

BLM

TR (TOP3A/RMI1-binding domain)

Human 1 ---MAAMPQNNLQEQLEHRSARTLNNKLSLSKPKFSGFTFKKKTSSDNNVSVT-NVSVAKTPVLRNKDVMNTEDFSFS-
 Mouse 1 MRI MAAMPQNNLQEQLEHRSARKLNQPSLSKPKSLGFTFKKKTSEG-DVSVT-SVSVKTPALSDKDVNVEAFSFTES
 Dog 1 ---MAAMPQNNLQEQLEHRSARKLSNKLSPSKPKSSVFTFKKKT SAN-NVSVT-SVSVAKTPVLRNKDVMNTEAFPFSE-
 Chicken 1 ---MAAMPQNNLREQLRLHSARGALSKVLPARSRPAAFTRRTHSPA-----AGPAALRDKDVMNTEAFSGGVA-
 Xenopus 1 ---MAAMPQNNLQEQLELFPAGKTSNKLSQLQKTKSSVFTFKKKT CSPN-VSAST-GFIPFQQHVLKDKVMNTEKQDGTHTA-
 Zebrafish 1 ---MSSLPQNNLKEHLERHNN-AAQNKL SLLKPKPGGFCFKKKTSSSG-ISKVEVPQKVTGSSVLANRSMNTPSNFEVTKN

Human 76 PLPNTTNQQRV---KDFFKNAFAGQETQRG--GSKSLLEDFLQTPKEVCTTQNTPT-VKKSRTALKKEFSSSPDLSL
 Mouse 79 PLHKPKQQAQI---EGFFKHFPGRQQSKGT--CSEPSLPATVQTAQDTCTTPKTPT-AKKLPVAVFKKEFSSSA---D
 Dog 75 PLPHATSQQTR---PSDLKNTPAGQQRRRT--VSKPLLEPDL SL-VSRVLCNTQNTPI-VKSSNATFKKEFSSSDSFV
 Chicken 66 -----RP---KDLR-VGPPG-----ARPALPGFAG-----SSGPT-AGAPPGSV--SVSLFSSGPAAY
 Xenopus 75 -LPKATERNKI---NCFFT--PVYTKS-----GQPPQVVALKDHVHGNSANK-PPSTEDAASKKTGINISFGSVT
 Zebrafish 76 PVTFSQKPERVAPKVNFF-TAPSKPKNTVNPLANPFALNKTPLVQSTKALPKSAALPKDSTNDQTVELKHDIS---QL

1

Human 150 TINDDWDDMDDFDTSSETSFSVTPPQSHFVRS-STAQKSKKGRNFFKAQLYTTNTVKTDLPFSSSESEQIDLTEEQKDD-
 Mouse 150 SLSDWADMDDFDMSADA-FASLAKNPATFV-STAQKMAKTKRNFKPPPRKANAVKTDLPSSPECLQVLDLTKESEEEE
 Dog 148 TINDDWDDMDDFDTS GNSK-LVTPCKNHFVRS-STAQKSKPKRNFKAQLPQANTVKADLPSSFESKQACLTKKQND-
 Chicken 112 TGDEWDDMDDFDLSGFEEKFSRP-AVLSFKG-P-----RTPQ-----GRGLRVSKARADVGEQEHGSEVSCS-Q-----
 Xenopus 139 SLEWDDMDDFDTSVSP-----KSHAGKGGKTPQKCNNTS-----PVASFKIQSLEEGPTTEKHDCAKLLYDNN
 Zebrafish 152 SFNEWDDMDDFETPVKSR-VASPVAGTSTKPK-PSV-SDQNTS-----S-----SCSSKCEETKVNEE-SQA-

Human 228 -----SEWLSSDVICIDDDGPIAEVHINEAQESDS-LKTH-----LEDER-----DN---
 Mouse 228 EE-----EEEAGADCLSRDVICIDNDSASEELTEKDTQESQS-LKAH-----LGAER-----GD---
 Dog 225 -----SEWFSNDVICIDDDPNPEELIHGDTPQESH-SLKH-----LEEER-----D---
 Chicken 173 -----GSSQGLICIDGAGAPAAVLSINGMEEARAAANG-----GSGESQKL-----SN---
 Xenopus 205 EVASEPRKNLHAKTAESPQSLVCLASVE-P-----IN-----L--ER-----DM---
 Zebrafish 209 -----TETITAPKDVLSAANGVST-ETAERPEPDSPI-KKSKRPKKSQHTALLSDTEDEEIIHCVSPDTNQK

2

Human 269 -----SEKKNLEEAEL-HSTEKVPICI-EFDDDDYDIDFVPPSPPEEII SASSSSSKCLSTLKDLDTSDRKEDVLSTSK
 Mouse 277 -----SEKKSHEDEAVF-HSVQNTFYF-EHNDNDYDIDFVPPSPPEEII STASSSLKCSMLKDLDDSDKEKGLSTSE
 Dog 265 -----SEK-KNWEETEL-CSLEKSPCV-ELDEDDYDIDFVPPSPPEEII SASSSSLKCFMMLKDLASGT-EDGPSTSE
 Chicken 218 -----GKSSQLEPGDV--GNELLADI-ELLEDDY-IDVPPSPPEEELPSFSPSVNVSIFKESPTDGRSAVHGTE-
 Xenopus 242 -----CRNTDYLGTDDLEHDQETLSQVLIIEEDDCEFDIIPPSPSDESLSSPPVLKVIISAQRKHKS-----SLT
 Zebrafish 275 NFKSVAVAEK-DKWGEPN--VIDSDDCE-ENNHYEGFEDFIIPPSPPIPEEISLSVSDKEKSSSEPVTPANKKESRSAS-

DHBN (dimerization domain)

Human 340 DLLSKPEKMSMQELNP--ETSTDCDARQI-SLQQQLIHVMTHICKLVDITPDDKLLKLLDCNELLQQRNTRRKLLETVDF
 Mouse 348 ELISKPEEMTTHKSDA--GTSKDCDAQI-RIQQQLIHVMTHICKLVDITPDELEALNCGTELLQQRNTRRKLLEAEAGF
 Dog 333 D-LPTPKGTTQQPNO--ETSTNCDARQP-SLQQQLIHVMTHICKLVDITPDELKALTCGNALHQQRDTRRKLLEAADF
 Chicken 286 ---SEPELMAKQPAEQDSSAEHADKGL-HLEQQLYSVMTHICKLVDITPHELTSISCKELLLQQRERLRRKLLEADSGA
 Xenopus 307 D-VNDCENTTDHLQGO--SVSTSLDS---KVPSQLLTMLEICDLVDKIPISELHVLSCGLDLKKKRDTRRKLLENSDSV
 Zebrafish 349 G-LPAEL-----DQSAKGLKGADDALFVMSICCLVDITPEHELIALTCGTELLLQRAHRKRILAKGGS

Human 417 -NKSDASLLGSLWR---YRPDSL-----DGPM-----EGDSCPTGNSMKE-----
 Mouse 425 -NGNDVRLGSLWR---HRPDSL-----DNTV-----QGDSCPVGHPNKE-----
 Dog 409 -NTSDASVLASVWT---RGPDSL-----GSPVEDMASLSAPDVFPKGNSHPTGNSVKE-----
 Chicken 362 LNTNSVNG-PRNWKACVQQDPSSRPGTPLCSGPG-----RGV-SSVGSTPKS-----
 Xenopus 380 FRSSPADS-----STV-----SLTSCSTSTQNRDFNVNAPKGAESLSGSSVSKV
 Zebrafish 413 -SRTSHS-----DSVSTPGFLNR-----

Human 453 LNFSPHPSNSVSPGD-----CLLTTTL-----GKTGFSATR--KNLFEERPLFN-----THLQK-----
 Mouse 461 LNSPYLHSHSPSTEE-----CLPTTTP-----GKTGFSATP--KNLFEERPLN-----SHLQK-----
 Dog 458 LNFPHLHSHSSSTGE-----CLLATTP-----GKTGFSATM--KNPSEIRLLFS-----PHLQK-----
 Chicken 407 TNLPSVLS-----RTV-----NSSSSFSTIR--NQTLDKL--DTSYSSKETDQEVICLEPAALPSP
 Xenopus 424 FKFNKLAVHDIGTKESENSANSAPNFMKIG----NKTSSFSFRAGGDSIMEN-SFN-----FHS-----
 Zebrafish 430 PTFGVTPSNL---T-----SLTPVTSKREGVKTGFSFRK--S-IASVM--SVGD--ESVFED-----

BLM

Human 499 -----S FVSSNWAET-----PRL-----
 Mouse 507 -----S FVSSNWAET-----PRM-----
 Dog 504 -----S FVSSNWAET-----PRI-----
 Chicken 458 KVNGKGSTLSRPSSEASFNQSWCEK-----PT-----
 Xenopus 478 -----S VLSNSRFNT-----PQN-----
 Zebrafish 478 -----S DCIINGVETPGGTWNPNSSTKI SAGRDTFNQSIQTLSKPEKSTDKCYSRSLSFNESSNQTDLFYS

