

..... Acidic region ..... C .....

DdisPdsA -----MALNKKLISLLLLLFIILNIVNSHQOEDCDDDEDIGISAERSERRSVKNSNDGSNFYNLNDYYTPENWNYY

DpurPdsA -----MVSNNKKKLSFLVLILFNLTFNSNNIDDCD--EDRGISAERSERRVIKNSNDGSNFYELNDYYQPENWNYYF

DmucPdsA -----

DrosPdsA -----

DdisPde7 -----MKYLILILIFFIEINNGS-----RLNSGNLFSSELKDYYIIPENLNYY

DpurPdsB MVFVHHTVTLFSIKMIIILNKFLFLILLNLIILINCHEDQDDSLR-----NLKNMGKGFNLNDYYVPEPNYY

DpurPdsC -----MLIHKKLIVALLVFFIFVNSSFAHNNDDCDEGGNPKD-----NIKKNSGKNFYDINDYYSNENYNY

DminPdsA -----MKSTLNLFKIIIIILINQISTNETADQNVNDAD-----DDYYSYGSPYI

DlacPdsA -----MKLIGIILVFILI--INNIKSEDALID-----DDISDYGSSYI

DrhiPdsA -----

PvioPdsA -----

PpalPdsA415 -----MYSNDLGKYHQRLRF-----KSKHNNFLKMKIKQQPQ

PpalPdsA802 -----MYQLTNVLRPLYIAFLIFILNITSLVKCEIPS [389 aa]

ADB2010642 -----MNYNDLGNY-----

ADB1008679 -----MKDTEGLLFLLLLLS-----

AanaPdsA-1 -----

DFA\_07709 -----MAPPKLYQN-----

ADB2010160 -----MLSTKSLIVLFIATSIIVSISADSIYD-----FEFDYDEYDGA

AanaPdsA-2 -----

DausPdsA -----

DFA\_01410 -----MYIKSLFLLAIVVFSGIVIPALGDAEGLD-----FDFFGGGPSSY

FjohPDE -----MTHFSRLLLCFILVSFNSF-----

LpnePDE -----MRRLLITILIFLLSNAG-----

NgruPDE -----MEAAAAAGAS

..... PDE-II domain .....

