

Additional file 7

Alignment of vertebrate p47phox, NOXO1, p67phox, NOXA1, and p22phox proteins to estimate substitution rates

To describe species of the genes, we used the following naming: human (*H. sapiens*), dog (*C. familiaris*), rat (*R. norvegicus*), mouse (*M. musculus*), chicken (*G. gallus*), frog (*X. tropicalis*), zebrafish (*D. rerio*), fugu (*T. rubripes*), and tetraodon (*T. nigroviridis*).

Amino acid sequences of p67phox, NOXA1 and p22phox listed in Additional file 6 were aligned. Several sequences of NOXO1 proteins contained partial sequences: the minimum length was 281 amino acids for frog NOXO1 (see Additional file 6). To accurately compare substitution rates, we prepared the trimmed NOXO1 and p47phox sequences corresponding to the region of the minimum length of the NOXO1 (e.g., residues 30-273 in human NOXO1 or residues 32-267 in human p47phox) for alignment.

Alignments of p47phox, NOXO1, p67phox, NOXA1 and p22phox were used to estimate R1 and R2 in Additional file 3.

p47phox (vertebrates)

human-p47phox	WQDLSEKVVYRRFTEIYEFHKTLKEMFPIEAGAINPENRIIPHLPAKWFWDGQRAAENHQ	122
dog-p47phox	WHDLSEKVVYRRFTEIYEFHKMLKEMFPIEAGDINPENRIIPHLPAKWFWDGQRAAESRQ	122
mouse-p47phox	WQDLSEKVVYRKFTTEIYEFHKMLKEMFPIEAGEIHTENRVIIPHLPAKWFWDGQRAAESRQ	122
rat-p47phox	WQDLSEKVVYRKFTTEIYEFHKMLKEMFPIEAGEIHTENRVIIPHLPAKWFWDGQRAAESRQ	122
chicken-p47phox	WNDLSEKLIYRRFTDIYEFHKALKEMFPIESGDINAENRIIPHLPAKWFWDGQRSTQSRQ	122
frog-p47phox	WQDLTEKLVYRKFTTEIYEFHKSLKEMFPIEAGDISKEHRTIIPHLPAKWFWDGLRSTENRQ	122
tetraodon-p47phox	WSDLTEKLIYRYPEIYTFHKALKEMFPIEAGKIEKRDRIPSLAPPWLDQSKSTETRQ	122

