

HsPKA/1-351

HsPKA/1-351
HsGSK3b/1-420
HsCAMK1/1-370
HsSrc/1-536
HsCK2A1/1-391
HsCDK2/1-298
TgPKAc/1-333
TgAGC/1-514
TgROP5/1-461
TgROP7/1-575
TgROP8/1-575
TgROP16/1-707
TgROP18/1-554
TgRON13/1-1375
TgRON13/1-1375

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TgROP18/1-554
TgRON13/1-1375
TgRON13/1-1375

HsPKA/1-351

```
9 ..... K . G ..... SE .....
HsGSK3b/1-420 .....
HsCAMK1/1-370 .....
HsSrc/1-536 181 . ETTKGAYCLSVSDFDNDKAGLNK . HYKIRKLDSSGGF . . . YITSRTQFNLSLQQLVAYYSKHADGLCHRLTTVCP . TSKPQ . . .
HsCK2A1/1-391 .....
HsCDK2/1-298 .....
TgPKAc/1-333 .....
TgAGC/1-514 148 ..... R . G ..... DSSLTSSRT .
TgROP5/1-461 59 ..... AQHFRRRLRGGFFRGLTPR . . . WLSG . . . . . LGRRRQRWWR . . . . . G . . . . . RQR
TgROP7/1-575 147 ..... LQHLRRRVGRFFRHHGIPA . . . . . A . . . . . AGRFFRRVWP . . . . . E . . . . . RPO
TgROP8/1-575 156 ..... LQYLRRVGTFFRRDIPA . . . . . A . . . . . ALRFFRRFR . . . . . V . . . . . RQP
TgROP16/1-707 261 ADSGASQLASSVSSVAVQTPHVKRSEIRRVRLSE . . . . . EGLE . EVQQLKAAAQQLLVAVPDPYEAMRAVLQE . . . . .
TgROP18/1-554 147 ..... VRQRLAQLWRRRAKSLFKR . . . . . GIRRYFPQGRNRQRSLRAQRR . . . . . K . D . . . . . DQALSFLGDT . . . . . SE
TgRON13/1-1375 275 ..... K . D . . . . . DQALSFLGDT . . . . .
TgRON13/1-1375
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HsPKA/1-351

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13 ..... QESV . KEF I AKAKED . . . . . FLKKWESP
HsGSK3b/1-420 28 ..... VSRDKDGSK . . . V . . . . . TTVV . . . . . ATPGQ
HsCAMK1/1-370 1 ..... M LGAVEG . . . . . PRW . . . . .
HsSrc/1-536 255 ..... TQGLAKDA . . . . . WEIP . . . . .
HsCK2A1/1-391 17 ..... THRPRE . . . . . YW . . . . . DYESH
HsCDK2/1-298 .....
TgPKAc/1-333 1 ..... M QKPLL . . . . .
TgAGC/1-514 160 ..... S . VAVECSPRATQP . . . PPNVADRE . . . SOILSQVRYD . . . . . L
TgROP5/1-461 94 PLLDPS . . . . . F HGLEAGDSFMRDLLKREKELIGYCREEALKEPAAMVEAVTATVWPQN
TgROP7/1-575 179 PVFTEGDDPDLT . . . . . NSLYRDKVPGEVILREVLGKVFAGFGPTSGHG . . VFAAYENAFSEMLWAE
TgROP8/1-575 188 VFPPDEFPEVDVT . . . . . NPIYFRGTDPGDVILLELFNRIPQANVRTTSD . . YMQSAADSLSVSTSLWNIG
TgROP16/1-707 329 ..... AVLSEQRVATRKRKRKQPAGVESAVDEVFPNE . . RVMM . . . . . INAN
TgROP18/1-554 189 LVFEKAD . . . . . SGCVIGKRILAHMQEQIG . . . QPQALENSERLDRILTVAAWPPDPV
TgRON13/1-1375 287 ..... KSASELNPPRLVCPDKPPTLPRE . EQVR . . . . . KAYA . . . . .
TgRON13/1-1375
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HsPKA/1-351

η1 β1 Subdomain I β2 Subdomain II N-lobe insertion

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35 ..... A QNTAHL DQFERIKT L G T G S F G R V M L V K H K E . . . . . T G N H Y A M K I L
47 ..... G P D R P Q E V S Y T D T K T I G N G S F C V V Y Q A K L C D . . . . . S G E L V A I K K V
11 ..... K Q A E D I R D I Y D F R D V L G T G A F S E V I L A E D K R . . . . . T Q K L V A I K C I
267 ..... . . . . . R E S L R . L E V K L G Q G C F G E V M G T W N G T . . . . . T . . . . . R V A I K T L
30 ..... . . . . . V V E W G N Q D D Y Q L V R K L G R G K Y S E V F E A I N I T . . . . . N N E K V V V K I L
1 ..... . . . . . M E N F Q K V E K I G E G T Y G V Y K A R N K L . . . . . T G E V V A L K K I L
7 ..... . . . . . P P G T K E A F E F G P T L G T G S F G R V K S A K Y L K S T S T N V D D P T Q V P P R V A V K L L
192 ..... . . . . . L A R N L S I D D F L F H E T V G T G S F C R V C I V D L R G A . . . . . A G W Y P P M A L K I L
248 A E T T V D S L L S Q G E R K L K L V Q P L R V G D R S V F L V R D V E . . . . . R L E Y F A L K V F
241 G A V T V I S E L G R P G R Q L V R G N L I N I V D G G L L F Q A T D Q A . . . . . T G E P M T V L V G
251 Q P F R V E S E L G E R P R T L V R G T L L G O E D P Y A V E A T D Q E . . . . . T G E S F V H V P
371 ..... . . . . . G V P . . . . . I A L Y N R G H L G S G H F G A V I K A S L D D . . . . . G T L Y A A K V P
