

Legends for supplemental figures

Figure S1. A portion of the unbiased electron density of the Fo map. This map was calculated from the phases of PHENIX modification without structural model information and contoured at 1 sigma. The sticks represent the structure after refinement.

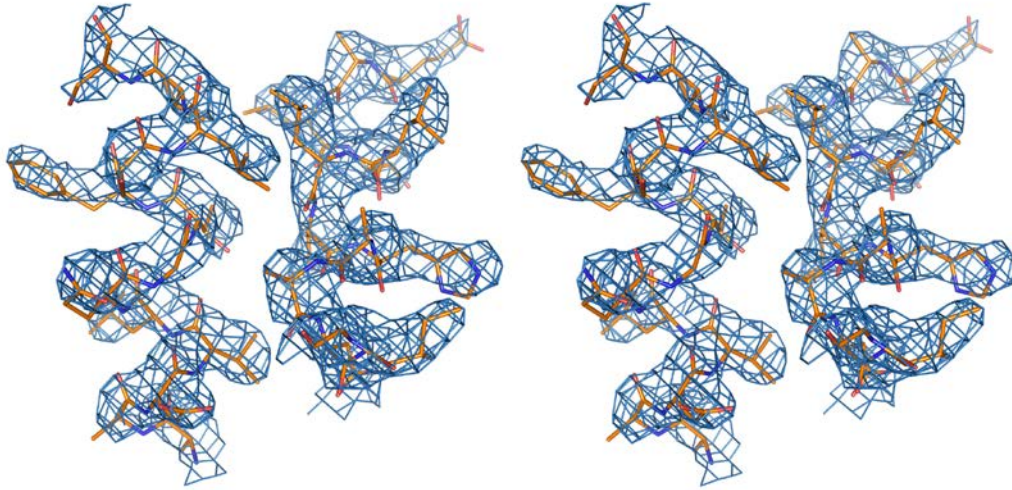


Figure S2. Multiple alignment of kinetoplastid PDECs and human PDE4D2 using the MAFFT algorithm. Grey boxes, α -helices H1 - H16 (human PDE4D2 numbering); red, the metal binding residues (His372, His409, Asp410, and Asp521 of TcrPDEC1); green, residues in inactive PDECs; open and closed circles, residues in the parasite pocket of TcrPDEC1; closed residues, gatekeepers Gly559 and Ser569.

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TcrPDEC1 289 QDTILAVVPPKSCAA-----IGTVDLRLDWGFDLTFEVAASRVPSV--LQSVAMHVALAWD 340
TviPDEC  258 KSTVLTVVSPVKFPT-----FFKGAKLDDWGFDTLEMSMCVPSV--LQVVAVEVANRWS 309
LmjPDEC  531 EELQYPCVADLDVRA-----IEPVGLELWEFDTVAAEQRGGEADVLLRVGHQIALDLH 582
LinPDEC  528 EELQYPSVADVDVRA-----IEPVGLELWEFDTVAAEQRGGEADVLLRVGHQIALDLH 581
LbrPDEC  528 EELQYVSVSNVNVGT-----IAPVPGLEKWEFDTVAAEQRGGEADVLMRIGHQIALNLN 581
HsPDE4D2 72  SSLTNSIIPRFVGRVTEQEDVLAKLEEDVNKWLGLVFPRIAE LSGNRP-LFVIMHTIFQERD 130
TbrPDEC  286 HATILTVVPTKLQVA-----LCEGIDFSDWGFDTLEVASLVPSA--LQTVAAEVVTRWK 337
TcoPDEC  339 QPIILSVVPPK-DVS-----LREGINLSSWAFDTMEVASLVPSA--LQSIALAIVKRW 389
TevPDEC  287 HATILTVVPTKLQVA-----LCEGIDFSDWGFDTLEVASLVPSA--LQTVAAEVVTRWK 338
      :. :      H1  . * :... : H2.  * : : H3

TcrPDEC1 341 FFASDE-EAQKWAFLVAAVENNYRPN-PYHNAIHAADV LQGFSLVSAAKFELMEHLTPLE 398
TviPDEC  310 LFDPTLD-EMGWASMTAALENNYRPN-PYHNAVHAADV LQGFSLVSTKVLRLHLSVE 367
LmjPDEC  583 LFPDRT-SLHRWACLLATVQANYRAN-QYHNRVHAADV LQGVYAMICSCPGLLPHMTTVE 642
LinPDEC  582 LFPDRA-SLHRWACLLATVQANYRAN-QYHNRVHAADV LQGVYALICSCPGLLAHMTTVE 639
LbrPDEC  582 LFPDRA-SQHRWVCLLATVQANYRAN-PYHNRVHAADV LQGVYALICRCPGLLAHMTTVE 639
HsPDE4D2 131 LLKTKFKIPVDTLITYLMTLEDHYHADVAHYHNVIHAADV VQSTHVLLS-TPALEAVFTDLE 189
TbrPDEC  338 MFASSEE-EMQRWCHMVAAIENNYRPN-PFHNAVRAADV VQAVFSLASATKPLMRHVTLVE 395
TcoPDEC  390 LFSSTTE-ELQKWSHMVAALENNYRAN-PFHNALRAADV LQAVFSLVSTHKPLMKYVTLLE 447
TevPDEC  339 MFASSEE-EMQRWCHMVAAIENNYRPN-PFHNAVRAADV VQAVFSLASATKPLMRHVTLVE 396
      ::  H4  H5 :: :*:. : ** :*****... : .H6  *  .. :*