3

Human 512 -----GKKNESSYFPGNVLSTAVK DQNKHTA--SINDLERETQPSMDIDNFDIDDFDD--DDWEDIMHNLAASKSS
 Mouse 520 -----ENRNESTDFPGSVLSTTVK AQSQA--SGWNVERHGQASMDIDNFDIDDFDDDDDDDDWENIMHNFPASKSS
 Dog 517 -----EKRNESSYFLGNVLTSTAVR DQNKRAA--PINDLE--IQAACDIDNFDIDGDFDD--DDWEDIMHDLAASRSS
 Chicken 485 -----GRDSGNWRVPERPTASTALKAQHTAPAGNPASGCWDVNDTDFDIDHFDIDDFDE-----GWE EAVAPEAAPEAP
 Xenopus 491 -----EKP-----ISSSTCTRP---YSQ--PIDDM-NPDLDFDIDNFDIIDLDDI---HCLD SP-AAPSVSSKN
 Zebrafish 543 PKRVDSGSRNADSSVEINL IAGSSSLRT---GAE--PVD-----DIDLDDFDIDDFDENIPDYVEEPPSVLESRNN

Helicase

Human 581 -TAAYQPIKEGRPIKVSERLSSAKTDCLEVS-STAQNINFSESIQNYTDKSAQNLASRNLKHERFQSLSFPHTKEMMKI
 Mouse 592 -TATYPPIKEGGPVKLSERISSAKAKFLFVV-STAQNTNLSESIQNCSDKLAQNLSKPKHEHFQSLNFPHTKEMMKI
 Dog 584 -TAACLPIKEGRPVKVSERISSAKTNCLFVA-STAQKN-SESIQNYTDKSAQNLASRNLKHERFQSLSFPHTKEMMKI
 Chicken 554 PAPQWQPLREGSA--SLRCRLLAAAAGSAGGPHPTAPKSG-----CGISAKSSSEPLVNP AHERFRGMKFSHSEEMTKI
 Xenopus 546 -VPQYPTIREAQLDSRNKEKNTNRN-----NTGDTN-----PSLLSDSLLKQIENPAHERFRGFNFPHSKEMMKI
 Zebrafish 610 -GVKTPSVEEGGSSKSFERKTF-----TFEAP-KSIK-----TPNPEPLYRNP AHRFRGFNFPHSPPEMKI

Helicase

Human 659 FHKKFGLNHFRFNQLEA INAALLGEDCFILMPTGGGKSLCYQLPACVSEGVTIVISPLRSLIVDQVQKLTSLDIPATYLT
 Mouse 670 FHKKFGLNHFRFNQLEA INAALLGEDCFILMPTGGGKSLCYQLPACVSEGVTIVISPLRSLIVDQVQKLTSLDIPATYLT
 Dog 661 FHKKFGLNHFRFNQLEA INAALLGEDCFILMPTGGGKSLCYQLPACVSEGVTIVISPLRSLIVDQVQKLTSLDIPATYLT
 Chicken 627 FHKKFGLNHFRFNQLEA INAALLGEDCFILMPTGGGKSLCYQLPACVSEGVTIVISPLRSLIVDQVQKLTSLDIPATYLT
 Xenopus 611 FHKKFGLNHFRFNQLEA INACLGGEDCFILMPTGGGKSLCYQLPACVSEGVTIVISPLRSLIVDQVQKLTSLDIPATYLT
 Zebrafish 670 FHKKFGLNHFRFNQLEA INASLLGEDCFILMPTGGGKSLCYQLPACVSEGVTIVISPLRSLIVDQVQKLTSLDIPATYLT

Helicase

Human 739 GDKTDEAATNIYQLSKKDPIIKLLYVTPEKICASNRLSTLENLYERKLLARFVIDEAHCVSQWGHDFRDYKRMNMLR
 Mouse 750 GDKTDEAANIYQLSKKDPIIKLLYVTPEKVCASNRLSTLENLYERKLLARFVIDEAHCVSQWGHDFRDYKRMNMLR
 Dog 741 GDKTDEATSIIYQLSKKDPIIKLLYVTPEKVCASNRLSTLENLYERKLLARFVIDEAHCVSQWGHDFRDYKRMNMLR
 Chicken 707 GDI TDAASKTYMQLSKKDPIIKLLYVTPEKVCASNRLSALENLYNRKLLARFVIDEAHCVSQWGHDFRDYKRLNMLR
 Xenopus 691 GDKTDEAASIIYQLSKKDPIIKLLYVTPEKVCASRLSTLENLYERKLLARFVIDEAHCVSQWGHDFRDYKRLNMLR
 Zebrafish 750 GDKTDEAARIYQLSKKDPIIKLLYATPEKVCASGRMISALONLYERKLLARLVIDEAHCVSQWGHDFRDYKRLHEL

Helicase

Human 819 QKFPSVPMALTATANPRVQKDILTQLKILRPQVFSMSFNRHNLKYVLPKKPKKVAFDCEWIRKHHHPYDSGIYCLSR
 Mouse 830 QKFPSVPMALTATANPRVQKDILTQLKILRPQVFSMSFNRHNLKYVLPKKPKKVAFDCEWIRKHHHPYDSGIYCLSR
 Dog 821 QKFPSVPMALTATANPRVQKDILTQLKILRPQVFSMSFNRHNLKYVLPKKPKKVAFDCEWIRKHHHPYDSGIYCLSR
 Chicken 787 KKFHSPVPMALTATANPRVQKDIQNQLEMLKQVFSMSFNRHNLKYVLPKKPKKVAFDCEWIRKHHHPYDSGIYCLSR
 Xenopus 771 QKFQSPVPMALTATANPRVQKDIINQLKILRPQVFSMSFNRDNLKYVLPKKPKKVAFDCEWIRKHHHPYDSGIYCLSR
 Zebrafish 830 RMFPNVPMALTATATPRVQKDIINQLKILRPQVFSMSFNRNNLKYVLPKKPKKVAFDCEWIRKHHHPYDSGIYCLSR

Helicase

Human 899 RECDTADTLQRDGLAALAYHAGLSDSARDEVQKWINQDGCQVICATIAFGMGIDKPDVRFVIHASLPKSEGGYYQESG
 Mouse 910 RECDTADTLQREGLAALAYHAGLSDSARDEVQHKWINQDNCQVICATIAFGMGIDKPDVRFVIHASLPKSEGGYYQESG
 Dog 901 RECDTADTLQKDGGLAALAYHAGLSDSARDEVQHKWINQDGCQVICATIAFGMGIDKPDVRFVIHASLPKSEGGYYQESG
 Chicken 867 HECDTAAAILQKEGLAALAYHAGLSDSNRDLVQKWINQDGCQVICATIAFGMGIDKPDVRFVIHASLPKSEGGYYQESG
 Xenopus 851 HECDTADTLQKEGLAALAYHAGLSDSNRDYVQHKWINQDGCQVICATIAFGMGIDKPDVRFVIHASLPKSEGGYYQESG
 Zebrafish 910 NDCDTADSLQRAAGLAALAYHAGLSDSDREYVQNKWINQDGCQVICATIAFGMGIDKPDVRFVIHASLPKSEGGYYQESG

Helicase

RQC

Human 979 RAGRDEISHCLLFYIYHDVTRLKRLIMMEKDGNIHTRETHFNNLYSMVHYCENITECRRIQLLAYFGENGFPNDFCKKH
 Mouse 990 RAGRDEISHCVLFYIYHDVTRLKRLIMMEKDGNYHTRETHVNNLYSMVHYCENITECRRIQLLAYFGEKGFNDFCKKY
 Dog 981 RAGRDEISHCLLFYIYHDVTRLKRLIMMEKDGNRHTRETHFNNLYSMVHYCENITECRRIQLLAYFGESGFNDFCKKY
 Chicken 947 RAGRDEISHCLLFYSYSDVTRLRLRLIMMEKDGNSHTRETHFNNLYSMVHYCENNVDCRRIQLLAYFGETDFNDFCKDH
 Xenopus 931 RAGRDEISHCLLFYSYHDVTRIRRLIQMEKDGNSHTRETHFNNLYSMVHYCENNVVECRRIQLLSYFGENNFNDFCKEH
 Zebrafish 990 RAGRDEISHCVLFYSYSDVTRIKRLIAMMEKDGNIHTRETHFNNLYSMVHYCENVAECRRIQLLAYFGEHTFNDFCKEH

BLM

RQC

Human	1059	PDVSCDNCCKTKDYKTRDVTDDVKSIIRFVQEHSSSQGMRNIKHVGPSGRFTMNMLVDIFLGSKSAKIQSGIFGKGSAYS
Mouse	1070	PDVSCDNCCKTKDYKTRDVTDDVKNIIRFVQEHSSSPGTRNI---GPAGRETNMLVDIFLGSKSAKIKSGIFGKGTYS
Dog	1061	PDVSCDNCCKTKDYKTRDVTDDVKNIIRFVQEHSSSQGTRIKNQLGPSGRFTMNMLVDIFLGSKSAKIQSGIFGQGSTYS
Chicken	1027	PEVICDNCGRKKDYKSRNVTDVVKSIIRFVQHQCGQVGGINGNRNTGSGRYTINMMVDIFLGAKSAKIQSGIFGKGAAYS
Xenopus	1011	TQVACDNCGLGKKNYKSRDVTDDVGNIRFVQDNCSLVQGRGKGR-SNNTRLTINMMVDIFLGSKSAKIQSGIFGKGAAYS
Zebrafish	1070	PEVICDNCARPKNKYKSRNVTDVVKTIIRFVQDNCSEKVNRYGKS-AQQNRLTINMLVDIFLGSKSAKIQSGIFGVGAAYS

