
Supplementary information

Direct observation of the conformational states of PIEZO1

In the format provided by the
authors and unedited

Supplementary Notes

PIEZO protein sequences used for binding energy calculations:

PIEZO2 6KG7

>Repeat_A

QIYVPIRQFFYDLIHPDYSAVTDVYVLMFLADTVDFIIIVFGFWAFGVPGPFLVMVLIQFGTMVVDRALYL
RKTVLGKVIFQVILVFGIHFWMFFILPGVTERKFSQNLVAQLWYFVKCVYFGLSAYQIRCGYPTRV

>Repeat_B

LLLLFYAMYNTLVARSEMVCYFVIIINHMTSASIIITLLLPIILFLWAMLSVPRPSRRFWMMMAIVYTEVAIV
VKYFFQFGNIIGVEKKEGYVLYDLIQLLALFFHRSILKCHGLWDE

>Repeat_C

ICMNLDAASFQHNVPDFIHCRSYLDMSKVIIFSYLEFWFVLTIIITGTTRISIFCMGYLVACFYFLLFGGD
LLLKPIKSILRYWDWLIAYNVFVITMKNILSIAGIWDSSICFAFLLLQRRVFMSY

>Repeat_D

SKTIFHDITRLHLDGDLINCAKYFVNYFFYKFGLETCLMSVNVIGQRMDFYAMIHACWLIGVLYRRRRK
AIAEVWPKYCCFLACIITFYFVCIGIPPAPCRDYPWRFKGAYFNDNIIKWLYFPDFIVRPNPVFLVYDFML
LLCASLQRQIFEDENKAAVRIMAGDNVE

>Repeat_E

TVLFLKFLEYFHKLQVFMWWILELHIIKIVSSYIIWVTVKEVSFLFNYVFLISWAFALPYAKLRRRAASSVCT
VWTCVIIVCKMLYQLQTIKPENFSVNCSLPNENQTNIPHELNKSLLYSAPVDPTEWVGLRKSSPLL VYLR
NNLLMLAILAFEVTVYRHQEYYRGRNNLTAPV

>Repeat_F

IMKVLGNLVVALFIKYWIYVCGGMFFFVSFEGKIVMYKIIYMVFLFCVALYQVHYEWWRKILKYFWM
SVVIYTMLVLIFIYTYQFENFPGLWQNMTGLKKEKLEDLGLKQFTVAELFTRIFPTSFLLCILHLHYFHD
RFLELTDLK

>Repeat_G

AVFQFIMKQSYICALIAMMAWSITYHSWLTFFVLLIWSTLWMIRNRRKYAMISSPFMVVYANLLLVLQY
IWSFELPEIKKVPFGFLEKKEPGELASKILFTITFWLLLRQHLTEQKALREKEALLS

>Repeat_H

LRRFASVASKLKEFIGNMITTAGKVVTILLGSSGMMLPSLTSVYFFVFLGLCTWWSWCRTFDPLLFGC
LCVLLAIFTAGHLIGLYLYQFQFFQEAVPPNDYYWYHHANPILLVMYYTLATLIRIWLQE

>Repeat_I

GLIFRLLLPICLAVACAFRYNGLSFVYLIYLLLIPLFSEPTKATMQGHTGRLLQSLCITSLSFLLLHIIHFHIV
VPDIGMFIASLTIWLVCRT

>Central_domain

YFLHVVADIKASQILASRGAELFQATIVKAVKARIEEEKKSMDQLKRQMDRIKARQQKYKKGKERVDH
ASMVRSGDYFLFETDSEFTWVFLATVDSFTTWLNSISREHIDISTVLRIERCMLTREIKKGNVPTRESIH
MYQQNHLTASDLLMSKMFHDDELEESEKFYVDQPRLGNFLTKSYNYVNLFLFQGFRLVPFLTTELRAVM
DWVWTDTTLSLSSWICVEDIYAHIFILKCWRESEKRYPQPRGQKKKKAVKYGMGGMIIIVLLICIVWFPLL
FGVINQPLDVSVTITLGGYQPIFTMSAQSQLKVMDSKYNEFLKSFGPNSGAMQFLENYEREDVTVAE
LEGNSNSLWTISPPSKQKMIQELTDPNSCFVSVFSWSIQRNMTLGAKAEIATDKLSFPLAVATRNSIAKMI
AGNDTESSNTPVTIEKIYPYVKAPSDSNSKPIKQLLENFMNITILFRDNVTKSNSEWWVLNLTGSRIF
NQGSQALELVFNDKVSPPSGIMGLYASVVLVIGKFVREFFSGISHSIMFEELPNVDRILKLCTDIFLVRET
GELELEDLYAKLIFLYRSPETMIKW TREKTN

PIEZO2 6KG7 – TMDs only

>Repeat_A

QIYVPIRQFFYDLIHPDYSAVTDVYVLMFLADTVDFIIIVFGFWAFGVPGPFLVMVLIQFGTMVVDRALYL
RKTVLGKVIFQVILVFGIHFWMFFILPGVTERKFSQNLVAQLWYFVKCVYFGLSAYQIRCGYP