fugu-p47 <i>phox</i>	WSDLTEKLIYRTYPEIYTFHKSLKEMFPPIEAGKIEKRDRIPSPSAPPWLDQSKSTETRQ	122
zebrafish-p47 <i>phox</i>	WSDQSEKLVYRRYPEVHTLHKTLKEMFPPIEAGDIDEKDRIPITLPAPKWLNDQKTTETRQ	122
	* * * * *	
human-p47 <i>phox</i>	GTLTEYCGTLMSLPTKISRCPHLLDFFKVRPDDLKLPD-NQTKKPETYLMPKD-GKST-	179
dog-p47 <i>phox</i>	GTLTEYNTLMGLPVKISRCPQLLDFFFRVRPDDLKLPD-SQVKKPETYLVPKD-GKSS-	179
mouse-p47 <i>phox</i>	GTLTEYFNGLMGLPVKISRCPHLLDFFKVRPDDLKLPD-SQAKKPETYLVPKD-GKNN-	179
rat-p47 <i>phox</i>	GTLTEYFNSLMGLPMKISRCPHLLNFFKVRPDDLKLPD-SQVKKPETYLTAKD-GKNN-	179
chicken-p47 <i>phox</i>	GTLAEYCYTLVNLPHKISRCRHVVSFFEVPRDDMNPVTD-SQIRKPEVFLPKD-AKKN-	179
frog-p47 <i>phox</i>	VTLSDYFSSLLSLPPKISRCPHVLFNFQVRSDDVNPVANNNGRKPETFLKLVDTAKKN-	181
tetraodon-p47 <i>phox</i>	TLSLDYQCALVNLPPHISRCTHLTSLFKVRPEDENPAAP-NLKRNETFVVSRLARGN-	180
fugu-p47 <i>phox</i>	TLSLDYCHSLVNLPPHISRCTHLTGFFTVRPEDENPPSP-NILKRNETFVVSRLARGN-	180
zebrafish-p47 <i>phox</i>	ATLAEYCRSLLNLPANISRCQLIRDFFKMRPEDETPPAP-HPYKRNETFIMSTNRVRSNT	181
	* * * * *	
human-p47 <i>phox</i>	ATDITGPIILQTYRAIANYEKTSGSEMALSTGDVVVEKSESQWFCQMKAKRGWIPAS	239
dog-p47 <i>phox</i>	VTDITGPIILQTYRAIADFEKTSSSQMALATGDDVDDVVEKSESQWFCQTKTKRGWVPAS	239
mouse-p47 <i>phox</i>	VADITGPIILQTYRAIADYEKSSGTEMTVATGDDVDDVVEKSESQWFCQMKTKRGWVPAS	239
rat-p47 <i>phox</i>	VADITGPIILQTYRAIADYEKSSGTEMTVATGDDVDDVVEKSESQWFCQMKTKRGWVPAS	239
chicken-p47 <i>phox</i>	TSDITGPIIVLQTYRAIADYEKSSKSEMAVKAGDAVDVVEKSETGWWFCQLKTKRGWVPA	239
frog-p47 <i>phox</i>	VSDITGPIILQSYRVIADYEKSSKSELAAKNGDVVEIVEKSENGWWFCQLRNKRGWMPAA	241
tetraodon-p47 <i>phox</i>	ASEISGPIILDMYRAIADYTKTKTYEINLLAGDQVEIVEKNQNGWWFCQMDSKRGWVPAS	240
fugu-p47 <i>phox</i>	VSEISGPIILDMYRAIADYTKTKTYEINLHAGDQVEIVEKNQNGWWFCQCDKSKRGWVPAS	240
zebrafish-p47 <i>phox</i>	TSEITGPIILETYRVIADYSSKSYELTLKMGDMVDIVEKSPNGWWFCQCESRRGWVPAS	241
	* * * * *	
human-p47 <i>phox</i>	FLEPLDSPDETEDPEPNYAG---EPYVAIKAYTAVEGDEVSLLEGEAVEVIHKLLDGWWV	296
dog-p47 <i>phox</i>	YLEPLDSPDEAEDPEPNYEG---EPYVTIKAYTAEMEDEMSELQEGEAIEVIHKLLDGWWV	296
mouse-p47 <i>phox</i>	YLEPLDSPDEAEDPDPNYAG---EPYVTIKAYAAVEEDEMSELSEGEAIEVIHKLLDGWWV	296
rat-p47 <i>phox</i>	YLEPLDSPDEAEDPDPNYAG---EPYVTIKAYAAVEEDEVSLSEGEAIEVIHKLLDGWWV	296
chicken-p47 <i>phox</i>	YLEPMDGPDESEEQEPNYAG---ELYVVQKSYTAVEEDELTLKEGDTIEVIHKLLDGWWV	296
frog-p47 <i>phox</i>	YLEPLDGPDESEEQDPNYEG---DLHITTKDYSGELDDELSELQEGENVEVIHKLLDGWWV	298
tetraodon-p47 <i>phox</i>	YLEPLDGPDESEEAADPDYEGS---ELFITIKAYKAEQEDEISLDLGESEIEVIHKLLDGWWV	298
fugu-p47 <i>phox</i>	YLEPLDGPDESEEAADPDYEGS---ELFITIKAYKAEQEDEITLDELGESEIEVIHKLLDGWWV	300
zebrafish-p47 <i>phox</i>	YLEPLDGADESEEPPEPNYAG---ELYKTRGRYKAVEQDEMTLEAGVIEVIHKLLDGWWV	298
	* * * * *	
human-p47 <i>phox</i>	IR	298
dog-p47 <i>phox</i>	VR	298
mouse-p47 <i>phox</i>	VR	298
rat-p47 <i>phox</i>	VR	298
chicken-p47 <i>phox</i>	IR	298
frog-p47 <i>phox</i>	VR	300
tetraodon-p47 <i>phox</i>	VR	300
fugu-p47 <i>phox</i>	VR	302
zebrafish-p47 <i>phox</i>	VR	300
	*	