RQC

HRDC

Human	1139	RHNAERLFRKKLILDKILDEDLYINANDQAIAYVMLGNKAQTVLNGNLKVFEMETENSSSVKQKAL-VAKV SQREEMVKK
Mouse	1147	RHNAERLFRKKLILDKILDEDLYINANDQPIAYVMLGTRKAHSVLSGHLKVFEMETENSSSIKQKAL-VAKV SQREEVVKK
Dog	1141	RHNAERLFRKKLILDKILDEDLYINANDQPIAYVMPGNKAQTVLNGHLKVFEMETENSTSIKQKAALVAKV SQREEVVKK
Chicken	1107	RHNVERLFRKKLVLDRITLDELYITFNDQAVAYVVLGEKAQAVLNGLLQVFEHETENASAIKORAS-VTKMSQREEMVKK
Xenopus	1090	RHNAERLFRKKLVLDRITLDELYITFNDQAVAYVKMGEKAQAVLNGFLKVFQTESASSIKQKASVVTNTSQREEMVKK
Zebrafish	1149	KHNAERLFRKKLVLDRITLDELYITNSGQAVAYISAGPKAMSVLNGCMQVFEHETENASSIKHRASVCEKMSKREEMVKK

HRDC

Human	1218	CLGELTEVCKSLGKIFGVHYFNIFNTVTLKKLAESLSDPEVLLQIDGVTEDKLEKYGAEMISVLQKYSEWTSVPAEDSSP
Mouse	1226	CLGELTEVCKLLGKIFGVHYFNIFNTATLKKLAESLSDPEVLLQIDGVTEDKLEKYGAEMIPVLQKYSEWTVPAEDGSP
Dog	1221	CLGELTEVCKSLGKIFGVHYFNIFNTVTLKKLAESLSDPEVLLQIDGVTEDKLEKYGAEMIPILQKYSEWTLPAEDGSP
Chicken	1186	CLGELTEVCKTLGKIFGVHYFNIFSTVTLKKLAETLSDAPEVLLQIDGVTEDKLEKYGAEMIKVMDKYSEWTPEDAACQ
Xenopus	1170	QVLELTELCKRLGKIFGVHYFNIFNTATLRRIAESLSDPEVLLQIDGVTEDKLDKYGAEMIDVLQKYSEWTLPEVICQ
Zebrafish	1229	CLGELNDLCKKLGKIFGVHYFNIFSTATLKKLAETLSADPEVLLQIDGVTEDKLEKYGAEMIEILLQKYSEWQLPAEAQAE

NLS

Human	1298	GISLSS-SRGPGRSAAE---ELDE-EIPVSSHVFASKTRNERKRRKMPASQSKRRKTASSG--SKAKGGSAT-CRKLSS
Mouse	1306	G-----ARGAPE-DTE---EEEE-EAPVSSHVFANQTRNERKRRKMSATHKPKRRRTSYGG--FRAKGGSTT-CRKTSS
Dog	1301	RISPS-SRSTRRSAPD---EFDE-ETSVSSHVFANKTKNERKRRKMSATHKPKRRRTGFGG--SKTKGGSAT-CRKTSS
Chicken	1266	SVDTAPGSAGTP--GSE---EAAA-DDVVTSSYFGGANQRKRRKRLPNSGESKRRKTSSGG--SQQFYSKGA-RYRRAR
Xenopus	1250	KSGGPA-NVSARR-SNS---DHDD-ESCDKSSYFSSNNKKGPKRKNSSYFGKSKRRKTGGDQQSRSKNINSSYARKNST
Zebrafish	1309	SSGWIDTRGHQN-DEDDNDDEGGGVSTYFRSNSGRGAKRQGSYRKPRRKGGSSQ--NSSAKGQYSS-NWSSSR

4

Human	1370	K-TKSS-SIIIGSSSAS-HTSQ-ATS-GANSKLGIMAPPKPI--NRPFLKPSYAFS
Mouse	1372	K-SKFY-GVTGSRAS-CASQ-ATS-SASRKLGIMAPPKPIV--NRTFLRPSYAFS
Dog	1373	K-SKSS-NIFGPHSSL-HGSQ-AAS-GAARKLGIMAPPKPI--NRPFLKPSYAFS
Chicken	1337	R-----APGSRAAAPQSS-ALR-GAGARLGIMAPPKPS--SRHFLQPSYAVL
Xenopus	1324	A--K-----TSSS-YISG-SKT-GADKRPGFMAPPMPO-PNRRFLKPSYSMF
Zebrafish	1386	GGGKGGGYRGGSRGAG-RGSRSAPSGSAAKRPGFMSLPTEQAAARPFLKPSYSHL

RM11

3H

OB1

Human 1 MNVT-SALRAETWLLAAWHVKVPPMWLEACINWIQEENNNVNLSQAQINKQVFEQWLLTDLRDLEHPLLPDGLILEIPKG
 Mouse 1 MSVA-SAVLRVETWLLATWHVKVPPMWLEACVNWIQEENNATLSQAQINKQVLEQWLLTDLRDLEHPLLPDILELIPKG
 Dog 1 MNVT-NALRVETWLLATWHVKVPLTWLEACVNWIQEENDNVNLSQAQINKQVFEQWLLTDLRDLEHPLLPDGLILEVPGK
 Chicken 1 MSTP-NVARTVETWLLSSTWHVKVPLTWLEACINWIQEENGGNLSQAQINKQVFEQWLLTDLRDLEHPLLPDGLILDAPKG
 Xenopus 1 MMATSGTANRVKTWLLISTWHVKVPPDWLEACINWIQEENG-SSLLQAEINKQVFEQWLLTDLRDLEFPVLPANITDSLKC
 Zebrafish 1 MSVG-EVQ-VIQAWLRSEWHIQVPPAWLLACVNWIKKEADRASIPQSQINKQVLEQWLLTDLRDLAHPVLPRISEAQKT

OB1

Human 80 EINGFYAQLQINSLVDVSPAYSQIQKLRGKNTTNDLVIAEAQVTPKPWEAKPSRMLMLQLTDGIVQIQGMEYQPIPIILHS
 Mouse 80 EINGFYAQLQINSLVDVSPAYSQIQKLRGKNTTNDLVIAETQSTPKPWEVFPSPRMLMLQLTDGIVTHIQGMEYQSIIPALHS
 Dog 80 ELTGFYALQINSLVDVSPAYSQIQKLRGKNTTNDLITAEATQVTPKPWEAKPSRMLMLQLTDGIVQIQGMEYQSIIPVLHS
 Chicken 80 ELSGFYSLQIDSLLDVSPAYSQIQKLRGKSTVNEEVIANQAFQKPWEAKPTRMLMLQLTDGIVHQIQGMEYQFVPIVLS
 Xenopus 80 EINGFHAVQMDSLVDLSTIPAYSQIQKLRGKDSITNEQVCTTQSQKPWEAKPTRMLMLQLTDGTQHIQAMEYRPIQAINA
 Zebrafish 79 VLSNRCCVQMDSLLDVSPAYNQLQRIRGTDCSNDQVSAVTOETQRPWEAKPTRMLMLQLTDGIVQNLGMEYRPIIPALNA

OB1

Human 160 DLPPGTKLILTYGNISFRLGVLLKPNVVKLGGEVDALIEEYAEKVLARLIGEPDLVSVIPNNSNENIPRVTDVLDPA
 Mouse 160 GLPPGTKLIVRGCILFRGLVLLKPNVVKLGGEVDGLSEENAQEKVLARLIGELDPTVPVIPNNSIHNVPKVSGLDAV
 Dog 160 DLPPGTKLILTYGNISFRLGVLLKPNVVKLGGEVDALIEEYAEKVLARLIGEPDPIVSVIPNPNQSIGITDVLDP
 Chicken 160 NLPPGTKLIVHGNVAYRGLVLLKPNVVKLGGEVDALIEEYSQERVLARLIGEAENPDSVRQPGHEQIVPGVDELGQT
 Xenopus 160 NLSPPGTKMVLQGTIVCRGLVLLKPNVVKLGGEVEALNAEYTOTKVLARLIGVEDNTVAQHSNVQEAHAGVAAGELGQA
 Zebrafish 159 NLPPGTKLQIVGPIAVRGLVLLKAEINKVGLGGEVEQLIEIHSQSRVLCGTGLPEETH-----

5

Human 240 LGPSDEELLASLDENDELNTSSR-CFTTGSSSN-----TIPTRQSSFE-----
 Mouse 240 LGPSDEELLASLDESEESAANNVAMRSCFSTGTSSN-----TPTNPSGFE-----
 Dog 240 LGPSDEELLASLDENE-FAAINDTSLDRRFFSTDSSSN-----TITRQSSFE-----
 Chicken 240 LGPSDEELLASLDENNDFILNNETSLSGYCSRSNNFSAATSCSLTYNENTTGFPLQ-----
 Xenopus 240 LGPSDEELLASLENEEFINSNGVPSISGYYSRNENSS-----ISSSTQHQTQDSIVRCWVDDDDILEFSINNGVPS
 Zebrafish 223 PQQEPGLVASVADSGYSSLASEASLRH-----PQ-----SQPLPQISRQ-----