DdisPdsA SGSFATKDCRDASYITIPLGTTGGLDEGNLSSFFLTKKGSN-LFLALDAGTIWQVRRRLTTFKY-FNTLFNITYPSWAVL

DpurPdsA SGSFATKDCRDASYITIPLGTTGGLDEGNLSSFFLTKKGSN-LFLALDAGTIWQVRRRLTTFKY-FNTLFNITYPSAWATL

DmucPdsA -----

DrosPdsA -----

DdisPde7 SGGYSEQHCKDSSYITIPLGVTGGLDEGSLSSFFLTKKGSN-LFIFLDAGTIWQVRRRLTMLQD-FNSVFNITYEPWATL

DpurPdsB SGFSFSEKYCKDAKYITIPLGTTGGLDEGNLSSFFLTKKGSN-TFLALDAGTIWQVRRRLTMMNQ-FNNYFGIEYEPWAIL

DpurPdsC SG--SNKDCASASYITIPLGTTGGLDEGGLSSFFLTKKGSN-LFLALDAGTIWQVRRRLTTFKY-FNSLFNITYEPDAVL

DminPdsA SGSISEKDCRGASFLTIPLGTTGGLDESNLSSFFLTKKGSN-LFLALDAGTIWQVRRRLTTFKY-FNSQYLNITYPSWAIL

DlacPdsA SGFSFSEKECKSASFITIPLGTTAGGLDESNLSSFFLTKKGSN-LFLALDAGTIWQVRRRLTTFKY-FNSQYLNITYPSWAIL

DrhiPdsA -----

PvioPdsA -----

PpalPdsA415 TNWMOEACKKASFITIPLGTAAGLDESNLSSFFLTKKGSN-VFIALDAGTIWQVRRRLTTFKY-FNARFISNRN-YNNLINITFEPWATQ

PpalPdsA802 NDLAQTEACKKASFITIPLGTAAGLDESNLSSFFLTKKGSN-VFIALDAGTIWQVRRRLTTFKY-FNARFISNRN-YNNLINITFEPWATQ

ADB2010642 -----IACKRSSFITIPLGTTAGGLDESNLSSFFLTKKGSN-VFIALDAGTIWQVRRRLTTFKY-FNARFISNRN-YNNLINITFEPWATQ

ADB1008679 SIELKYVSCRDSSYITIPLGTTAGGLDESNLSSFFLTKKGSN-LFIFLDAGTIWQVRRRLTTFKY-FNARFISNRN-YNNLINITFEPWATQ

AanaPdsA-1 -----

DFA\_07709 ----YDYDCSRASFITIPLGTAAGLDESNLSSFFLTKKGSN-VFIALDAGTIWQVRRRLTTFKY-FNARFISNRN-YNNLINITFEPWATQ

ADB2010160 DSYLTHRACRGKSFITIPLGTTAGGLDESNLSSFFLTKKGSN-VFIALDAGTIWQVRRRLTTFKY-FNARFISNRN-YNNLINITFEPWATQ

AanaPdsA-2 -----

DausPdsA -----

DFA\_01410 DSYLSLRSCRNKNFITIPLGTAAGLDESNLSSFFLTKKGSN-VFIALDAGTIWQVRRRLTTFKY-FNARFISNRN-YNNLINITFEPWATQ

FjohPDE -----SQKEHKASFOVPLGKCGIDEKNLSAYLLAPSNSK-DFICLDAGTIWQVRRRLTTFKY-FNARFISNRN-YNNLINITFEPWATQ

LpnePDE -----CCAPVFEIIPLGVTGGLDEGNLSSFFLTKKGSN-NYALDAGTIWQVRRRLTTFKY-FNARFISNRN-YNNLINITFEPWATQ

NgruPDE EDEIKSTLNDKCTFGLVISCREGGLLESDFLNVLLRNTSSRGNFISLDAGTIWQVRRRLTTFKY-FNARFISNRN-YNNLINITFEPWATQ

..... HxHxD motif .....