TcrPDEC1 399 CKAFAAALHDVCHPGRINAFLAAVODPVSFVSGKCTLEQLHTATAFELINVTEFDFT 458
TviPDEC  368 LKAIFAAAAHDVRRHGRSNGFLTAVNDPLCFQFPGCGTLEQMHAHALQLLEVPLNFA 427
LmjPDEC  643 KRAVFAAAVHDIRHPGRSEVFLKNTFDATYVHYNGLVLEQMHTATAFHLLATPELDFT 702
LinPDEC  640 KRAVFAAAVHDIRHPGRSEIFLKHTFDATYMHYNGLVLEQMHTATAFHLLATPELDFT 699
LbrPDEC  640 KRAVFAAAVHDIRHPGRSEMFLRNTFDAMYRYNASQVLEQMHTATAFHLLATPELDFT 699
HsPDE4D2 190 ILAAIFASALHDVDPGVSNQFLINNSSELALMYNDSVLENHHLAVGFRLLQEENCDIF 249
TbrPDEC  396 LKALVFAAVLDRHHPGRTNEFLVRTCDPLCYRYPGPGTLEQMHVATAFQLVEVPELNFT 455
TcoPDEC  448 LKALVFATVLDVRRHPGYTNDFLVRTCDPLCHRHPGPGTLEQMHVDTAFHLLVEPELNFT 506
TevPDEC  397 LKALVFAAVLDRHHPGRTNEFLVRTCDPLCYRYPGPGTLEQMHVATAFQLVEVPELNFT 456
      *  ** :H7 * : ** :. : * H8  .H9 .** : *  ...* :H10  ::

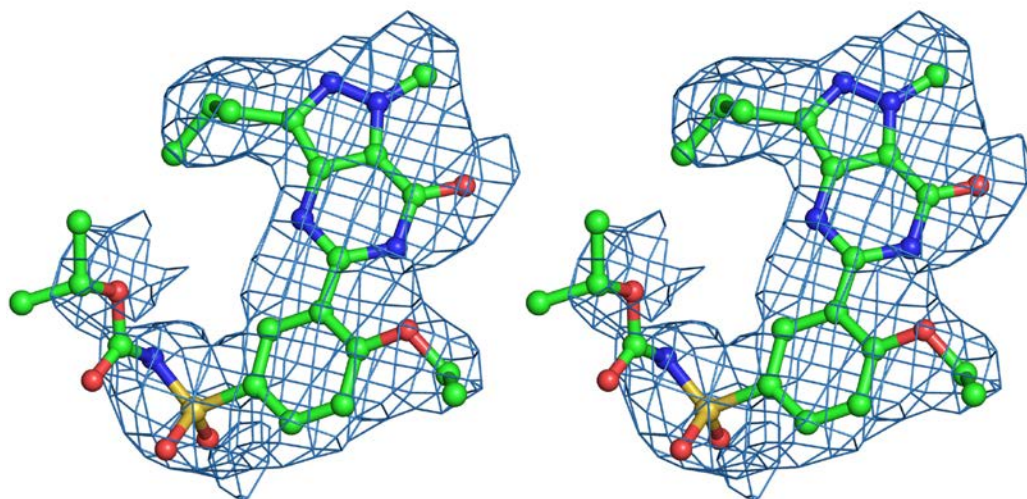
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TviPDEC  428 -GLMNDATYLSFRNSVVRLIMCTDMGMHSRRLEHWRMKIR-----NG-GFDFTKAEDRI 479
LmjPDEC  703 RGMMDTEALEPHGLVAALIGCTFMGRHASLMEQWSRPLQ-----DGKTYDMAVATDRQ 756
LinPDEC  700 RGSMDTEALEPHGLVAALIGCTFMGRHASLMEQWSRPLQ-----DGKTYDVTVTADRQ 753
LbrPDEC  700 HGDMSDEALEPHGLVAALIGCTFMGRHASLMEQWSRPLQ-----EGKTYDVTVADRQ 753
HsPDE4D2 250 -QNLKQRQSLRKMVIDIVLADMSKINLLADLKTMTVEPKKVTSSG-VLLLDNYSDRI 307
TbrPDEC  456 -CRMNDESFLRFKTI VSKLICRTDAVLEHLEHWRKAKAR-----EG-GFDYGPADDRV 507
TcoPDEC  507 -YRMSEASLKFKAIVTHLINRTDYAAHSEHLEHWSAKAR-----DG-GFDYGSMDDRV 559
TevPDEC  457 -CRMNDESFLRFKTI VSKLICRTDAVLEHLEHWRKAKAR-----EG-GFDYGPADDRV 508
      :. :      : * H11 *  . :.  H12  *  **