6

Human 287 -----PEFVISPSPKLEPSNLS-----IHVMDGELDDFSLLEFALLLEETVQKEQMETKELQPIITFNR
 Mouse 288 -----PGCNISSRPKLEKPPNQP-----THFTDGEFDDFSLLEFALLLEETVQKEQMETKASQPLTLKE
 Dog 287 -----EQRIISPSPKLEKPPDPS-----MCFTDGEELDDFSLLEFALLLEETVQKEQMETTELQPLTLNR
 Chicken 297 -----QESVNLPRSDIQT-PS-----VEYNDAFLNDFLEDDILLEETVQRELEEV----SVARNG
 Xenopus 313 GYYSRNENSSISSSTQHQTQDSIVRQTSFPMLDQTVVHVNVANNHAIIEEQDIDDELFLLEETVQRELEEMSMSQAEV---
 Zebrafish 258 -----DDWDMDEIPDIDFRSIP-----DHFDLPLQNNNPLEDVPEDFDIDIP--LDEL--NVMCPI

Human 344 NADRSI-----ERFSHPNPTNNFSLTC--KNGNNWSEKN-----VSEQM
 Mouse 345 NTGKCM-----EIFSHKPSLNHTALIH--KQGNFDEKT-----SEQM
 Dog 344 TPDESIEIVSQMETEELQPLTLNRPDESTIERVSHKPNLTGNFSLTC--KSRNNWNKKN-----LSEQM
 Chicken 351 NVNLST-----ERIPHTYRSCGSSLNETSEKDDGCGSEKPEVETSKQKNLARTVSTGDG
 Xenopus 390 -----
 Zebrafish 310 DVEVSA-----GTLEDPERNKHDSS-----

Human 383 TNEKDSFGCPSVRDQNRSIFSVHCNVPLAHDFTNKEKNLETDNKIKQT-SSSDSHSLNNKIL--NREVVNYVQKRNLSQIS
 Mouse 383 IHEDKFFDCASTRNHHR-F-----SAHDFTNDSKISEVDDAAQQTLSNNVHCLRNKIL--NRKLD--LSEKSSQIS
 Dog 408 INEGSFCSPSAGDQNSVFSVHNNVPLPHDFTNK--DSETDNKIKQTFSSIDGHSNNKISISNGELVNYVPKSSSHIS
 Chicken 406 TSTGGSLLQCNSVSQACSSAIVLLK---NPHEERN--DLGPDESSCQSRHAPDSRQLNKD-----PVSSSKTD
 Xenopus 390 -----THGS
 Zebrafish 330 -----LLNGSKPEEVS-----FPSRSRLIGNT-----YQSRTLN

OB2

Human 460 NENDCNLQSCSLRSEENSINLSIAMDIYSPPEFVYLSVLMNA--SKPKETITVVKAFIVTLTGNLSSSGGIWSTAKVSDG
 Mouse 451 KENGHPFQACSSRSFENNTYLSIGMDLHSPPEFIYLSVLMNA--SKPKETITVVKAFIVTLTGNLSSSGGFVGTAKVSDG
 Dog 486 NENDHLLQTCSSRSSEYSTPLSSAMDIYSPPEFIYLSVLMNA--SRPKETITVVKAFIVTLTGNLSSSGGIWSTAKISDG
 Chicken 469 PEADQQAILCR-P-----GNACDLIDSPPEFTYLSLILNA--KPKETITLVKVKCFIVTLTGNLSSNGSWGAKAVSDG
 Xenopus 394 TDLPTTSLATS--HASSAS-CTSDQNNIDIPPYTYLSTILNA--SKSRSTITVVKLKSFIVTLTGNLSSHSCGLWNTAKAKISDG
 Zebrafish 358 KVPNTSLASCSTST-----LDSSACKETP-MYLCSLQAGCWPEKSPQVFRLOAFIVTLTGNLRISSGGVWKGATISDG

RM11

OB2

Human	538	TAYLDVDFVDEILTSLIGFSVPPEMKQSEKDPDLQYQKFLRGLQKCQRDLIDICCLMTISNFSLSKAMVLAIQDVMNEHLE
Mouse	529	TAYLDVDFIDEILTSWIGYVPEMKQLKDPDKYKTFLEGLQKCQRDLIDICCLMTISNDFSSCKGVVLEIQDVMGMEHVE
Dog	563	TAYLDVDFADEILTSLIGFSVPPEMKQSEKDPDLQYQKFLRGLQKCQRDLIDICCLMTISNFSLSKAMVLAIQDVMKTEHLE
Chicken	540	SAYLDVDFADDILTSLIGFSVPPEMHTLEKDPALQPKLKGLEERCQKQLIDICCLMTIEENFFQSKATVLIQDVTDARHLE
Xenopus	470	TGYLNVDFESDDVLTSLIGFTVPEMKTLKDPSSQQSTLMRGLQKCQRMLIDFCGVMTVSNFAKEEAVVLSIQDVTTEEIMQ
Zebrafish	430	SGYLDVDLSDNMLSELIGFSAAEITRVLEKDLARRGEVDSGTQHCQRELVDMCCMMSVQVDLT-GRGVVLSASFTSDRECS

OB2

Human	618	NLKKRLN---K
Mouse	609	NLKKRLN---K
Dog	643	NLKKRLN---K
Chicken	620	QLKKRLN---K
Xenopus	550	SLQKTLR---S
Zebrafish	509	EMQKRVKEARR

RM12

OB3

Human	1	MAAA	DS-FS	-----	GGPAGVRLPR	S	P	L	K	V	L	A	E	Q	L	R	R	D	A	E	---	G	P	C	A	W	R	L	S	-	R	A	A	A	G	R	C	P	L	D	L	A	A	V	W	M	Q	G	R	V					
Mouse	1	MAAA	SESLS	-----	SGGPGAVRLPRL	P	P	L	K	V	L	A	G	Q	L	R	R	H	A	E	---	G	P	C	A	W	R	L	S	-	R	A	A	V	G	R	A	P	L	E	I	V	A	V	W	M	Q	G	T	V					
Dog	1	MAAA	AP-VGAAGSVAGGGG	FPVAVRLPR	S	P	L	K	V	L	A	E	Q	L	R	R	D	A	E	---	G	P	C	A	W	R	L	S	-	R	A	A	T	G	R	C	P	L	E	L	V	T	V	W	M	Q	G	T	V						
Chicken	1	MAGEA	-----	-----	AS	P	L	K	V	L	A	A	Q	L	R	A	A	G	R	---	G	A	G	T	W	R	L	S	-	R	T	E	T	G	R	A	P	L	C	I	R	A	V	W	M	Q	G	T	V						
Xenopus	1	MATR	ET-SA	-----	SGG	---	F	Q	F	S	P	P	M	K	L	A	G	K	L	R	E	C	T	K	R	S	-	G	A	T	P	S	F	W	L	E	W	-	G	P	S	G	G	P	L	D	V	S	L	V	L	Q	G	N	L
Zebrafish	1	MMCASFL	-SA	-----	DRARS	P	P	M	K	V	L	S	S	Q	L	R	E	A	S	E	S	Q	S	S	G	K	E	V	V	-	R	R	L	G	A	S	G	R	R	S	L	Q	V	S	V	W	M	Q	G	T	V				

OB3

Human	66	MAD	---	R	G	E	A	R	L	R	D	P	S	G	D	F	S	V	R	G	L	E	R	V	P	R	G	P	C	L	I	V	P	G	K	Y	V	M	V	M	G	V	V	Q	A	C	S	P	E	E	C	L	O	A	V	K	M	T	D	L	S	D	N	-	P	H	E	S	M	W	E	L	E	V	E	D			
Mouse	68	AAE	---	G	Q	A	R	L	R	D	S	S	G	A	F	S	V	R	G	L	E	R	V	P	R	G	P	C	L	L	P	G	K	Y	V	M	V	M	G	V	V	Q	A	C	S	P	E	E	C	L	O	A	V	K	M	T	D	L	S	D	N	-	P	M	H	E	S	M	W	E	L	E	V	E	D				
Dog	75	TAG	---	G	G	E	A	R	L	R	D	P	S	G	A	F	S	V	R	G	L	E	R	V	P	R	G	P	C	L	I	V	P	G	K	Y	V	M	V	M	G	V	V	Q	V	C	S	P	E	E	C	L	O	A	V	K	M	T	D	L	S	D	N	-	P	M	H	E	N	M	W	E	L	E	V	E	D		
Chicken	53	Q	V	E	R	G	G	G	S	A	R	L	R	D	G	S	G	H	F	T	V	L	G	V	E	D	V	P	R	G	P	C	L	S	A	G	K	Y	V	M	V	M	G	V	V	R	A	C	S	P	E	P	V	L	R	A	T	K	M	T	D	L	S	E	N	-	P	M	H	E	E	M	W	G	L	E	V	E	E
Xenopus	66	Q	V	R	P	D	R	G	T	T	L	R	L	D	D	T	H	T	F	V	C	G	A	D	K	V	P	K	G	P	C	L	E	I	G	K	Y	V	M	V	M	G	V	V	L	S	S	P	E	E	I	L	R	A	V	K	I	T	D	L	S	D	N	-	P	M	H	S	L	M	W	K	T	E	V	H			
Zebrafish	65	E	L	Q	A	D	-	N	N	T	L	L	L	D	E	T	G	N	F	T	V	N	G	I	N	S	V	P	R	G	P	C	L	S	P	G	K	Y	V	M	V	M	G	V	V	Q	S	H	S	P	E	P	V	L	R	A	V	K	M	A	D	L	S	A	N	A	A	H	R	R	N	W	I	E	V	E	D		

OB3

Human	142	L	H	R	N	I	-	-	P
Mouse	144	L	H	R	N	I	-	-	P
Dog	151	L	H	R	I	I	-	-	P
Chicken	132	L	H	R	V	I	-	-	P
Xenopus	145	L	H	R	N	I	L	R	P
Zebrafish	144	L	Q	R	V	I	-	-	P

