501    MFEGHDTTTSAISFCLYEISRHPEVQQRLQQEIRDVLG..........EDRKSPVILRD
2IAG/23-504     QLWATQGNMGPAAFWLLLFLLKNPEALAAVRGELESILWQAEQPVSQIT.....TLP.QK


                 α17       α18            β5     β6   T....T   β7      β8   α19
CG3466/1-501    .ϙϙϙ ϙϙϙϙϙϙϙϙϙϙϙϙϙ        →      →              →        → ϙϙϙϙ.ϙ
                360       370       380       390       400       410
CG3466/1-501    .LGELKFMENVIKESLRLHPPVPMIGRWFAEDVEI.R....GKHIPAGTNFTMGIFVL.L
2IAG/23-504     VLDSTPVLDSVLSESLRLTA.APFITREVVVDLAMPMADGREFNLRRGDRLLLFFFLSPQ


                              η2            T.T      η3                    TT       TT        ϙϙϙϙϙϙϙ
CG3466/1-501                  ϙϙϙϙ                  ϙϙϙ
                             420       430            440       450
CG3466/1-501    RDPEYFESPDEFRPBRFD....A.DVPQIH.......PYAYIPFSAGPRNCIGQKFAMLE
2IAG/23-504     RDPEIYTDPEVFKYNRFLNPDGSE.K.KDFYKDGKRLKNYNMPNGAGHNHCLCRSYAVNS
                                                                       ★


                  α20        β9          β10       β11       β12
CG3466/1-501    ϙϙϙϙϙϙϙϙϙϙϙ.ϙ   →.      →          →         →..→
                460       470       480       490       500
CG3466/1-501    MKSTVSKLLR.HFELL.PL..GPE.PRHSM.N...IV.IRSANGVHLGL..KP.....RA
2IAG/23-504     IKQFVFLVLVHLDLBLI.NADV.EIPEFDLSRYGFGLMQPEHDVPVRYRI.RPHHHH..
```

C.

```
CG3466/1-501     1 MLGVVGVLLLVAFATLLLWDFLWRRRGN---GILPG-PRPLPF-LGNLLMY-RGLDPEQIMDFVKKNQRK-YGRL  68
2IAG/23-504     23 -----------------------RT--RRPGEPPLDL-GSIPWLGYALDFGK-----DAASFLTRMK-EKHGDI  64

CG3466/1-501    69 YRVWILHQLAVFSTDPRDIEFVLSSQQ--HITKNNLY-KLL-NC--WLGD--GLLMSTGRK-WHGRRKIITPTF 133
2IAG/23-504     65 FTILVGGRYVTVLLDPHSYDAVV-WEPRTRLDFHA-YAIF-LMERIFDVQLPH--------YSPSDEKARMKLTL 128

CG3466/1-501   134 HFKILEQFVEIFDQQSA-VMVE--Q----LQS--RADGMTPINIFPVICLTALDIIAETAMGT----------- 187
2IAG/23-504    129 LHRELQALTEAMYTNLHAVL-LGDATEAG--SGWH----E-MGLLDFSYSFLLRAGYLTLYGIEALPRTHESQAQ 195

CG3466/1-501   188 KIN--AQKNPN--LPYVQAVNDVTN--ILIKR-FIHAW--QRVDWIFRLTQPTEAKRQDK-AIKV-MHDFTENIIR 252
2IAG/23-504    196 D-RVHS---ADVFHTFRQLDRL-LPKLA--RG----SLS---------V--GDKDHM-CSVK-SRLWKLLS--PA 244

CG3466/1-501   253 ERRET-LVNNSKETTPEEEVNFLGQKRRMA-LLDVLLQSTIDGAPLSD--EDIR-EEVDTFMFEGHDTTTSAISF 322
2IAG/23-504    245 RLA-RR--------A-----------HRSKWLESYLLHLE--EMGVSEEM-QARA-LVLQLWATQGNMGPAAFW 294

CG3466/1-501   323 CLYEISRHPEVQQRLQQEIRDVLG----------EDRKSPVTLRD-LGELKFMENVIKESLRLHPPVPMIGRWFA 386
2IAG/23-504    295 LLLFLLKNPEALAAVRGELESILWQAEQPVSQTT-----TLP-QKVLDSTPVLDSVLSESLRLTA-APFITREVV 362

CG3466/1-501   387 EDVEI-R-----GKHIPAGTNFTMGIFVL-LRDPEYFESPDEFRPERFD----A-DVPQIH------PYAYIPFS 443
2IAG/23-504    363 VDLAMPMADGREFNLRRGDRLLLLFPFLSPQRDPEIYTDPEVFKYNRFLNPDGSE-K-KDFYKDGKRLKNYNMPWG 435