NOXO1 (vertebrates)

zebrafish-NOXO1	WSDGNEITVYRSLEDFFKMKHRQLKKKFPF-SNPFKRSARIVPEFK-----GNKWSG-	112
tetraodon-NOXO1	WSDHNEIVVYRTFQDFRKMHK-----LKRS-----GKKKSP-	135
chicken-NOXO1	WSDQNNILYRTLLEEFKRFHKELKRKFPPIESGLRRSDRTIPRFKD----INGKQKSGK	93
fugu-NOXO1	WSDHNEILYRTFEDFKLNRQLKKKFPLEAGLFRKSDNLLPKLKD----VPIFRKNRTT	56

human-p67 *phox* SVPMMP-YTLKVHYKYTVVMKTPGLPYSQVRDMVSKKLELREHTKLSYRPRDSNELVPL 405
 dog-p67 *phox* RVPMP-YTVKVHYKYTVVMEIQAGLPYSQLRDMVAKKLELLPEHTKLSYRPPDSHELEPL 407
 rat-p67 *phox* SVPMMP-YMLKVHYKYTVVMEIQLGLPYSQLRDMVSKKLELLPEHTKLSYRQRDSPELLLL 405
 chicken-p67 *phox* DIPKP-YVLKVHYKYTVAMQVKPDLSEKLLGLVCDKLELQPEHTMLRYKSAASGELVPL 407
 frog-p67 *phox* AVAVASYLVKVVYKYTVAIQISSKLPFADLLTLISSKQLLPSRMKLSFK--EDQDDVLL 401
 tetraodon-p67 *phox* QLVDDSYVVKVRFVTFVAVIPRGSYATLAQKVGEKLSVPADAVILSLSEAAEEDVIN 410
 fugu-p67 *phox* ELADDSCVVKVRYTFVAVIPRGSYATLAEKISEKLSVPANAIVLSLSEATEQNVID 403
 zebrafish-p67 *phox* REFSG-CVVKVHFQFTIAIAIAHGQPYGVILQMISSKLLKPASTLTLYAKEGSAERVII 410

:** : :*.:. : . : : : .** : . * :

human-p67 *phox* SEDSMKDAWQVKNYCLTLWCENTVGDQGFDPDEPKESEKADANNQTTEPQLKKSQVEAL 465
 dog-p67 *phox* SEDNMKAAWQVKNYCLTLWCENTVGDQGFDPDEPQSEKSEANNQTTEPTLKEGGHVVAL 467
 rat-p67 *phox* SEESMKDAWAQVKNYCLTLWCEHTVGDQGFVDEPKEKENSADNRTEPQKPEGTQVVAI 465
 chicken-p67 *phox* SAQNLEEAWSHSDQCLTVWCDCTEGE-GFLPDSKPEEPQAAAETGP-----TQVVAQ 460
 frog-p67 *phox* NEENTEKAWSLATDNCLKTKCT-----EVQVRQARSLYCSTMQGYFKAQKYPIAL 452
 tetraodon-p67 *phox* GSTDMEAVWGRASGRCLTLWCR-----LAEQTSETEPRETFLAL 451
 fugu-p67 *phox* GGTDMEGVWSRVSGRCLTLWCR-----LAQTNERVQ--KESSLAL 442
 zebrafish-p67 *phox* EDSEMEAVWNSAKDGRLLTWCS-----VTEGKSASH----AKVVAL 447

. : .* . : : *

human-p67 *phox* FSYEATQPEDLEFQEGDIILVLSKVNEDWLEGECKGKIGIFPKVVEDCATTDLESTRRE 525
 dog-p67 *phox* FTYEATQPEDLEFQQGDI IQIISMVNDWLEGECKGKIGIFPKAFVEEHATDLESSPRG 527
 rat-p67 *phox* FSYDATQPEDLEFVEGDVILVLSHVNEEDWLEGECKGKIGIFPKAFVEGCAAKNLEGTPRE 525
 chicken-p67 *phox* YSYEATQPEDLEFQAGDVILVLSKVNEDWLEGCNGKIGIFPSAFVRDGTNDKDP----- 514
 frog-p67 *phox* FEYEATQPEDLPFCKGDI IKILSHVSEDWWECEQGRMGIFPKVFTEE----- 500
 tetraodon-p67 *phox* HTYDSPNPEDLTFQQGDKILLSKVNQDWLEGCNGKIGIFPAAFVEEVSVSE----- 504
 fugu-p67 *phox* HSYDSSNPEDLSFHQDRITLLSKVNQDWLEGEFNGNTGIFPAAFVEEVVANG----- 495
 zebrafish-p67 *phox* YSYESSTPEDLEFQGNVITVLSKVNEDWLEGCNGKIGIFPSSFVEPLNGDPH----- 501

. * : . ***** * * : * : * * : * * : * : * * : * . ***** * .