DdisPdsA PEQRTSWFLKN-----HVMYSYFTGHSHLDHVGGLIIVSPEDYLA--KNWIDVQ-PPHNGIMGLIRK

DpurPdsA PEQRTSWFLKN-----HILGYFTGHSHLDHVGGLIIVSPEDYLA--KSWIDLQ-PPHNGIMGLIHQ

DmucPdsA -----HLDHVGGLIIVSPEDYLA--KNWIDVQ-PPHNGIMGLIKK

DrosPdsA -----VILGHSHLDHVGGLIIVSPEDYLA--KNWIDVQ-PPHNGIMGLIRK

DdisPde7 PEQRATWFIKN-----HILGYFTGHSHLDHVGGLIIVSPEDYLA--AGYLTAT-PPHNGIMGLIRK

DpurPdsB PEQRATWFIKN-----HILGYFTGHSHLDHVGGLIIVSPEDYLA--KMDLNTST--HKTGLGLIDK

DpurPdsC PEQRTSWFIKN-----HILGYFTGHSHLDHVGGLIIVSPEDYLA--AGYLTAT-PPHNGIMGLIRK

DminPdsA PEQRATWFIKN-----HILGYFTGHSHLDHVGGLIIVSPEDYLA--AGYLTAT-PPHNGIMGLIRK

DlacPdsA PEQRTSWFIKN-----HILGYFTGHSHLDHVGGLIIVSPEDYLA--AGYLTAT-PPHNGIMGLIRK

DrhiPdsA -----

PvioPdsA -----

PpalPdsA415 IDQOVAFWIRN-----HILGYFTGHSHLDHVGGLIIVSPEDYLA--PSALDMQPPHNGIMGLIRK

PpalPdsA802 IDQOVAFWIRN-----HILGYFTGHSHLDHVGGLIIVSPEDYLA--PSALDMQPPHNGIMGLIRK

ADB2010642 IDQOVAFWIRN-----HILGYFTGHSHLDHVGGLIIVSPEDYLA--PSALDMQPPHNGIMGLIRK

ADB1008679 EDQOIAWVFNK-----HILGYFTGHSHLDHVGGLIIVSPEDYLA--SGVLNIHPPHNGIMGLIRK

AanaPdsA-1 -----

DFA\_07709 VDQKVAFWIRN-----HILGYFTGHSHLDHVGGLIIVSPEDYLA--SIAFDKPPHNGIMGLIRK

ADB2010160 KDQKIAWVFNK-----HILGYFTGHSHLDHVGGLIIVSPEDYLA--KATLDYQPPHNGIMGLIRK

AanaPdsA-2 -----

DausPdsA -----

DFA\_01410 TDQKAAWFLRN-----HILGYFTGHSHLDHVGGLIIVSPEDYLA--YTHLNYG--HKTGLGLIDK

FjohPDE KVS-TSEVLKK-----HILGYFTGHSHLDHVGGLIIVSPEDYLA--YTHLNYG--HKTGLGLIDK

LpnePDE PSKKVDDLLQK-----HHPAYLISHAHLHDHVMGLVMAQPELREKQ-----  
NgruPDE LSSVDMSSLKTTSEKNQYYLSLSGYIMKQFTLGYFTGHAHLHDHLSGLVVISSEPGTFMD-----

.....  
DdisPdsA LG--FKPTDFTSSS--ILQKKTIIVGLPSTINSTLNLENNOVWPNLPSFGRYQYFSLASGIE--YPFTELVPYNATMTSLVA  
DpurPdsA LG--FKPSDFTTG--ILQKKTIIVGLPSTINSTLNLENNOVWPNLPSFGRYQYFSLAAGID--YPFTELIPYNETIMAPVK  
DmucPdsA LG--FKPSDFSTG--ILQKKTIIVGLPSTINSTLNLENNOVWPNLPSFGRYQYFSLAAGIE--YPFTELVPYNATIMSASVS  
DrosPdsA LG--FKPTDFASSSSILQKKTIIVGLSSTINSTLNLENNOVWPNLPSFGRYQYFSLASGIE--YPFTELVPYNATIMAQVA  
DdisPde7 MG--YVSDFPNITSIIDQKKPTIIGINETLYSMATDLENGFVWPSLBNYGRYSYYLGNNGQ--YSFKDLTPYANKVVTKVQ  
DpurPdsB MQ--LEKKNYVFPNSVLQMKTIIVGLTNTIQSITKDDLENGKVVPTLPLFGFEDYVVEPRRE--YAFSSLSAYNTSILAPVI  
DpurPdsC MG--LNTNHNFTANLLTSKPTIIGLPTNKYIQEDLENFWFIPNLPLQLSRYSYVTVASGIENNVAESLIQFNASLTGAVA  
DminPdsA LR----ITDAPTQSAILQKKTIIVGLSSTILMATQNNLENNOVWPNLPGYGRYDYNNLSPYKE--YFLSDLIPLNDTQKEIIK  
DlacPdsA LR----ITDAPTQSAILQKKTIIVGLQSTLIAIQNHLENLWPNLPGYGRYDYNNLQADRE--YFLSDLIPLNESQKEIIK  
DrhiPdsA -----  
PvioPdsA -----  
PpalPdsA415 ILDPTISIGG--SPNVLKKKATVGLPFTVNAIKTHLENNIWPNLPGYGRYDYVYTLTDIAQN--YDLSQLVFLNETQKQALN  
PpalPdsA802 ILDPTISIGG--SPNVLKKKATVGLPFTVNAIKTHLENNIWPNLPGYGRYDYVYTLTDIAQN--YDLSQLVFLNETQKQALN  
ADB2010642 LLNPILGT-----SILTKKATVGLPFTINSTIQNHLENLWPNLPGFGRYDYFTMIEGRG--YNLTDVIFLNDTQRQSLV  
ADB1008679 IIDPILLD----SKQILSKKTIIVGLPNTIQAKDNLENLWPNLPGFGRYDYVYTMKEGHS--YDLMELVFLNNSDRENLG  
AanaPdsA-1 -----  
DFA\_07709 LLSPAQQQSNPSPPTIILQKKSIIIGLPTINAIQTHLENNIWPNLPSFGRYDYVYTLTDNTVK--YNLIDLVTVNETQKSSMK  
ADB2010160 QFPNVTAAP-----VMLKKKVLVGLPQTVNAVKNLENNIWPNLPMFGRYDYVYVMTSNVS--AKLSDVALLNTATANIAG  
AanaPdsA-2 -----  
DausPdsA -----  
DFA\_01410 YLAPNTTAG----VLRKRPILG--LNSITLQAIQTHLENNIWPDLALYGRYSYVNLTNAST--QNFAAASGWN--VNANIAG  
FjohPDE -----TVYATEKCMEMMENHYENDQIWANFQDQKPG-----FPLKKYHFQTLNLSEET  
LpnePDE -----TIMAREETMQALQDNIFNWSVWGNFGDSCAI-----PHLNFQHYQTLPLQLWL  
NgruPDE -----TSTKDYQIPSSKRITITSTEVIASINSSLENDKVPDIPKYTPWYQYQPIEHNINYYVNDLIYMSPNSEFNPKI