CG3466/1-501   444 AGPRNCIGQKFAMLEMKSTVSKLLR-HFELL-PL--GPE-PRHSM-N--IV-LRSANGVHLGL--KP-----RA 501
2IAG/23-504    436 AGHNHCLGRSYAVNSIKQFVFLVLVHLDLELI-NADV-EIPEFDLSRYGFGLMQPEHDVPVRYRI-RPHHHH-- 504
```
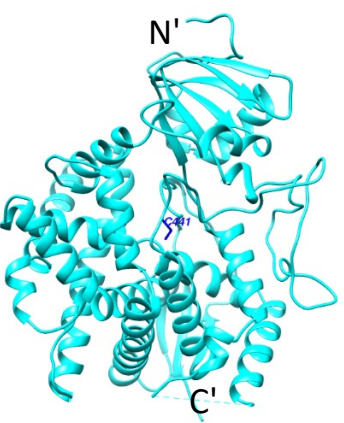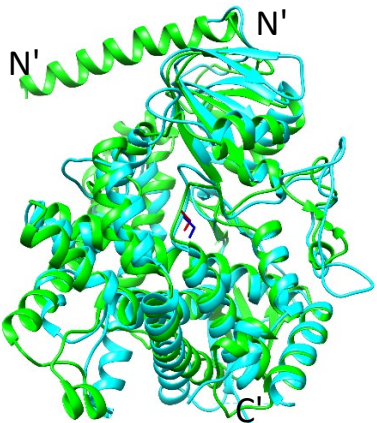
D.

Z-Score: **-8.59**

Model Quality — Max — Min
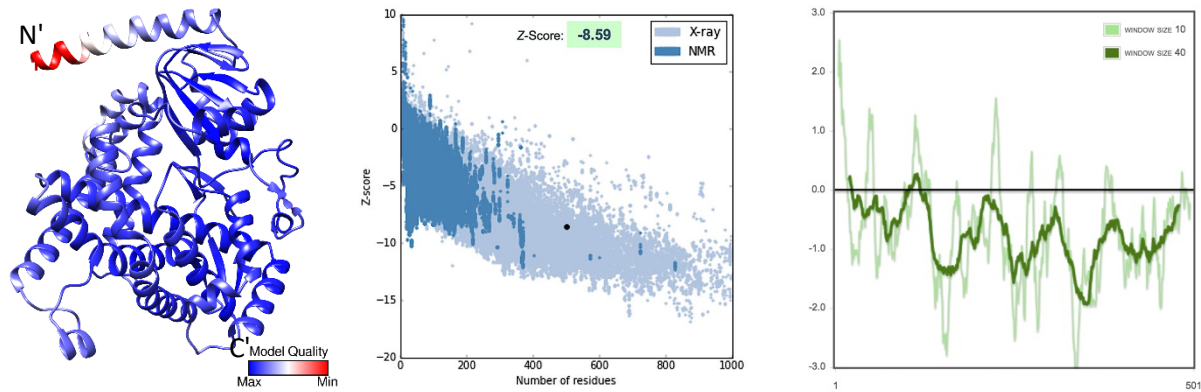
E.

PTGIS Structure	*D. melanogaster* Model	Superimposed

F.	Length (AA)	Domain Architecture (Pfam, range)	Functional Residues (aligned matches in *D. melanogaster*)	Sequence ID%	Structural Overlap (RMSD)
Prostacyclin synthase (PTGIS, NP_000952.1, PDB: 2IAG)	500	Cytochrome p450 family (PF00067) 30-494	C441	14% ID 30% SIM	1.213 Å
Cytochrome p450-4d2 (CG3466, NP_525043.1)	501	Cytochrome p450 family (PF00067) 31-495	C449		

S16 Fig. Sequence and structural details of the modeled fly PTGIS candidate. A. Domain architecture of PTG1S and CG3466 and known/predicted functional residues B. Pairwise alignment of CG34666 and 2IAG generated from structural superposition showing shared secondary structure elements and known/predicted functional residues (marked with a red asterisk) C. Pairwise alignment of CG3466 and 2IAG generated from structural superposition with conserved residues highlighted using the physiochemical color scheme (CLUSTALX) D. Validation of the CG3466 model: ProQ2 quality score mapped to a 3D model of CG3466 (left); ProSA global quality score ranking (middle) and per-residue quality graph (right) E. PTG1S (2IAG, cyan-blue) superimposed on the predicted structure of CG3466 (green-red) with potential matches for conserved functional residues highlighted F. Summary of features shared by PTG1S and potential *D. melanogaster* ortholog CG3466.