239 K R . . F V S V T T G E T R T L V R G A P L G S G G F A T V Y E A T D V E . . . . . T N E E L A V K V F
319 ..... . . . . . L P L C E L P W D D L G P M L G S G T F G R V Y P L R R P A C T E V T . . . . . K G F V G R K F A V K I F W L K R K G M M N L F D T I S Q G G T P S A E Q T D P
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β1 β2 β3 α2 β4 α3

N-lobe insertion

HsPKA/1-351

α2 Subdomain III α3

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76 ..... D K Q K V V K L K Q I E H T L N E K R I L . . . . . Q A V N . F P F
88 ..... . . . . . L Q D K R F K N R E L Q I M . . . . . R K L D . H C N
52 ..... . . . . . A K E A L E G K E G S M E N I A V L . . . . . H K I K . H P N
301 ..... . . . . . K P G T M S P E A F L Q E A Q V M . . . . . K K L R . H E K
71 ..... . . . . . K P V K K . K K I K R E I K I L . . . . . E N L R G G P N
36 ..... . . . . . R L D T E T E G V P S T A I R E I S L L . . . . . K E L N . H P N
58 ..... . . . . . K K A A I I K L K H V D H I T N E K K I L . . . . . L A L D . H P L
236 ..... . . . . . S K H I V K M K Q V E H V K D E K R I L . . . . . S S I E . H P F
195 ..... . . . . . T M G A E N S R S E L E R L H E A T F A A A . R L L G . E S P E E . A R D R R R L L . . . . .
288 ..... . . . . . S T W N K P S G K D L K L R H Q A L A I G . L F Q K V K N P Y L A N R Y L R F L . . . . .
298 ..... . . . . . L S K E K P S N T I K Q M K Q E V L R L R . L L R G I K N Q K Q A K V H L R F I . . . . .
407 ..... . . . . . Y S Q I V P N A . . . . . D A T S A E L E A I S S A R A E L V K T I R Q E L D V
284 ..... . . . . . M S E K E P T D E T M L D L Q R E S S C Y R N F S L A K T A R D A Q E S C R F M . . . . .
394 G T I A A I K S E I R S L P T S S A F R D M V R I A D P T V D V E K I K G M A D S L T V E T I M K E A K T L R T V I N T N G E Y T E V G E T G T I . F T Q M E K F V Q A
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α4 α5 α6 α7

HsPKA/1-351

β4 β5 TT α4

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104 L V K L E F S F K D N . . . . . S N L Y M V M E Y V P G G E M F S H . . . . . L R R . . . . .
109 I V R L R Y F F Y S S G . . . . . E . . . . . K K D E V Y L N L V L I D Y P E T V Y R V A R H . . . . . Y S R A . . . . .
78 I V A L D D I Y E S G . . . . . G H L Y L I M Q L V S G G E L F D R . . . . . I V E . . . . .
325 L V Q L Y A V V S . E . . . . . E P I Y I V T E Y M S K G S L L D F L . . . . . K G E T G K Y L R
94 I I T L A D I V K D P V . . . . . S R T P A L V F E H V N N T D . . . . . F K Q L . . . . .
63 I V K L L D V I H T E . . . . . N K L Y L V F E F L H Q D L K K F M D . . . . . A S A . . . . .
86 T V R C F G S F Q D S . . . . . R Y L Y L V M E L V P G G E F F T H . . . . . L R K . . . . .
264 I V N L L A A F Q D E . . . . . K R L F I L M E Y V N G G E L F S H . . . . . L R R . . . . .
234 . . . . . L P S D V V A V Q S Q . . . . . P P F A Q L S P G Q S D Y A V A N Y L L L M P A S G G E . . . . .
328 . . . . . A P F D L V T I P G K . . . . . P L V Q A K A S H N E V G W V I N L L L L P A I E I D M G R F V E E L . Y E L P T E D R . . . . .
338 . . . . . P P F D L V K D P Q K . . . . . K . . . . . K M I Q G V S D E G A G W I V N G F L Y P R M Q T N L Q T L G E V L . L S H S S T H K . . . . .
443 R D K L V A G L T L T E T . . . . . A E Q Y G L P L C Q M T L L P E N K A T V V R R G S R L V V V S K E V M L L P L I D G S P S N S L . . . . . V Q . . . . .
324 . . . . . V P S D V V M L E G Q . . . . . P A S T E V V I G L T T R W V P N Y F L L M R A E A D M S K V . . . . . I S W V F G D A S V N K S . . . . .
478 H R P E I W S T L S K A S Q E A Q A S K Y A E I G L A D N H W S L P L A R V L V K D . . . . . K N D V K H W A L L I E L F D G D L Q P K T D K T G Y S L D G W N A K S G G N V V
```