TOP3A

		TOPRIM																																																																												
Human	1	M	I	F	P	V	A	R	Y	A	---	L	R	W	L	R	R	P	-	E	D	R	A	F	S	-	R	A	A	M	E	M	A	L	R	-	G	V	R	K	V	L	C	V	A	E	K	N	D	A	A	K	G	I	A	D	L	L	S	N	G	R	M	R	R	E	G	L	S	K	F	N	K	I	Y	E	F	D
Mouse	1	M	I	F	P	V	T	L	L	A	---	F	Q	W	H	R	R	P	-	G	G	R	A	L	S	-	R	A	A	M	E	V	A	F	R	-	G	V	R	K	V	L	C	V	A	E	K	N	D	A	A	K	G	I	A	D	L	L	S	N	G	R	M	R	R	E	G	L	S	K	F	N	K	I	Y	E	F	D
Dog	1	M	I	F	P	V	A	R	S	A	---	L	R	W	L	R	P	-	G	A	R	T	L	S	-	R	A	A	M	E	V	A	F	R	-	G	V	R	K	V	L	C	V	A	E	K	N	D	A	A	K	G	I	A	D	L	L	S	N	G	R	M	R	R	E	G	L	S	K	F	N	K	I	Y	E	F	D	
Chicken	1	M	N	F	Q	A	R	L	L	A	S	C	G	V	R	M	P	Q	-	W	-	R	G	F	S	-	R	A	A	E	G	P	A	V	Q	-	R	I	K	V	L	C	V	A	E	K	N	D	A	A	K	G	I	A	D	L	L	S	N	S	R	M	R	R	E	G	L	S	K	F	N	K	I	Y	E	F	D	
Xenopus	1	M	V	I	L	S	R	V	L	A	L	S	K	F	K	V	L	R	P	-	A	V	R	F	C	S	H	R	T	A	E	M	A	L	R	I	P	V	Q	K	V	L	C	V	A	E	K	N	D	A	A	K	G	I	A	D	L	M	S	N	S	R	M	R	R	E	G	L	S	K	F	N	K	I	Y	E	F	D
Zebrafish	1	M	N	V	L	F	R	---	---	---	A	R	K	T	V	N	S	R	F	Y	R	-	H	I	S	V	S	M	I	R	T	Q	I	K	V	L	C	V	A	E	K	N	D	A	A	K	G	I	A	D	L	M	S	N	G	S	R	R	R	E	G	S	V	N	K	I	Y	E	F	D								

		TOPRIM																																																																											
Human	75	Y	H	L	Y	G	Q	N	V	T	M	V	M	T	S	V	S	G	H	L	A	H	D	F	Q	M	Q	F	R	K	W	C	S	C	N	P	V	L	F	A	E	T	E	K	Y	C	P	E	N	F	I	D	I	K	T	L	E	R	E	T	R	Q	C	A	L	I	V	I	W	T	D	C	D	R	E	G	E
Mouse	75	Y	H	L	Y	G	Q	N	V	T	M	T	M	T	S	V	S	G	H	L	A	H	D	F	Q	M	Q	F	R	K	W	C	S	C	N	P	V	L	F	A	E	T	E	K	Y	C	P	E	N	F	I	D	I	K	T	L	E	R	E	T	H	H	C	A	L	I	V	I	W	T	D	C	D	R	E	G	E
Dog	75	Y	H	L	Y	G	Q	N	V	T	M	V	M	T	S	V	S	G	H	L	A	H	D	F	Q	M	Q	F	R	K	W	C	S	C	N	P	V	L	F	A	E	T	E	K	Y	C	P	E	N	F	I	D	I	K	T	L	E	R	E	T	Q	Q	C	A	L	I	V	I	W	T	D	C	D	R	E	G	E
Chicken	77	Y	Q	M	F	G	Q	N	V	T	M	V	M	T	S	V	S	G	H	L	A	H	D	F	K	L	F	E	R	K	W	H	S	C	N	P	A	L	F	A	E	T	E	K	Y	C	P	E	N	F	I	D	I	K	T	L	E	R	E	V	Q	C	A	L	I	V	I	W	T	D	C	D	R	E	G	E	
Xenopus	80	Y	H	L	F	G	K	D	V	T	M	V	M	T	S	V	S	G	H	L	A	E	F	M	D	H	M	K	W	H	S	C	N	P	S	L	F	A	E	V	Q	K	Y	C	P	E	N	F	I	D	I	N	I	K	T	L	E	R	E	V	R	Q	C	A	L	I	V	I	W	T	D	C	D	R	E	G	E
Zebrafish	72	Y	N	L	F	G	Q	N	V	T	M	T	M	T	S	V	S	G	H	L	A	E	F	K	A	F	Q	K	W	H	S	C	S	P	L	L	F	A	E	V	E	K	Y	C	P	E	N	F	I	D	I	K	T	L	E	R	E	V	R	Q	C	A	L	I	V	I	W	T	D	C	D	R	E	G	E		

		TOPRIM														TopA																																																															
Human	155	N	I	G	F	E	I	H	V	C	K	A	V	K	P	N	L	Q	V	L	R	A	R	F	S	E	I	T	P	H	A	V	R	T	A	C	E	N	L	T	E	P	D	Q	R	S	D	A	V	D	V	R	Q	E	L	D	R	I	G	A	A	F	T	R	F	Q	T	L	R	L	Q	R	I	F	P	E	V	L	
Mouse	155	N	I	G	F	E	I	H	V	C	K	A	V	K	P	N	L	Q	V	L	R	A	R	F	S	E	I	T	P	H	A	V	R	T	A	C	E	N	L	T	E	P	D	Q	R	S	D	A	V	D	V	R	Q	E	L	D	R	I	G	A	A	F	T	R	F	Q	T	L	R	L	Q	R	I	F	P	E	V	L	
Dog	155	N	I	G	F	E	I	H	V	C	K	A	V	K	P	N	L	Q	V	L	R	A	R	F	S	E	I	T	P	H	A	V	R	T	A	C	E	N	L	T	E	P	D	Q	R	S	D	A	V	D	V	R	Q	E	L	D	R	I	G	A	A	F	T	R	F	Q	T	L	R	L	Q	R	I	F	P	E	V	L	
Chicken	157	N	I	G	F	E	I	H	V	C	K	A	V	K	P	N	L	Q	V	L	R	A	R	F	S	E	I	T	P	H	A	V	R	T	A	C	E	N	L	T	E	P	D	Q	K	T	S	D	A	V	V	R	Q	E	L	D	R	I	G	A	A	F	T	R	F	Q	T	L	R	L	Q	R	I	F	P	E	V	L	
Xenopus	160	N	I	G	F	E	I	H	V	C	K	A	V	K	P	N	L	Q	V	L	R	A	R	F	S	E	I	T	P	R	S	I	R	M	A	C	B	H	L	V	Q	P	D	O	N	I	N	D	A	V	D	V	R	T	E	L	D	R	I	G	A	A	F	T	R	F	Q	T	L	R	L	Q	R	I	F	P	S	V	L
Zebrafish	152	N	I	G	F	E	I	D	V	C	K	A	V	K	P	N	L	Q	V	L	R	A	R	F	S	E	I	T	P	N	S	I	R	R	A	C	E	L	T	E	P	D	I	N	S	D	A	V	D	V	R	Q	E	L	D	R	I	G	A	A	F	T	R	F	Q	T	L	R	L	Q	R	I	F	P	E	S	L		

		TopA																																																																															
Human	235	A	E	Q	L	I	S	Y	G	S	C	Q	F	P	T	L	G	F	V	V	E	R	F	K	A	I	Q	A	F	V	P	E	I	F	H	K	I	K	V	T	H	-	H	K	D	G	I	V	E	F	N	W	K	R	H	R	L	F	N	H	T	A	C	L	V	L	Y	Q	L	C	V	E	D	P	M	A	T	V	E		
Mouse	235	A	E	Q	L	I	S	Y	G	S	C	Q	F	P	T	L	G	F	V	V	E	R	F	K	A	I	Q	A	F	V	P	E	I	F	H	K	I	K	V	T	H	-	H	K	D	G	I	V	E	F	N	W	K	R	H	R	L	F	N	H	T	A	C	L	V	L	Y	Q	L	C	M	E	D	P	M	A	T	V	E		
Dog	235	A	E	Q	L	I	S	Y	G	S	C	Q	F	P	T	L	G	F	V	V	E	R	F	K	A	I	Q	A	F	V	P	E	I	F	H	K	I	K	V	T	H	-	H	K	D	G	I	V	E	F	N	W	K	R	H	R	L	F	N	H	T	A	C	L	V	L	Y	Q	L	C	M	E	D	P	T	A	T	V	E		
Chicken	237	A	D	Q	L	I	S	Y	G	S	C	Q	F	P	T	L	G	F	V	V	E	R	F	K	A	I	Q	A	F	V	P	E	I	F	H	K	I	K	V	T	H	-	H	E	D	G	N	V	F	N	W	K	R	H	R	L	F	N	H	T	A	C	L	V	L	Y	Q	L	C	M	E	D	P	T	A	T	V	E			
Xenopus	240	S	N	Q	L	I	S	Y	G	S	C	Q	F	P	T	L	G	F	V	V	E	R	F	K	A	I	Q	A	F	I	P	E	I	F	F	Y	K	I	K	V	T	H	E	-	H	E	D	G	L	V	E	F	S	N	K	R	N	R	L	F	N	H	T	A	C	L	V	L	Y	Q	L	C	M	E	D	P	M	A	T	V	E
Zebrafish	232	S	D	Q	L	I	S	Y	G	S	C	Q	F	P	T	L	G	F	V	V	E	R	F	K	A	I	Q	A	F	I	P	E	I	F	F	K	I	K	V	T	H	E	-	P	N	E	E	S	V	E	F	N	W	K	R	H	R	L	F	N	H	T	A	C	L	V	L	Y	Q	L	C	M	E	D	P	M	A	T	V	E	

