

**Additional file 4: Figure S2. Alignment of the protein kinase domain in ICK, MAK and MOK in different species.** The protein kinase domain in ICK, MAK and MOK is a conserved region, and it includes both described mutations in ICK, i.e. p.G120C and p.R272Q. The alignment is based on sequences from proteins with the following UniProt identifiers; Q9UPZ9 (*H. sapiens* ICK), Q9JKV2 (*M. musculus* ICK), B3WFY8 (*C. elegans* DYF-5b), P20794 (*H.sapiens* MAK), Q04859 (*M. musculus* MAK), Q7ZTX0 (*D. rerio* MAK), Q9UQ07 (*H. sapiens* MOK), Q9WVS4 (*M. musculus* MOK), Q9VL64 (*D. melanogaster* CG42366). The alignment was made using the online tool Clustal omega 1.2.1: <http://www.ebi.ac.uk/Tools/msa/clustalo/>. The annotations made by this tool visualize the conservation of each residue; an asterisk indicates “positions which have a single, fully conserved residue”, a colon and a period indicate “conservation between groups of strongly similar properties” and “weakly similar properties”, respectively. The colors assigned by Clustal omega inform about the properties of individual amino acids; red indicates small residues, blue indicates acidic residues, magenta shows basic residues, and green refers to amino acids with hydroxyl, sulfhydryl and amine groups or to glycine residues. The protein sequences for each of the presented species was obtained from UniProt ([www.uniprot.org](http://www.uniprot.org)), TreeFam ([www.treefam.org](http://www.treefam.org)), and ZFIN (<http://zfin.org>) websites were used to identify proteins that are homologues to ICK.

*H. sapiens* ICK YTTIRQLGDGTYGSVLLGRSIE SGELIAIKMKRKFYSWEECMNLRVKS LKKLN-HANV 59  
*M. musculus* ICK YTTIKQLGDGTYGSVLLGRSIE SGELIAIKMKRKFYSWEECMNLRVKS LKKLN-HANI 59  
*C. elegans* DYF-5b YLMTKRLGDGT FGEVMLAKKIDTGDRAIKMKKKFYSWEEAMS LREVKS LKKLN-HPNI 59  
*H. sapiens* MAK YTTMRQLGDGTYGSVLMGKSNE SGELVAIKMKRKFYSWDECMNLRVKS LKKLN-HANV 59  
*M. musculus* MAK YTTMKQLGDGTYGSVLMGKSNE SGELVAIKMKRKFYSWDECMNLRVKS LKKLN-HANV 59  
*D. rerio* MAK YTTLTKQLGDGTYGSVLMGKSNE SGELVAIKMKRKFYSWEECMNLRVKS LKKLN-HANV 59  
*H. sapiens* MOK YKAIGKIGEGT FSEVMKMQSLRDGNYYACKQMKQRFESIEQVNNLREIQALRRRLNPHPHNI 60  
*M. musculus* MOK YKAIGKIGEGT FSEVMKMQSLRDGNYYACKQMKQHFESIEQVNSLREIQALRRRLNPHPHNI 60  
*D. melanogaster* CG42366 YITLTQLGDGT YGT VVLGRKDTGKVKVAIKMKRKYYSWEEAMNLRVKS LKKLS-HPNI 59  
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*H. sapiens* ICK VKLKEVI-----RENDHLYFIF EYMK-ENLYQLIKER-NKLFPE SAIRNIMYQILQGLAF 112  
*M. musculus* ICK VKLKEVI-----RENDHLYFIF EYMK-ENLYQLIKER-NKLFPE SAIRNIMYQILQGLAF 112  
*C. elegans* DYF-5b IKLREVI-----RENDILYFVFEFMQ-ENLYELMKDRD-RYFPE SVIRNIIYQVLQGLAF 112  
*H. sapiens* MAK IKLKEVI-----RENDHLYFIF EYMK-ENLYQLMKDR-NKLFPE SVIRNIMYQILQGLAF 112  
*M. musculus* MAK IKLKEVI-----RENDHLYFVFEYMK-ENLYQLMKDR-NKLFPE SVIRNIMYQILQGLAF 112  
*D. rerio* MAK VKLKEVI-----RENDHLYFVFEYMK-ENLYQLMKDRENKMFTENEIRNIMFQVLSGLAF 113  
*H. sapiens* MOK LMLHEVV---FDRKSGSLALICE LMD-MNIYELIRGRR-YPLSEKKIMHYMYQLCKSLDH 115  
*M. musculus* MOK LALHEVV---FDRKSGSLALICE LMD-MNIYELIRGRR-HPLSEKKIMLYMYQLCKSLDH 115  
*D. melanogaster* CG42366 VKLKEVI-----RENDTLYFVFEYMK-ENLYQMIKDRD-THLPEPELKSILFQVLTGLAF 112  
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**G120C**