α8 α9 β5 TT β6 TT

HsPKA/1-351

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HsGSK3b/1-420
HsCAMK1/1-370
HsSrc/1-536
HsCK2A1/1-391
HsCDK2/1-298
TgPKAc/1-333
TgAGC/1-514
TgROP5/1-461
TgROP7/1-575
TgROP8/1-575
TgROP16/1-707
TgROP18/1-554
TgRON13/1-1375
TgRON13/1-1375

935 IGNAVKEAVAATYKFDPN...
alpha30 alpha31 alpha32

HsPKA/1-351

HsPKA/1-351
HsGSK3b/1-420
HsCAMK1/1-370
HsSrc/1-536
HsCK2A1/1-391
HsCDK2/1-298
TgPKAc/1-333
TgAGC/1-514
TgROP5/1-461
TgROP7/1-575
TgROP8/1-575
TgROP16/1-707
TgROP18/1-554
TgRON13/1-1375
TgRON13/1-1375

1020 QVYEQLLSGEKPSSESEK...
alpha33 alpha34 alpha35 alpha36

HsPKA/1-351

HsPKA/1-351
HsGSK3b/1-420
HsCAMK1/1-370
HsSrc/1-536
HsCK2A1/1-391
HsCDK2/1-298
TgPKAc/1-333
TgAGC/1-514
TgROP5/1-461
TgROP7/1-575
TgROP8/1-575
TgROP16/1-707
TgROP18/1-554
TgRON13/1-1375
TgRON13/1-1375

1105 RVTVRGLNASLPA...
alpha37 alpha38 alpha39 alpha40

HsPKA/1-351

HsPKA/1-351
HsGSK3b/1-420
HsCAMK1/1-370
HsSrc/1-536
HsCK2A1/1-391
HsCDK2/1-298
TgPKAc/1-333
TgAGC/1-514
TgROP5/1-461
TgROP7/1-575
TgROP8/1-575
TgROP16/1-707
TgROP18/1-554
TgRON13/1-1375
TgRON13/1-1375

1190 NLSDEDIEKQLEGMLPA...
eta4 alpha41 alpha42 beta11 beta12

HsPKA/1-351

HsPKA/1-351
HsGSK3b/1-420
HsCAMK1/1-370
HsSrc/1-536
HsCK2A1/1-391
HsCDK2/1-298
TgPKAc/1-333
TgAGC/1-514
TgROP5/1-461
TgROP7/1-575
TgROP8/1-575
TgROP16/1-707
TgROP18/1-554
TgRON13/1-1375
TgRON13/1-1375

1275 AFKKDISV...
alpha43 alpha44 alpha45 beta13 beta14

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HsCAMK1/1-370
HsSrc/1-536
HsCK2A1/1-391
HsCDK2/1-298
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TgAGC/1-514
TgROP5/1-461
TgROP7/1-575
TgROP8/1-575
TgROP16/1-707
TgROP18/1-554
TgRON13/1-1375 1360 FLWTQAEFLDDKTIVVS
TgRON13/1-1375 $\frac{\eta\eta}{\eta 6}$ TTT \rightarrow $\beta 15$