		TopA																																																																													
Human	314	V	R	S	K	P	K	S	K	W	R	Q	A	L	D	T	V	E	L	E	K	L	A	S	R	K	L	R	I	N	A	K	E	T	M	I	A	E	K	L	Y	T	Q	G	I	S	Y	P	R	T	E	T	N	I	F	P	K	D	L	N	L	V	L	V	E	Q	O	T	P	D	R	W	G	A	F	A			
Mouse	314	V	R	S	K	P	K	S	K	W	R	Q	A	L	D	T	V	E	L	E	K	L	A	S	R	K	L	R	I	N	A	K	E	T	M	I	A	E	K	L	Y	T	Q	G	I	S	Y	P	R	T	E	T	N	I	F	P	K	D	L	N	L	V	L	V	E	Q	O	T	P	D	R	H	W	G	A	F	A		
Dog	314	V	R	S	K	P	K	S	K	W	R	Q	A	L	D	T	V	E	L	E	K	L	A	S	R	K	L	R	I	N	A	K	E	T	M	I	A	E	K	L	Y	T	Q	G	I	S	Y	P	R	T	E	T	N	I	F	P	K	D	L	N	L	V	L	V	E	Q	O	T	P	D	R	W	G	A	F	A			
Chicken	316	V	G	S	K	P	K	S	K	W	R	P	L	P	L	D	T	V	E	L	E	K	L	A	S	R	K	L	R	I	N	A	K	E	T	M	I	A	E	K	L	Y	T	Q	G	I	S	Y	P	R	T	E	T	N	I	F	P	K	E	L	N	L	S	A	L	V	O	H	O	T	O	D	R	N	W	G	A	F	A
Xenopus	319	V	G	S	K	P	K	S	K	W	R	P	V	A	L	D	T	V	E	L	E	K	L	A	S	R	K	L	R	I	N	A	K	E	T	M	I	A	E	K	L	Y	T	Q	G	I	S	Y	P	R	T	E	T	N	I	F	P	K	D	L	N	L	S	L	V	E	Q	O											

TOP3A

		Zinc finger	
Human	713	VYRLKLLKFKRGS	LPPTMPLEFVCCIGGCD
Mouse	713	VYRLKLLKFKRGS	LPPTMPLEFVGCIGGCD
Dog	713	VYRLKLLKFKRGS	LPPTMPLEFVGCIGGCD
Chicken	715	VHRLKLLKFKRGS	VPPMPLFVGCIGGCD
Xenopus	718	VHRLKLLKFKRGS	IPPTMPLEFVGCIGGCD
Zebrafish	712	VHMLKLLKFKRGS	IPPMMPLEFVGCIGGCD
Zinc finger			
Human	785	DSR--QTGSSK--ALAQT-LP-	PP-TAAGESNSVTCNCGQ
Mouse	787	VNR--HTRPSK--TVAQA-LL-	PP-TTAGESNSVTCNCGR
Dog	785	-----M-LPLPA-AADGES	NSVTCNCGQ
Chicken	792	TNM--ATGHLLYLSSTRAPRPA	PSAAPDDGNNAVVCNCGN
Xenopus	797	TKTLKPPVVKP--STSRG-AP-	PI-PGNSESNVVCNCGV
Zebrafish	787	ENI-RPPAPRP--RADFG-LQ-	PP-P-STQGGALVTCNCGQ
Zinc finger			
Human	858	GP-----PALA-YRPLGASLGCP	-----PGPGIHLGGF
Mouse	860	GT-----PTSA-SCPPGSSVGC	-----SSVGSHMDGF
Dog	846	GP-----PASA-LGPPAGSLGHP	-----PAMGDRRGGF
Chicken	870	NAAPRGSAPRRA-FGARGPANSQR	-----PGGKRGPEHF
Xenopus	872	NA-----PAGPSTGRPSNAFNNS	-----RAPDSFRSGG
Zebrafish	858	GV-----PERN-RGPLSQNVQPPR	PSNGFGNVSQQRQNHRS
Zinc finger			
Human	923	AKPREQQCGFFQWVDENTAPG	ISGAPS-----
Mouse	925	AKPREQQCGFFQWVDENVAPG	FAAPA-----
Dog	911	AKPREQQCGFFQWVDENVAPG	ILRTPT-----
Chicken	942	SKPREQQCGFFQWADENVAPG	ASGDFS-----
Xenopus	939	SKPREQQCGFFQWADENVVPG	SSGFSGSSGGSS
Zebrafish	928	GKPREQQCGFFQWADENVAPG	ATA-----
Zinc knuckle			
Human	996	F	CPQNR
Mouse	998	F	CPQNR
Dog	984	F	CPQNS
Chicken	1015	T	CPFLD
Xenopus	1017	N	CPQNR
Zebrafish	993	T	CPQAR

Fig. S1. Sequence alignments of (a) BLM, (b) RMI1, (c) RMI2 and (d) TOP3A orthologs from representative vertebrates. Underlined regions in red denote conserved protein domains/motifs.

Numbered motifs in BLM and RMI1 correspond to sequences synthesized as biotinylated peptides (see main text for further details).

a

Human	1	MAAVPQNNLQEQLERHSARTLNNKLSLSKPKFSGFTFKKKTSSDNNVSVT	50
Mouse	1	MAAVPLNNLQEQLQRHSARKLNNQPSLSKPKSLGFTFKKKTSE-GDVSVT	49
Dog	1	MAAVPQNNLQEQLERHSARKLSNKLSPSKPKSSVFTFKKKTSA-NNVSVT	49
Chicken	1	MAAVPQNNLREQLRLHSARGALSKVLPARSRPAAFTFRRTHSP-AAGPAA	49
Xenopus	1	MAAVPQNNLQKQLELFPKGTSNKLSLQKTKSSVFTFKKKTSP-NVSAST	49
Zebrafish	1	MSSLPQNNLKEHLERHNN-AAQNKLSLLKPKPGGFQFKKKTSS-GISKVE	48
Sgs1	1	MVTKPSHNLRRERKWL-----KETATLQEDKDFEQAIQKHIANKRPK	43
Δ4-37	1	MAA-----KTKTSSDNNVSVT	16

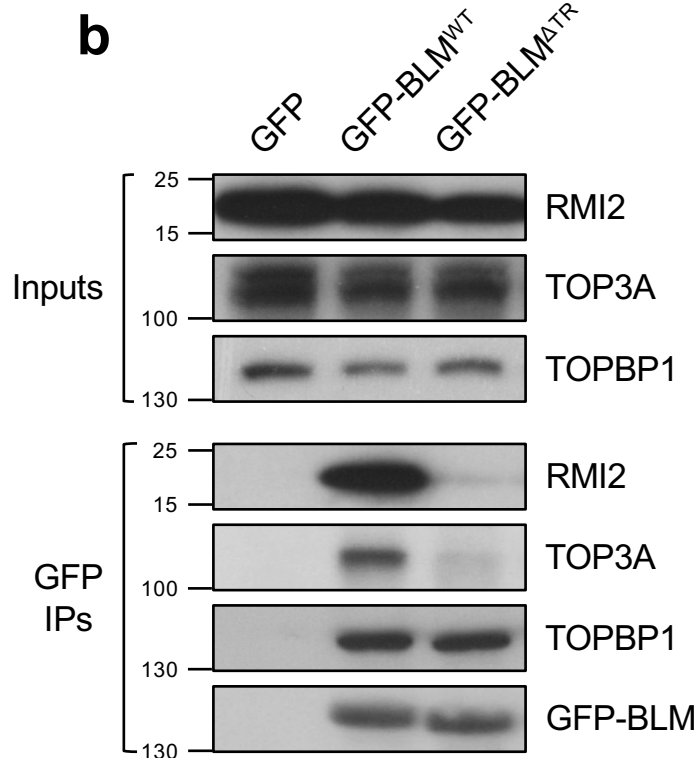


Fig. S2. Identification of a critical region required for BLM to associate with other BTR complex components.

- a) Sequence alignment of the N-terminal TR region of vertebrate BLM orthologs and Sgs1. Residues in red indicate those required for Sgs1 to promote resistance to HU³¹.
- b) Deletion of residues 4-37 in the TR domain of BLM abrogates interaction with the BTR complex. 293FT cells were transfected with the indicated constructs and GFP-pulldowns were carried out from cell lysates, followed by western blotting for the indicated proteins.