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DdisPdsA NEFPFVVKVPFELCHDNLISTSFLFT----DSISGEQIAFFSDTCVPS--VACDWEKGIYAVWVKQIKIDKIKAIY  
DpurPdsA SQEPFSLNVRPFELCHDNLISTAFLFT----DSITQEQFAFFSDTCVPS--TACDWEKGIYVWRNRIHIEKIKAIY  
DmucPdsA NEFPFSLKVKPFELCHDNLISTSFLFT----DSVTGEQIAFFSDTCVPS--VACDWEKGNYSVWVKQIKIEKIKAIY  
DrosPdsA NDYFSLKVKPFELCHDNLISTAFLFT----DSVTGEQIAFFSDTCVPS--VQCDWEKGIYSVWVKQIKIDKIKAIY  
DdisPde7 NDEFPNHLVKSFEICHDSLTSAFLFT----DSQSEQIVFFSDTCIST--TKCDWEKILQVWRNRIKIDKIKAVY  
DpurPdsB NEFPYNLKVPYDICHDTLISAFVFT----DSLTDGQIVFFSDTCVPSPSNFQATCDWENKIFDVRRTIKIDKIKAVY  
DpurPdsC NDEFPFHKFKTFDVCCHDTLISAFVFT----DKISGEQVAFSSDTCVPSSTG--LTCDEWAKIINVEKSIITLGLKIKAIY  
DminPdsA NDEPHNIKIKSYELCHDSVMSAFLFT----DTSTNQOMVFFSDTCVPSSTYS--PCDWKQKIYNLWSEVNIHNSLEBAIF  
DlacPdsA NDEPHNIKIKSYELCHDSIMSFAFLFQ----DTQTNQOIVFFSDTCVPSNTF--GCDWKQKIYNVWRDVMNHTTQQAIF  
DrhiPdsA -----SSNSF--PCDWKQKIYNVWRDVMNHTTQAIF  
PvioPdsA -----SDEKND--LCGWRDKIHNVWRNRIKIDKIKAVY  
PpalPdsA415 GFEPPTMEMMPFETCHNDILSTSFLFT----DKTITGEQIIFSSDTCVPSGNYN--CDWQQRILYNVWRKVKIDKIKAIY  
PpalPdsA802 GFEPPTMEMMPFETCHNDILSTSFLFT----DKTITGEQIIFSSDTCVPSGNYN--CDWQQRILYNVWRKVKIDKIKAIY  
ADB2010642 NTFPNAQLTAYSTCHNDIQSTAFIYN----DQITAEQVFFSDTCVPSGNYN--CDYQOKIYNVWRKVRIDKIKAIY  
ADB1008679 KNEFPNNVEIKPEPTCHNDMMSFAFLT----DKITGDQIVFFSDTCVPSNVIGITCDYLKIRIILWQSIHINKIKAIY  
AanaPdsA-1 -----SGNYN--CDYQOKIYAVWRNVRIDKIRGII  
DFA\_07709 GQEPNNIQITPFELCHNDIMSFAFLFQ----DMTITNEQIVFFSDTCVPSGNYN--CDWKEKINVWRNRIKIDKIKAVY  
ADB2010160 TTFEN--MTLTPYEVCHNDIISTAYLFT----DDVTGEQIVFFSDTCVPSGNYP--CNWQERLWAVWRNINISKLRKAIY  
AanaPdsA-2 -----STYFA--CNWQERLWAVWRNIRLDRKIRAVY  
DausPdsA -----SGNYP--CDWKQRILHNVWSQIKIDKIKAVY  
DFA\_01410 TIFAN--MDVSTFETCHNDIFSAFLFT----DQITITGEQVFFSDTCVPSGTYN--CDWKQRILHNVWAVQVKIDKIRAVY  
FjohPDE PLSNNTMSVKAFLPSLHVNPFFESTAFI----KNDN--DYALYLGDTGPDSEKNS--DKLKTLTWAVVAPVRSORLKGIF  
LpnePDE AIPDPTDLHVKVPFLSG--MASSAFLI----RYKT--EYALYFGDTGADRLEKS--TNMNIWKEIAPLIRNKQIHAIM  
NgruPDE DTHQLIGSNYLESDTIVKSFSLCHSLPSAAFLFEHDNVQLIFFSDTGSNTYSS--CDWRSKLTAVWNAVDLISKIRVII