human-p67 *phox* V 526
 dog-p67 *phox* V 528
 rat-p67 *phox* V 526
 chicken-p67 *phox* -
 frog-p67 *phox* -
 tetraodon-p67 *phox* -
 fugu-p67 *phox* -
 zebrafish-p67 *phox* -

NOXA1 (vertebrates)

human-NOXA1 MASLGDVLRVHLAGAQRDGRDWARALHLFSGVPAPPARLCFNAGCVHLLAGDPEAALRA 60
 dog-NOXA1 MPSLGDVLDVHWRGVQAVARGDWGCALRLFSGDPDPPAKMCFNLGCVHLLAGDPEAALRA 60
 mouse-NOXA1 MSSLGDQIRDWHRGVLAVAREDDWSDALCFSDVREPLARMYFNRCVHLMAGDPEAALRA 60
 rat-NOXA1 MSSLGDQIRDWHRGVLAVAREDDWSDALCFSDVREPLAKMYFNMGCVHLMAGDPEAALRA 60
 frog-NOXA1 -MHYKEVVRWHEGVVAEKGDYDAALRSFTAIEDPPSRIWVFNVGGIYLLRGDLPRALEA 59
 zebrafish-NOXA1 -MLYIELIRLWDEAVKAIDIRDWQGALSCLNQTIDHNCRTMFVASTHIALGQVDLAIKA 59

* * * ** * * *

human-NOXA1 FDQAVTKDTCMAVGGFFQRGVANFQLARFQEALSDFWLALQLRGHAAIDYTLGLRFLKQ 120
 dog-NOXA1 FDQAVTKDTCMAVGGFFQRGVANFQLERFQEALSDFRLALQLRGHAAIDYTLGLRFLK 120

human-NOXA1 LAPGEDGHWVPIPEEESLQRAWQDAAACPRGLQLQCRG-AGGRPVLYQVVAQHSYSAQGP 415
 dog-NOXA1 RDPSHEARWVALPGEALQGAWRDTAASPRGLQLQCRA-AGSRPVLYQAVAQHNYCAQGP 393
 mouse-NOXA1 KAPGEERSWIPISTEESLQSIWRNVVPGGGLQLQCG- VWGRPVLYQVVAQYNYRAQRP 385
 rat-NOXA1 KARGEDRAWVPISTEDSLQSVWRNVVSPRGLQLQCRG-AWGRPVLYQVVAQYDYRAQRP 387
 frog-NOXA1 RDPE-SRGLTPVTGSKDWQEVLLKSRANQVTLCKETTLCAGRPVLYRMRQAQYDYLAAQGP 536
 zebrafish-NOXA1 RRPG-TRVLTPLNGDDGLDCLGVAESGRAQIWCQNEPLANRTILYQMVALYDYNAQGP 447

* ** * * ** *

human-NOXA1 EDLGRFRQDGTVDVLCV--PDVPL-AVDQAWLEGHCDGRIGIFPKCFVVPAGPRMSGAPG 472
 dog-NOXA1 EDLDRRQGDMDVLCAGQGPVPLHVVDPAWLEGHCDGRIGIFPKCFVVPAG----- 445
 mouse-NOXA1 EDLDFHQDGTVDVLCV-----DEAWLEGHDRDGCVGIFPKCFVVPAGAYVEAML- 434
 rat-NOXA1 EDLDFRQDGTVDVLCV-----DEAWLEGHDRDGRVIGIFPKCFVVPAAATCVEALP- 436
 frog-NOXA1 ADLSFQQGDLISILSEVN-----GEWLEGHCHRIGIFPKCFQAQR-AEGI----- 580
 zebrafish-NOXA1 EDLEFSEGDTIDILSEVN-----EEWLEGHVAGNIGIFPQSFHRDTSISGAST 497