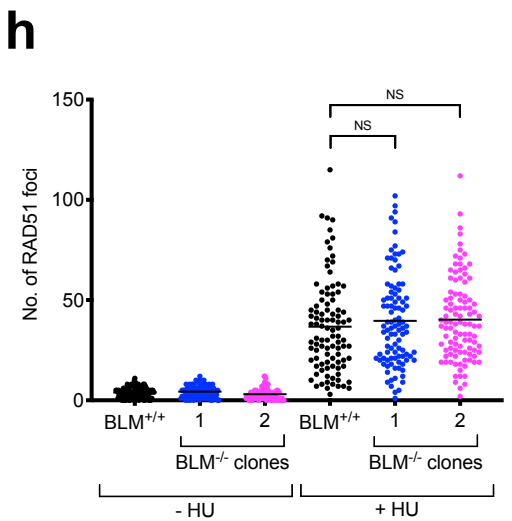
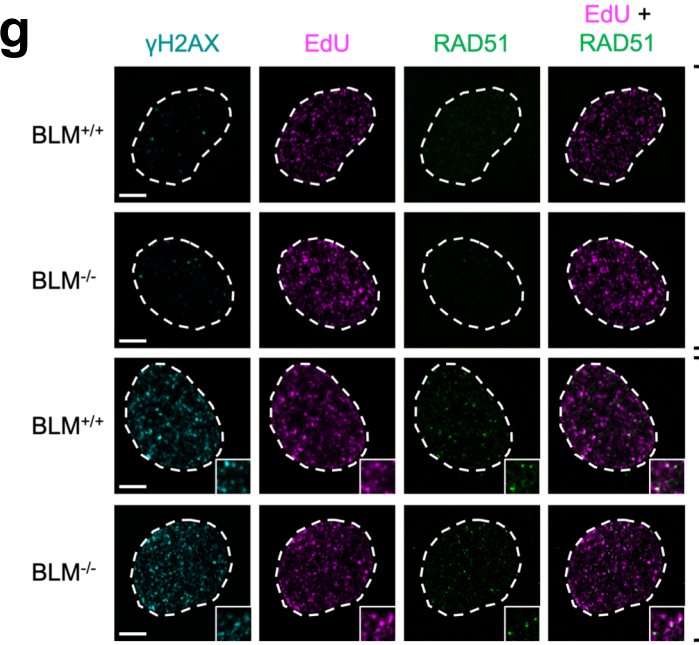
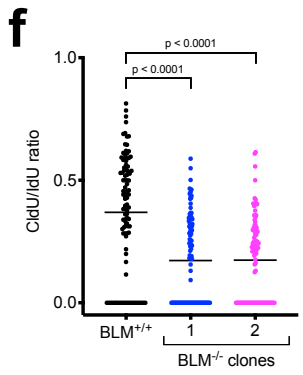
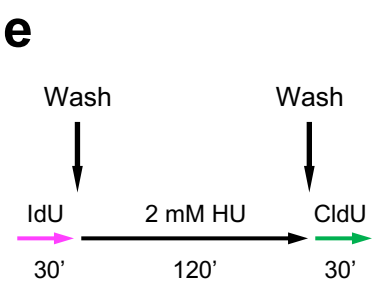
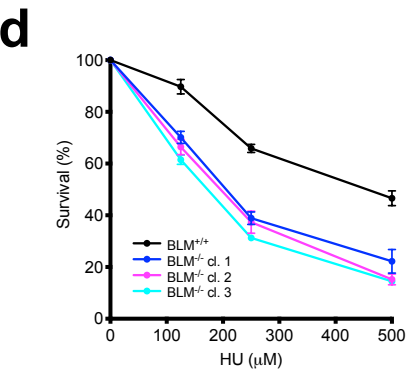
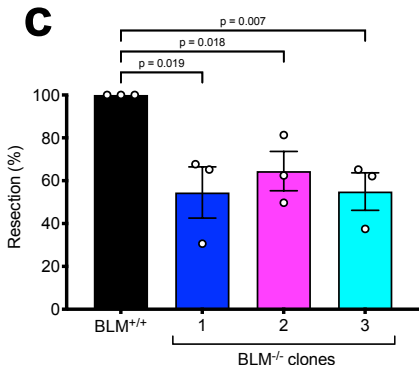
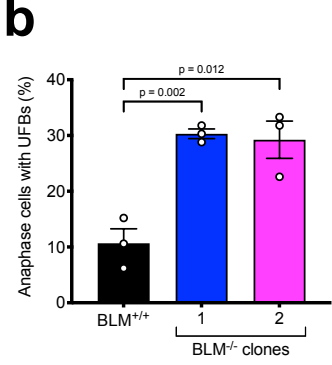
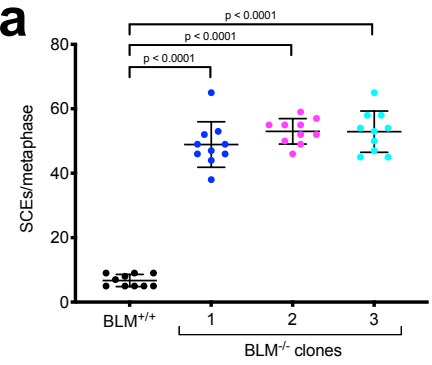


Fig. S3. Characterization of *BLM*^{-/-} RPE-1 cells.

- a) SCE assay showing that all three *BLM*^{-/-} clones have very high levels of SCEs (n=3, one representative experiment shown). At least 10 metaphases were scored per sample. Error bars denote SD. Significance was determined using the two-sided Mann-Whitney *U* test.
- b) Quantification of the increase in UFBs observed in *BLM*^{-/-} cells by immunofluorescence (n=3). Error bars denote SEM. Significance was determined by two-sided unpaired t test.
- c) DNA-end resection is defective in *BLM*^{-/-} cells as measured by RPA loading on chromatin in response to 1 μ M CPT treatment for 1 hr in a FACS-based assay (n=3). Error bars denote SEM. Significance was determined by two-sided unpaired t test.
- d) Colony survival assay showing that *BLM*^{-/-} cells are hypersensitive to HU (n=3). Cells were treated with the indicated doses of HU for 24 hr. "cl." = clone. Error bars denote SEM.
- e) Experimental outline of the DNA fibre assay to measure replication fork restart.
- f) Quantification of the replication fork restart defect in *BLM*^{-/-} cells by DNA fibre assay (n=2, one representative experiment shown). At least 100 DNA fibres were analysed per sample. Significance was determined using the two-sided Mann-Whitney *U* test.
- g) RAD51 foci are not affected by BLM loss in RPE-1 cells. Cells were pulsed with 10 μ M EdU for 15 min to mark sites of active DNA replication and treated where indicated with 2 mM HU for 2 hr. Scale bars, 5 μ m.
- h) Quantification of RAD51 foci in Cyclin A-positive cells, treated where indicated with 2 mM HU for 24 hr (n=2, one representative experiment shown). ~100 cells were analysed per sample. Significance was determined using the two-sided Mann-Whitney *U* test.

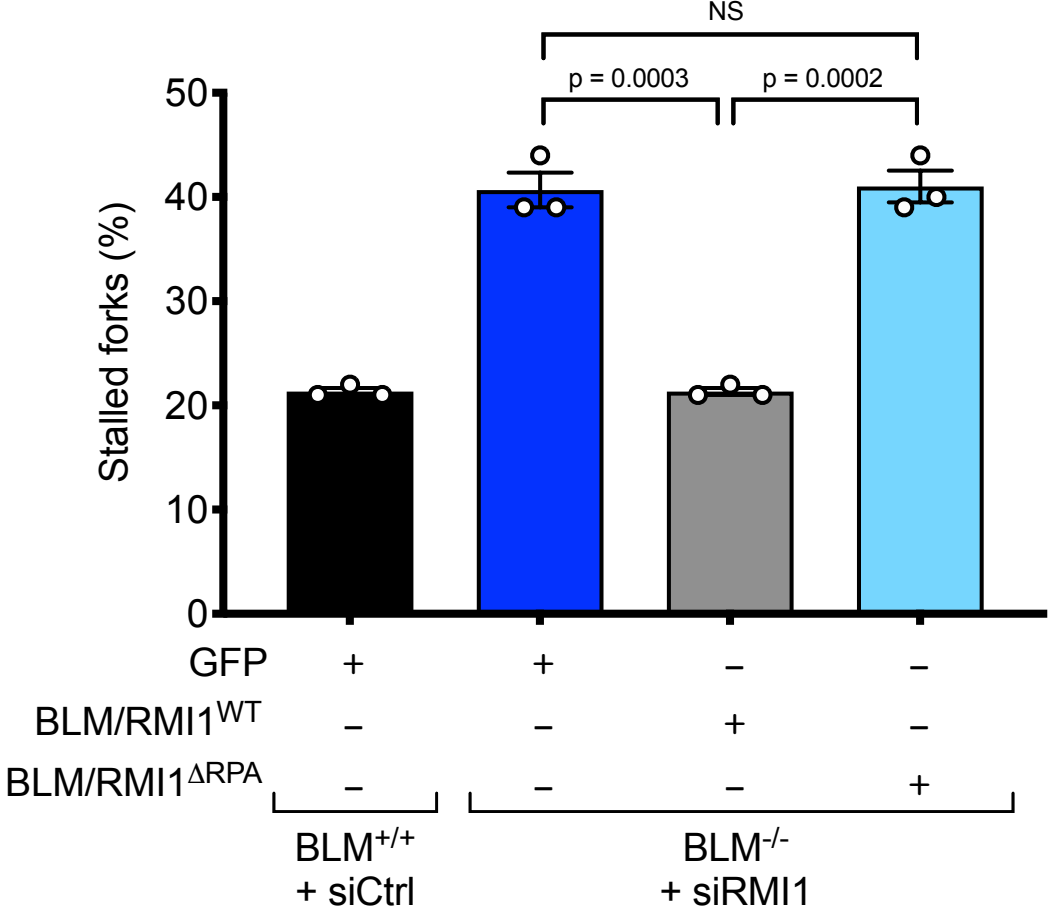


Fig. S4. RPA-binding by BLM and RMI1 suppresses increased stalled replication forks.