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DdisPdsA IETSFPNTPDSAMFGLHRPRDVMKLDQLLVQSIQTSPPMNLKHKVLIIEHIKQVQVSEDVNG--WTTQRVIVYQQLKE  
DpurPdsA IEVSFPDATPDSAMFGLHRPRDVMKLDQLLVQSRQINPEPTNLKHKVLIIEHIKQVQVSDPENG--WTTQRVIVYQQLKD  
DmucPdsA IETSFPNITPDSAMFGLHRPRDVMKLDQLLVQSIQTSPPMNLKHKVLIIEHIKQVQVSEDVNG--WTTQRVIVYQQLKE  
DrosPdsA IETSFPNTPDSAMFGLHRPRDVMKLDQLLVQSIQTSPPMNLKHKVLIIEHIKQVQVSEDVNG--WTTQRVIVYQQLKE  
DdisPde7 IESSFLDDAADVVMFGLHRPRDVMKLDQLLVQSIQTSPPMNLKHKVLIIEHIKQVQVGMNQY--LTSQRVIVYQQLQE  
DpurPdsB IESSFLDDAADVVMFGLHRPRDVMKLDQLLVQSIQTSPPMNLKHKVLIIEHIKQVQVSKSDYG--LTAQRVIVYQQLMK  
DpurPdsC IECSEFLNEAADSTLFGHLRPKDVMMKLDYLLTQSVNSG--YTNLKHVKLIIEHIKQVQVQATNN--WTAQKAVYBOLKA  
DminPdsA IECSEFPNSTPDNMLFGHLRPKDVMMKLDYLLTQSVNSG--YTNLKHVKLIIEHIKQVQVQATNN--WTAQKAVYBOLKA  
DlacPdsA IECSEFPNSTPDNMLFGHLRPKDVMMKLDYLLTQSVNSG--YTNLKHVKLIIEHIKQVQVQATNN--WTAQKAVYBOLKA  
DrhiPdsA IECSEFPNATPDQLLYGHLRPKDVMMKLDYLLTQSVNSG--YTNLKHVKLIIEHIKQVQVQATNN--WTAQKAVYBOLKA  
PvioPdsA IECSEFPNDTPDNMLFGHLRPKDVMMKLDYLLTQSVNSG--YTNLKHVKLIIEHIKQVQVQATNN--WTAQKAVYBOLKA  
PpalPdsA415 IECSEFPNATDASLFGHLRPKDVMMKLDYLLTQSVNSG--YTNLKHVKLIIEHIKQVQVQATNN--WTAQKAVYBOLKA  
PpalPdsA802 IECSEFPNATDASLFGHLRPKDVMMKLDYLLTQSVNSG--YTNLKHVKLIIEHIKQVQVQATNN--WTAQKAVYBOLKA  
ADB2010642 IECSEFPNATDASLFGHLRPKDVMMKLDYLLTQSVNSG--YTNLKHVKLIIEHIKQVQVQATNN--WTAQKAVYBOLKA  
ADB1008679 IECSEFPNATDASLFGHLRPKDVMMKLDYLLTQSVNSG--YTNLKHVKLIIEHIKQVQVQATNN--WTAQKAVYBOLKA  
AanaPdsA-1 IETSFPNTPDSAMFGLHRPRDVMKLDYLLTQSVNSG--YTNLKHVKLIIEHIKQVQVQATNN--WTAQKAVYBOLKA  
DFA\_07709 IESSFLDDAADVVMFGLHRPRDVMKLDYLLTQSVNSG--YTNLKHVKLIIEHIKQVQVQATNN--WTAQKAVYBOLKA  
ADB2010160 IESSFLDDAADVVMFGLHRPRDVMKLDYLLTQSVNSG--YTNLKHVKLIIEHIKQVQVQATNN--WTAQKAVYBOLKA  
AanaPdsA-2 IETSFPNTPDSAMFGLHRPRDVMKLDYLLTQSVNSG--YTNLKHVKLIIEHIKQVQVQATNN--WTAQKAVYBOLKA