*H. sapiens* ICK IHKHGFFHRDLKPENLLCMGPE---LVKIADEGLAREIRSKPPYTDYVSTRWYRAPEVLL 169  
*M. musculus* ICK IHKHGFFHRDLKPENLLCMGPE---LVKIADEGLAREIRSRPPYTDYVSTRWYRAPEVLL 169  
*C. elegans* DYF-5b MHKNGFFHRDMKPENIMCNGTE---LVKIADEGLAREIRSKPPYTDYVSTRWYRAPEILL 169  
*H. sapiens* MAK IHKHGFFHRDMKPENLLCMGPE---LVKIADEGLAREIRSQPPYTDYVSTRWYRAPEVLL 169  
*M. musculus* MAK IHKHGFFHRDMKPENLLCMGPE---LVKIADEGLAREIRSQPPYTDYVSTRWYRAPEVLL 169  
*D. rerio* MAK VHKHGFFHRDMKPENLLCMGPE---LVKIADEGLAREIRSRPPYTDYVSTRWYRAPEVLL 170  
*H. sapiens* MOK IHRNGIFHRDVKPENILIK-QD---VLKLGDFGSCRSVYSKQPYTEYISTRWYRAPECLL 171  
*M. musculus* MOK MHRNGIFHRDVKPENILVK-QD---VLKLGDFGSCRSVYSKQPYTEYISTRWYRAPECLL 171  
*D. melanogaster* CG42366 MHRHGFHRDLKPENLLCSGPD---LIKIADEGLAREIRSRPPFTDYVSTRWYRAPEVLL 169  
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*H. sapiens* ICK RSTNYSSPIDVWAVGCIMAELYTLRPLFP GASE-I--DTIFKICQVLGT PKKTDWPEGYQ 226  
*M. musculus* ICK RSTNYSSPIDIWA VGCIMAELYTLRPLFP GASE-I--DTIFKICQVLGT PKKTDWPEGYQ 226  
*C. elegans* DYF-5b RSTSYNSPIDMWA LGCIMAELYTLRPLFP GTSE-M--DQLFKIISILGT PNKDEWPEGYQ 226  
*H. sapiens* MAK RSSVYSSPIDVWAVGSIMAELYMLRPLFP GTSE-V--DEFKICQVLGT PKKSDWPEGYQ 226  
*M. musculus* MAK RSSVYSSPIDVWAVGSIMAELYTFRPLFP GTSE-V--DEFKICQVLGT PKKSDWPEGYQ 226  
*D. rerio* MAK RSPVYSSPIDIWA VGCIMAELYTLRPLFP GNSE-V--DEFKICQVLGT VKKSDWPEGHQ 227  
*H. sapiens* MOK TDGFYTYKMDLWSAGCVFYEIASLQPLFP GVNE-L--DQISKIHDVIGT PAQKIL-TKFK 227  
*M. musculus* MOK TDGFYTYKMDLWSAGCVFYEIASLQPLFP GVNE-L--DQISKIHDVIGT PCQKTL-TKFK 227  
*D. melanogaster* CG42366 HSTNYGSTIDLWAMGCIMAELYTFRPLFP GSSE-V--DQLFKICSVLGT PDKDDWPDGYR 226  
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**R272Q**

*H. sapiens* ICK LSSAMNFRWPQCVPNNLKTLPNASSEAVQLLRDMLQWDPKKRPTASQALRYPYF 281  
*M. musculus* ICK LSSAMNFWPQCI PNNLKTLPNASSEAIQLLRDLLQWDPKKRPTASQALRYPYF 281  
*C. elegans* DYF-5b LASAMNFRFPQVVATPMEQVVNTISKEGMKLMMDMLWNPEKRPANQSLRYKYF 281  
*H. sapiens* MAK LASSMNFREFPQCVPINLKTLPNASNEAIQLMTEMLNWDPKKRPTASQALKHPYF 281  
*M. musculus* MAK LASSMNFREFPQCI PINLKTLPNASSEAIQLMTEMLNWDPKKRPTASQALKHPYF 281  
*D. rerio* MAK LASAMNFRFPQCVPTPLKTLIPNATNEALDIMRDLLQWDPKKRPSAVKALRYPYF 282  
*H. sapiens* MOK QSRAMNFRFPFKKSGIPLLTNLS PQCLSLLHAMVAYDPPERIAAHQALQHPYF 282  
*M. musculus* MOK QSRAMNFRFPFKKSGIPLLTANLS PQCLSLLHAMVAYDPPERIAAHQALQHPYF 282  
*D. melanogaster* CG42366 LASMIHFRYPDCIKVPLSSVVSRCSONGLDLEDMLAYDDEKRPATAQSLKYPYF 281  
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