TcrPDEC1 511 EALSLLHAADIGASSRGAIAKRWL-VLQEFADQAEDERRGLPVTGPFET-PSSVEK 568
TviPDEC  480 DALSLILVAADLGACTRGVAIAKRWL-VVLDMAEQAEEEKRELVPVTPGFAR-QECLEG 537
LmjPDEC  757 QVLSLFLHAADIGAQARGLTVARKWL-GIVEEMRAQGDEEAARGLPLSPGSSR-SASLER 814
LinPDEC  754 QVLSLLLHAADIGAQARGLAVALKWL-GVVEEMRAQGDEEAARGLPLSPGSSR-SASLER 811
LbrPDEC  754 QALSFLHAADIGAQARGLAVAPKWL-GIVEEMRAQGDEEAARGLPPSPGSSR-SASLER 811
HsPDE4D2 308 QVLQNVHCADLSNPTKPLQYRQWTRIMEEFFRQGDRE RERGMEISPMCKKHNASVEK 367
TbrPDEC  508 DALSLLLAADFGVISRGADIAAKWL-VLTEEHAQAQEERRRGLPVTGPFDL-PTSVGR 565
TcoPDEC  560 DALSLLLVAADFSANTRGPEIAKKWL-VVIEEHAQAQEERRRGLSVTPGFEL-PTSVGR 617
TevPDEC  509 DALSLLLAADFGVISRGADIAAKWL-VLTEEHAQAQEERRRGLPVTGPFDL-PTSVGR 616
      :.*. :. : ** :H13: : : * : : *H14* : * * : : *  .:

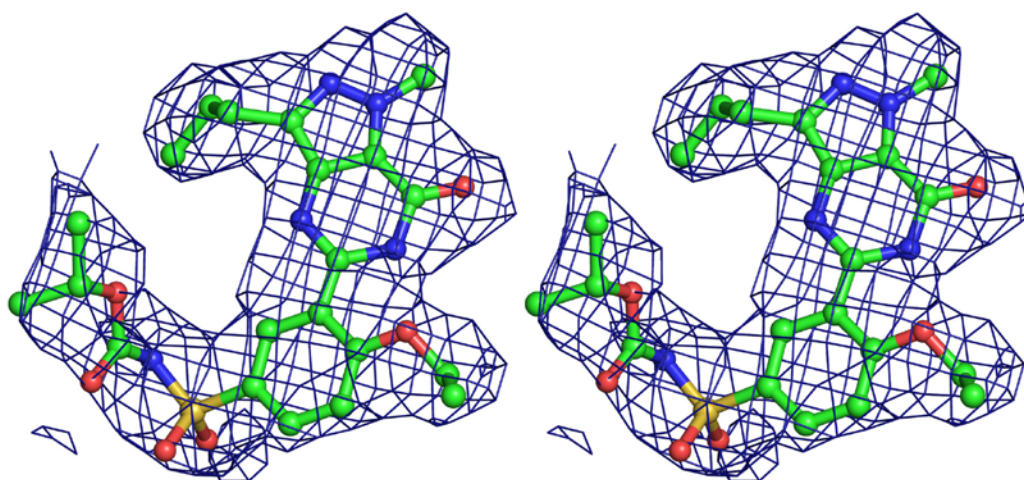
TcrPDEC1 569 SQIPFLDFFVIPTFDLLHQIF-PSIEEPLNLRKRLRELYAAK-AGVT 613
TviPDEC  538 SQIAFLDHVVIPFDVVQQLL-PGIEVPMKNLRELRLALYAEK-AGVS 582
LmjPDEC  815 QGIFFMEMFVVPLFDLVHQMF-PSIESPMRNLRTVHAHYCAA-LQET 859
LinPDEC  812 QGIFFMEMFVVPLFDLVHQMF-PSIESPMRNLRTVHAHYCAA-LQET 856
LbrPDEC  812 QGLFFMEMFVVPLFDLVHQMF-PSIESPMRNLRALHAHYCAA-LQET 856
HsPDE4D2 368 SQVGFIDYIVHPLWETWADLVHFDQADILDTLLEDNREWYQSTIPIQSP 414
TbrPDEC  566 SQIAFLDSVVIPLFNQVQQLF-PGIVEPSRNLRALRSKYAAM-ANPP 610
TcoPDEC  618 SQMVLDSVVIPLFDKVVQQLF-PGVVEPSQNLRLILRTRYAAM-AHAK 662
TevPDEC  567 SQIAFLDSVVIPLFNQVQQLF-PGIVEPSRNLRLRSKYAAM-ANPP 611
      .* :. :. : * * :H15:. : *  .*. : * H16

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Figure S3. Stereo view of the electron density for inhibitor wyq16. (A) The $(F_o - F_c)$ map that was calculated from the structure with omission of the inhibitor and contoured at 2.0 sigmas. (B) The $(2F_o - F_c)$ map that was calculated after the structure refinement and contoured at 1.0 sigma.



(A)



(B)