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DausPdsA      LEVSEFPNSTPDASMFGRPKELIDLLDDLVDSLVSQTTPHTENLSHVKLIHQHIKPYANAATFT---IPVSKVIENELKQ
DFA_01410    LEVSEFPNSTPDASMFGRPKDVLAALDDLVDSLVSQTTPFTESLSHVKLIHQHIKPYANAATFT---IPVSKVIENELKA
FjohPDE      LEVSEFPNEQPKFLFGHLTPNHLMTETLVLEELAG----KGSINNEKIIITHLKPPAKSIKIK--EQ-----LKN
LpnePDE      LECSEFLNSQPPDKLFGHLKPNLFMSELRHLASIVDPFDS-RNSLRGLPVVVTHIKPKLADFSNTN--EDTEKQVINELSQ
NgruPDE      LEVSEFTNEAQDSELYGHRPKDLVLLIKELSNLKGD-----KLSLTIIVVTHIKPTFTSTFSESAQVLIQQLQSGLKE

.....
DdisPdsA      AN--NNGVRIIIEPNOGDPICI
DpurPdsA      SN--TNGIRVIEPNOGDPICI
DmucPdsA      AN--TNGIRVIEPNOGDPICI
DrosPdsA      AN--TNGIRVIEPNOGDPICI
DdisPde7      IN--NHGVKVIIEPNOGVPICL
DpurPdsB      AN--TNSIKIIIIEPNOGDPICI
DpurPdsC      LN--THNVKIIIIEPNOGDPICI
DminPdsA      DN--NLGLNIIIEPQGEPICI
DlacPdsA      SN--TLGLNIIIEPQGEPICI
DrhiPdsA      DN--NLGLNII-----
PvioPdsA      AN--RVGINVI-----
PpalPdsA415  NN--PTGINVVIEPQOGEIICI
PpalPdsA802  NN--PTGINVVIEPQOGEIICI
ADB2010642   YN--PVGIQVNIIEPQGEPICI
ADB1008679   SNKFLGIQIIEPQGEPICL
AanaPdsA-1   LN--TVGLKVI-----
DFA_07709    NN--PFNINVIIIEPQGEPICI
ADB2010160   DN--NMHVKVVIEPKQGVPICF
AanaPdsA-2   NN--TVGLQVV-----
DausPdsA      AN--NHNIQIV-----
DFA_01410    GN--THNIQVVIEPQGVPICF
FjohPDE      QN--NLGLKIIIEPQGGKIEL
LpnePDE      EN--DIGVELIKPEQGITLSL
NgruPDE      AS--LDCAVTIEPQOQLCF

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**Figure S1. Alignment of Dictyostelid and outgroup PDE-II sequences**