>Repeat_B

RSEMV⁻CYFVILNHMTSASIITLLLPIILFLWAMLSVPRPSRRFWMMAIVYTEVAIVVKYFFQFGNIIGVEK
KEGYVLYDLIQLLALFFHRSILKCHGLWDE

>Repeat_C

VIIISYLFWFVLTIIFITGTTRISIFCMGYLVACFYFLLFGGDLLLKPIKSILRYWDWLIAYNVFVITMKNILSI
AGIIWDSICFAFLLLQRRVFMSYYFL

>Repeat_D

FYKFGLETCLMSVNVIGQRMDFYAMIHACWLIGVLYRRRRKAIAEVWPKYCCFLACIITFQYFVCVFLV
YDFMLLLCASLQRQIFEDE

>Repeat_E

LHIIKIVSSYIIWVTVKEVS⁻LFNYVFLISWAFALPYAKLRRRAASSVCTVWTCVIIVCKMPLLVYLRNNLL
MLAILAFEVTVYRHQEY

>Repeat_F

IMKVLGNLVVALFIKYWIYVCGGMFFFVSFEGKIVMYKIIYMVFLFCVALYQVHYEWWRKILKYFWM
SVVIYTMLVLIFIYTYQAE⁻LFTTRIFPTSFLLVCILHLHYFHDRFLELTDLK

>Repeat_G

AVFQFIMKQSYICALIAMMAWSITYHSWLT⁻TFVLLIWSCTLWMIRNRRKYAMISSPFMVVYANLLLVLQY
IWSGELASKILFTITFWLLLRQHLTEQKALREKEALL

>Repeat_H

LRRFASVASKLKEFIGNMITTAGKV⁻VVTILLGSSGMMLPSLTS⁻AVYFFVFLGLCTWWSWCRTFDPLLFGC
LCVLLAIFTAGHLIGLYLYWYHHANPILLLVMYYTLATLIRIWLQE

>Repeat_I

GLIFRLLLPICLAVACAFRYNGLSFVYLIYLLLIPLFSEPTKATMQGHTGRLLQSLCITSLSFLLLHIIHFHIV
VPDIGMFIASLTIWLVCRT

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>Repeat_A

SFYQPLQ⁻RFFHDILHTKYRAATDVYALMFLADIVDIIIIIFGFWAFGK⁻HSAATDIASSLSDDQVPQAFLFML
LVQFGTMVIDRALYLRKTVLGKLA⁻FQVVLVVAIHIWMFFILPAVTERMFSQNAVAQLWYFVKCIYFALS
AYQIRCGYPTRI

>Repeat_B

TLRLLRAGYQCVA⁻AHSELLCYFIILNHMVTASAASLVLPVLVFLWAMLTIPRPSKRFWMTAIVFTEVMV
VTKYLFQFGFPWNSYVVLRRYENKPYFPPRILGLEKTDSYIKYDLVQLMALFFHRSQLLCYGLWD

>Repeat_C

LEPLRGEPNPIPNIHCRSYLDMLKVAVFRYLFWLVLVVVFVAGATRISIFGLGYLLACFYLLLFGTTLLQ
KDTRAQLVLWDCLILYNVTVIISK⁻NMLSLLSCVFVEQM⁻QSNFCWVIQLFSLVCTVKGYYPKEMMTRD
RDCLLPVEEAGIIWDSICFFFLLLQRRIFLSHY

>Repeat_D

AQAVCADGTRQRLDQDLLSCLKYFINFFFYKFGLEICFLMAVNVIGQRMNFMVILHGCWLVAILTRRRR
EAIARLWPNYCLFLTLFLLYQYLLCLGMPPALCIDYPWRWSKAIPMNSALIKWLYLPDFFRAPNSTNLIS
DFLLLLCASQQWQVFS⁻AERTEEWQRMAGINTDH

>Repeat_E

LDLAASFS⁻AVLTRIQVFVRRLLELHVFKLVALYTVWVALKEVSVMNLLLVLWAFALPYPRFRPMASCL
STVWTCIIIVCKM⁻LYQLKIVNPHEYSSNCTEPPNNTNLQPLEINQSLLYRGPVDPANWFGVRKGYPNLG
YIQNHLQI⁻LLLVEAVVYRRQE⁻HYRRQHQA⁻PLP

>Repeat_F

TQTQTLLRSLGELVTGIYVKYWIYV⁻CAGMFIVVSFAGRLVVYKIVYMFLFLLCLTLFQVYYTLWRKLLR
VFWWL⁻VVAYTMLVLI⁻AVYTFQFQD⁻FPTYWRNLTGFTDEQLGDLGLEQFSVSELFSSILIPGFFLLACILQL
HYFHRPFMQLTDLEH