DNA fibre assays were carried out as in Supplementary Fig. 3e. The number of IdU-positive, CldU-negative tracts was quantified as a percentage of total fibres. At least 100 DNA fibres were analysed per sample. Significance was determined by two-sided unpaired t test (n=3, error bars denote SEM).

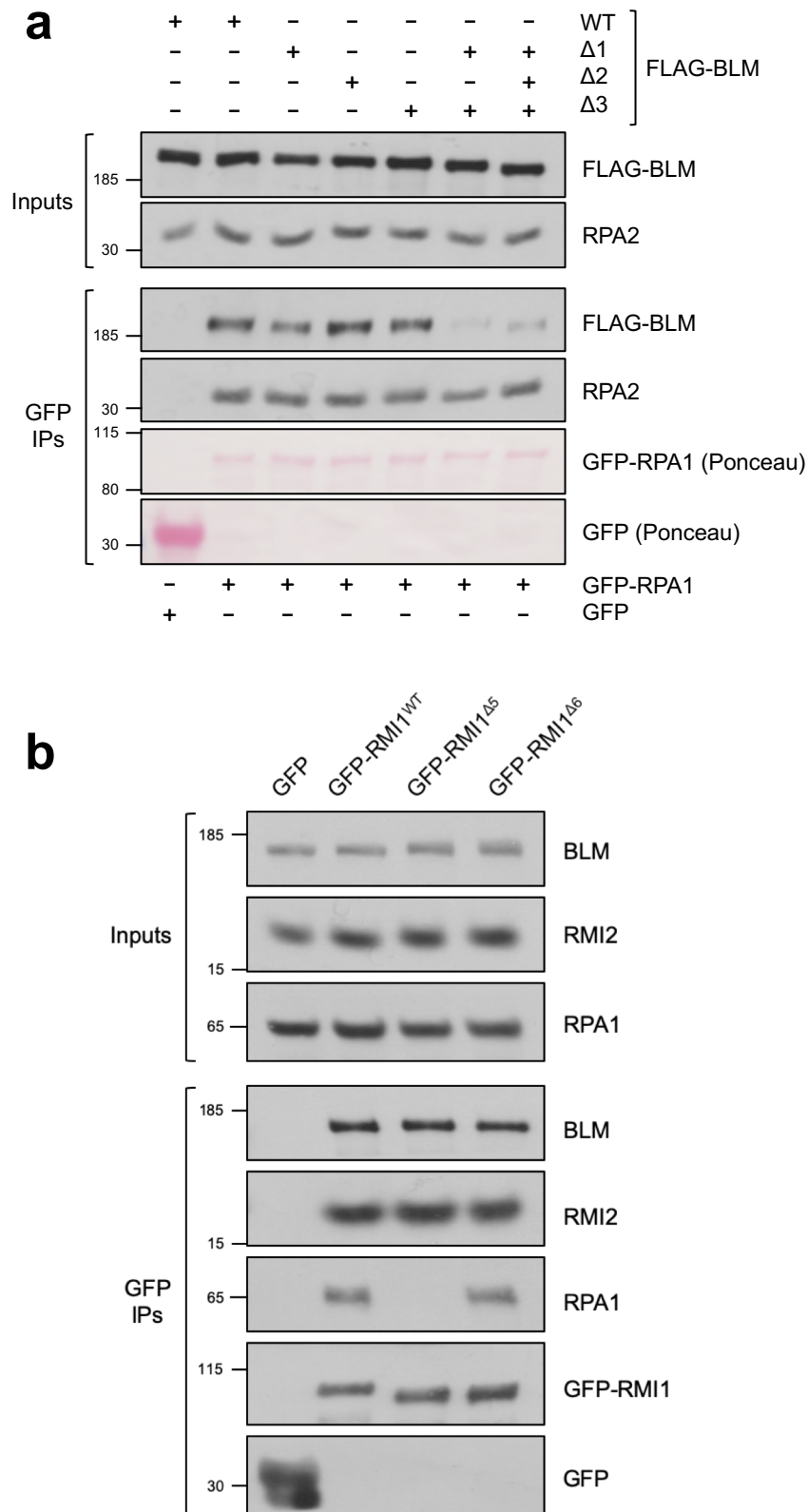


Fig. S5. BLM motif 2 and RMI1 motif 6 are not required for RPA-binding.

- a) GFP-pulldowns from 293FT cells transfected with constructs expressing either GFP or GFP-RPA1, and the indicated FLAG-tagged BLM variants, showing how loss of motifs 1 and 3 but not motif 2 of BLM impacts on RPA-binding.
- b) GFP-pulldowns from 293FT cells transfected with constructs expressing GFP or the indicated GFP-tagged RMI1 variants, showing that loss of motif 5 disrupts RPA-binding but motif 6 does not.

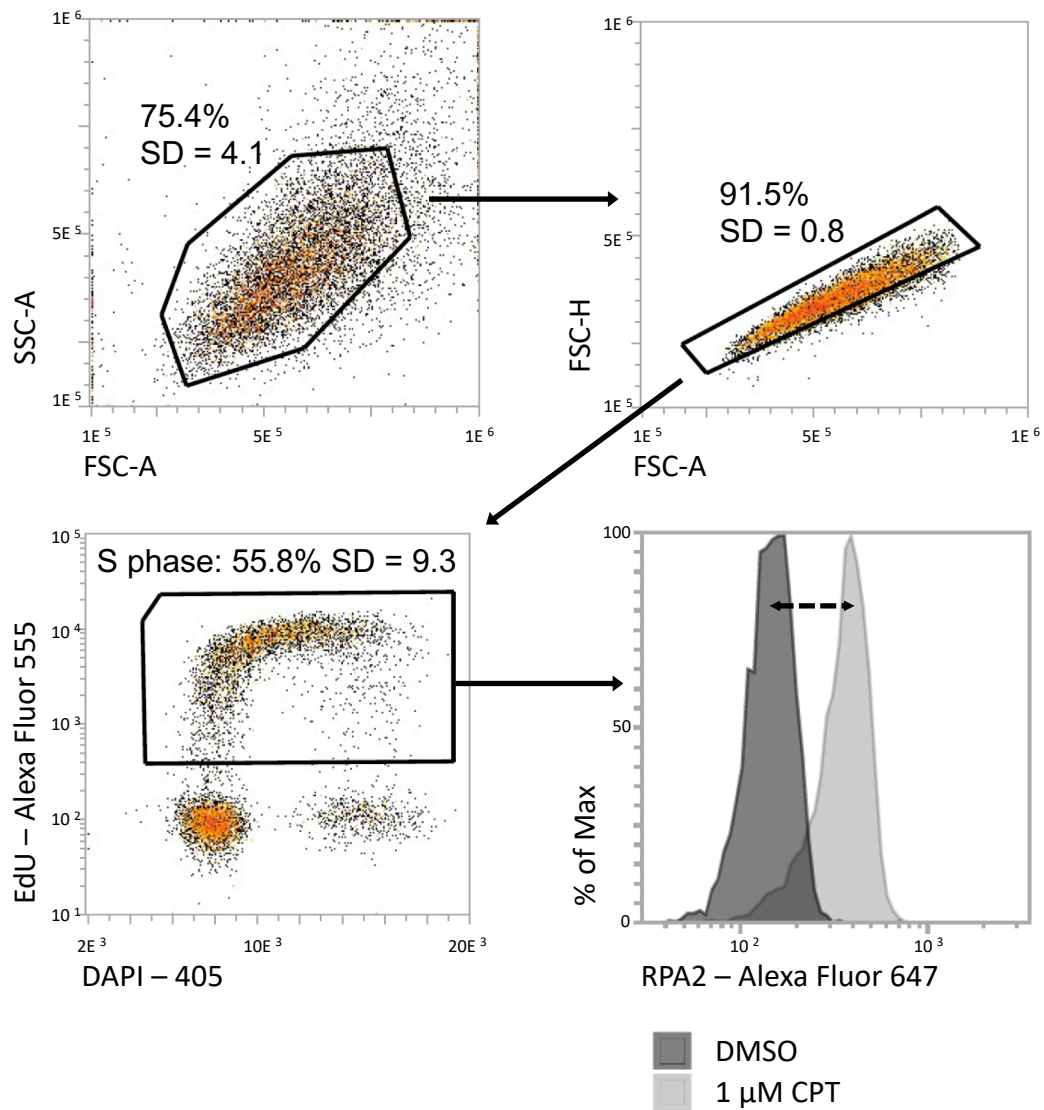


Fig. S6. Flow cytometry gating strategy.

Single RPE-1 cells were identified using Forward Scatter (FSC) and Side Scatter (SSC) and gated as indicated (top left panel, top right panel). EdU pulse-labelling was used to identify replicating cells in S phase and DAPI was used to quantify DNA content, before gating as indicated. Fluorescent marker/excitation wavelengths used are indicated on the axes (bottom left panel). Mean RPA2 intensity was calculated from the S phase population and the difference between DMSO- and CPT-treated cells found to quantify CPT-induced resection, as indicated by the dotted arrow. Fluorescent marker and excitation wavelength used are indicated on the x-axis (bottom right panel). The percentage of cells gated at each step is indicated on the panels ($n = 3$, SD = standard deviation).