** ** * ***** ** *

human-NOXA1 RLPRSQQGDQP 483
 dog-NOXA1 -----
 mouse-NOXA1 -VLGPQPGDQN 444
 rat-NOXA1 -VPEPQPGEQH 446
 frog-NOXA1 -----
 zebrafish-NOXA1 D----- 498

p22phox (vertebrates)

mouse-p22phox MGQIEWAMWANEQALASGLILITGGIVATAGRFTQWYFGAYSIAAGVLICLLEYPRGKRK 60
 rat-p22phox MGQIEWAMWANEQALASGLILITGGIVATAGRFTQWYFGAYSIVAGVLICLLEYPRGKRK 60
 Human-p22phox MGQIEWAMWANEQALASGLILITGGIVATAGRFTQWYFGAYSIVAGVFCVCLLEYPRGKRK 60
 dog-p22phox MGQIEWAMWANEQALASGLILIMGGIVATAGFTKWYFGAYSIGAGVFCVCLLEYPRGKRK 60
 frog-p22phox MGQIEWAMWANEQALASGLILLAGGIVAVAGQFKGWQFGAYGVAAGVFITLLEYPRSKRK 60
 tetraodon-p22phox MGKIEWAMWANEQALASGFILLAGGIVGVAGFRGWEFAAYAVAAGVFCVCLLEYPRSKRS 60
 fugu-p22phox MGKIEWAMWANEQALASGFILLTGGVVGAGQFRGWQFAAYAVAAGVFCVCLLEYPRSKRS 60
 zebrafish-p22phox MAKIEWAMWANEQALAAGLIYLTGGIVGVAGQFRGWQFAAFGIAAGVFCVCLLEYPRSKRG 60

* ***** * * ** * ** * * * * ** ***** **

mouse-p22phox KGSTMERCQKYLTSVVKLFGPLTRNYVRAALHFLLSVPAFLLATILGTVCLAIASVI 120
 rat-p22phox KGSTMERCQKYLTAUVKLFGLPLTRNYVRAVLHLLLSVPAFLLATILGTVCLAIASVI 120
 Human-p22phox KGSTMERCQKYLTAUVKLFGLPLTRNYVRAVLHLLLSVPAFLLATILGTACLAIASGI 120
 dog-p22phox KGSTMERCQKYLTAUVKLVFGLPLSRNYVIRAFHLGLSVPAFLLATILGTACLAIASI 120
 frog-p22phox KGSTMERCQKYLAAVVKLFGPLTRNYVRAILHAGLAVPGGFILSTILGTVCLGII 120
 tetraodon-p22phox KGTSVERPGQCFIVCVKAFGPVTRNYVRAVLHAAICVPGGFMLATVLCVCLGII 120
 fugu-p22phox KGTSVERPGQCFIVCVKAFGPVTRNYVRAVLHAAICVPGGFMLATVLCVCLGII 120
 zebrafish-p22phox KGTSIERSGQYCFIVCVKSFGLPLTRNYVRAFLHAAICVPGGFMLATVLCVCLGII 120

** ** ** ** ** ** * ** ** * ** * * ** * ** * ** *

mouse-p22phox YLLAAIRGEQWPIIEPKKERPVGGTIKQPPTNPPRPPAEVRKKPSEEEEEASAG-- 178
 rat-p22phox YLLAAIRGEQWPIIEPKKERPVGGTIKQPPTNPPRPPAEVRKKPSEEEEEASAG-- 178
 Human-p22phox YLLAAVIRGEQWPIIEPKPRERQIGGTIKQPPSNPPRPPAEARKKPSEEEAAVAGGPP 180
 dog-p22phox YLLAAVIRGEQWPIIEPKKERPVGGTIKQPPSNPPRPPAEARKKPSEEEAAVAGVVS 180
 frog-p22phox YFLAAIRGEWRPIIEKQAEKPRAGETIKRPPENPPRPPAEVRRK----QADEVSVG-- 174
 tetraodon-p22phox YLVAAIRGEHWEPILPKKEIQKVAESIKNPPQNPPRPPAEVRRKRVDDLEAAAYDN-- 178
 fugu-p22phox YLVAAIRGEHWEPILPSKEIRKVAESIKNPPQNPPRPPADTRRRKRVDDLEAAAYDN-- 178
 zebrafish-p22phox YLSAPIHGEHWEPILH-IETKRLGESIKEPQNPPRPPPELRRKADNLDAAAYDN-- 177

* * ** * ** ** ** * ** ***** * *

mouse-p22phox -GPQVNPMPVTDEVV 192
 rat-p22phox -GPQVNPMPVTDEVV 192
 Human-p22phox GGPQVNPMPVTDEVV 195

dog-p22 <i>phox</i>	GGPQENPVPVIDEVV	195
frog-p22 <i>phox</i>	-GGHVNPIPVTDNV-	187
tetraodon-p22 <i>phox</i>	-----P-----	179
fugu-p22 <i>phox</i>	-----PISVTANE-	186
zebrafish-p22 <i>phox</i>	-----PMSVTINE-	185

*