>Repeat_G

PLHGLGHLIMDQSYVCALIAMMVWSIMYHSWLTfVLLLWACLIWTVRSRHLAMLCSPCILLYGLTLC
CLRYVWAMELPELPTTLGPVSLHQLGLEHTRYPCLDLGAMLLYLLTFWLLLRQFVKEKLLKKQKVP

>Repeat_H

RRLWLASRFRVTAHWLLMTSGRTLIVVLLALAGIAHPSAFSSIYLVVFLAICTWWSCHFPLSPLGFNTLC
VMVSCFGAGHLICLYCYQTPFIQDMLPPGNIWARLFGLKNFVDLPNYSSPNALVLNTKHAWPIYVSPGIL
LLLYYTATSLLKLHKS

>Repeat_I

MEPHVLGAGLYWLLLPCITLLAASLLRFNALSIVYLLFLLLPLWLPGPSRHSIPGHTGRLLRALLCLSLLFL
VAHLAFQICLHTVPHLDQFLGQNGSLWVKVSQHIGVTRLDLKDIFNTTRLVAPDLGVLLASSLCLGLCGR

>Central_domain

YFLHVVADIKASQILASRGAELFQATIVKAVKARIEEEKKSMDQLKRQMDRIKARQQKYKKGKERVDH
ASMVRSGDYFLFETDSEFTWVLFATVDSFTTWLNSISREHIDISTVLRIERCMLTREIKKGNVPTRESIH
MYEQNHLTASDLLMSKMFHDDELEEESEKFYVDQPRLGNFLLTKSYNYVNLFLFQGFRLVPFLTELRAVM
DWVWTDTTLSLSSWICVEDIYAHIFILKCWRESEKRYPPQPRGQKKKKAVKYGMGMIIVLLICIVWFPLL
FGVINQPLDVSVTITLGGYQPIFTMSAQQSQLKVMDNSKYNEFLKSFGPNSGAMQFLENYEREDVTVAE
LEGNSNSLWTISPPSKQKMIQELTDPNSCFVSVFSWSIQRNMTLGAKAEIATDKLSFPLAVATRNSIAKMI
AGNDTESSNTPVTIEKIYPYVVKAPSDSNSKPIKQLLENFMNITILFRDNVTKSNSEWWVLNLTGSRIF
NQGSQALELVVFNDKVSPPSGIMGLYASVVLVIGKFVREFFSGISHSIMFEELPNVDRILKLCTDIFLVRET
GELEEDLYAKLIFLYRSPETMIKWTRKTN

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>Repeat_A

QIYVPIRQFFYDLIHPDYSVAVTDVYVLMFLADTVDFIIIVFGFWAFGVPGPFLVMVLIQFGTMVVDRALYL
RKTVLGKVIFQVILVFGIHFWMFFILPGVTERKFSQNLVAQLWYFVKCVYFGLSAYQIRCGYP

>Repeat_B

RSEMVCFVFIILNHMTSASITLLLPIILFLWAMLSVPRPSRRFWMMMAIVYTEVAIVVKYFFQFGNIIGVEK
KEGYVLYDLIQLLALFFHRSILKCHGLWDE

>Repeat_C

VIIFSILFWFVLTIIFITGTTRISIFCMGYLVACFYFLLFGGDLLLKPIKSILRYWDWLIAYNVFVITMKNILSI
AGIWDSSICFAFLLLQRRVFMSSYYFL

>Repeat_D

FYKFGLETCLMSVNVIGQRMDFYAMIHACWLIGVLYRRRRKAIAEVWPKYCCFLACIITFQYFVCVFLV
YDFMLLLCASLQRQIFEDE

>Repeat_E

LHIIKIVSSYIIWVTVKEVSLFNIVFLISWAFALPYAKLRRRAASSVCTVWTCVHIVCKMLPLLVLRRNNLL
MLAILAFEVTVYRHQY

>Repeat_F

IMKVLGNLVVALFIKYWIYVCGGMFFVVSFEGKIVMYKIIYMVFLFLFCVALYQVHYEWWRKILKYFWM
SVVIYTMLVLIFIYTYQAEFTRIFPTSFLVCILHLHYFHDRFLELTDLK

>Repeat_G

AVFQFIMKQSYICALIAMMAWSITYHSWLTfVLLIWSTLWMIRNRRKYAMISSPFMVVYANLLLVLQY
IWSGELASKILFTITFWLLLRQHLTEQKALREKEALL

>Repeat_H

LRRFASVASKLKEFIGNMITTAGKVVVITLLGSSGMMLPSLTSVYFFVFLGLCTWWSWCRTFDPLLFGC
LCVLLAIFTAGHLIGLYLYWYHHANPILLVMYYTLATLIRIWLQE

>Repeat_I

GLIFRLLLPICLAVACAFRYNGLSFVYLIYLLLIPLFSEPTKATMQGHTGRLLQSLCITSLSFLLLHIIFHIVE
VPDIGMFIASLTIVLVCRT