

RdDM-independent *de novo* and heterochromatin DNA methylation by plant CMT and DNMT3 orthologs

Yaari *et. al.*

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--Motif I--
KfDNMT3 31 RQH-PKMGDGLVVISFDGCGTAAATNLGIP-EVKMGYSCLKEKPNAYKSEPPVWILGSGTA/TQDMIPSHVDLTVGGFPQDLSMGNQRLGAGA
PpDNMT3a 90 ADAEPKSGGERLVVISLFDGCGTAAATNLGIP-GGYSSCLAPAIQVVKSEPPVWILGSGTANLSAIPSHVDLTVGGFPQDLSMGNKREGSLGAS
PpDNMT3b 84 AEA-PKSGGERLVVISLFDGCGTAAATNLGIP-GGYSSCLAPAIQVVKSEPPVWILGSGTANLSAIPSHVDLTVGGFPQDLSMGNKREGSLGAS
MpDNMT3i 50 LKG-EWTKGKPLVVISLFDGCGTAAATNLGIP-GGYSSCLADAMQVVKSEPPVWILGSGTANLSAIPSHVDLTVGGFPQDLSMGNKREGSLGAGQ
MpDNMT3ii 54 QKA-PKRSKPLVVISLFDGCGTAAATNLGIP-GGYSSCLADAMQVVKSEPPVWILGSGTANLSAIPSHVDLTVGGFPQDLSMGNKREGSLGAS
SfDNMT3i 101 KDA-PNNGEKLVLVISLFDGCGTAAATNLGIP-GGYSSCLAPLEVVKSEPPVWILGSGTANLSAIPSHVDLTVGGFPQDLSMGNKREGSLGAGQ
SfDNMT3ii 86 KKA-PKMGKPLVLVISLFDGCGTAAATNLGIP-GGYSSCLAPAIQVVKSEPPVWILGSGTANLSAIPSHVDLTVGGFPQDLSMGNKREGSLGAGQ
SmDNMT3i 52 RNLLAL-DRRLVLVISLFDGCGTAAATNLGIP-GGYSSCLAPAIQVVKSEPPVWILGSGTANLSAIPSHVDLTVGGFPQDLSMGNKREGSLGAGQ
SmDNMT3ii 52 RNLLAL-DRRLVLVISLFDGCGTAAATNLGIP-GGYSSCLAPAIQVVKSEPPVWILGSGTANLSAIPSHVDLTVGGFPQDLSMGNKREGSLGAGQ
WmDNMT3 7 LQSQMEEEKPLVLVISLFDGCGTAAATNLGIP-GGYSSCLAPAIQVVKSEPPVWILGSGTANLSAIPSHVDLTVGGFPQDLSMGNKREGSLGAGQ
EbDNMT3 9 LKSGDMLGKPLVLVISLFDGCGTAAATNLGIP-GGYSSCLAPAIQVVKSEPPVWILGSGTANLSAIPSHVDLTVGGFPQDLSMGNKREGSLGAGQ
PsyDNMT3 1 -----
McDNMT3 1 -----
PtaDNMT3 1 -----
PjDNMT3 1 -----
SeDNMT3_F1 7 NKA-DITGKPLVLVISLFDGCGTAAATNLGIP-GGYSSCLAPAIQVVKSEPPVWILGSGTANLSAIPSHVDLTVGGFPQDLSMGNKREGSLGAGQ
SeDNMT3_F2 1 -----
SaDNMT3_F1 1 -----
SaDNMT3_F2 1 -----
QDQVNLTVGGFPQDLSMGNKREGSLGAGQ

----Motif VI-----
KfDNMT3 130 RSGFFHPFPF-SMKAKWFLVENVK-CRQDPAETKYLDWLPHELDADPESSEVNEWTNHLEPNLGRDAPETSCHEFNAPFPVFTGT
PpDNMT3a 189 RSLFFDLVLVQIKERKWLVENVASMSWDRDEIRH-LKVPHELDSDLTASRRRLWNTNHHPEPLPARRHPSTSQSCLEGLALBQRCQGV
PpDNMT3b 183 RSLFFDLVLVQIKERKWLVENVASMSWDRDEIRH-LKVPHELDSDLTASRRRLWNTNHHPEPLPARRHPSTSQSCLEGLALBQRCQGV
MpDNMT3i 149 RSLFFDLVLVQIKERKWLVENVASMSWDRDEIRH-LKVPHELDSDLTASRRRLWNTNHHPEPLPARRHPSTSQSCLEGLALBQRCQGV
MpDNMT3ii 153 RSLFFDLVLVQIKERKWLVENVASMSWDRDEIRH-LKVPHELDSDLTASRRRLWNTNHHPEPLPARRHPSTSQSCLEGLALBQRCQGV
SfDNMT3i 200 RSLFFDLVLVQIKERKWLVENVASMSWDRDEIRH-LKVPHELDSDLTASRRRLWNTNHHPEPLPARRHPSTSQSCLEGLALBQRCQGV
SfDNMT3ii 185 RSLFFDLVLVQIKERKWLVENVASMSWDRDEIRH-LKVPHELDSDLTASRRRLWNTNHHPEPLPARRHPSTSQSCLEGLALBQRCQGV
SmDNMT3i 146 RSLFFDLVLVQIKERKWLVENVASMSWDRDEIRH-LKVPHELDSDLTASRRRLWNTNHHPEPLPARRHPSTSQSCLEGLALBQRCQGV
SmDNMT3ii 146 RSLFFDLVLVQIKERKWLVENVASMSWDRDEIRH-LKVPHELDSDLTASRRRLWNTNHHPEPLPARRHPSTSQSCLEGLALBQRCQGV
WmDNMT3 106 RSLFFDLVLVQIKERKWLVENVASMSWDRDEIRH-LKVPHELDSDLTASRRRLWNTNHHPEPLPARRHPSTSQSCLEGLALBQRCQGV
EbDNMT3 108 RSLFFDLVLVQIKERKWLVENVASMSWDRDEIRH-LKVPHELDSDLTASRRRLWNTNHHPEPLPARRHPSTSQSCLEGLALBQRCQGV
PsyDNMT3 1 -----
McDNMT3 1 -----
PtaDNMT3 1 -----
PjDNMT3 1 -----
SeDNMT3_F1 106 RSLFFDLVLVQIKERKWLVENVASMSWDRDEIRH-LKVPHELDSDLTASRRRLWNTNHHPEPLPARRHPSTSQSCLEGLALBQRCQGV
SeDNMT3_F2 1 -----
SaDNMT3_F1 1 -----
SaDNMT3_F2 30 RSLFFDLVLVQIKERKWLVENVASMSWDRDEIRH-LKVPHELDSDLTASRRRLWNTNHHPEPLPARRHPSTSQSCLEGLALBQRCQGV

----Motif IX-----
KfDNMT3 229 LNTNDNTSNCA-KSYDIA-SGGARVDEHELEAMGSAVYKPYNKHGCI L PFS SSK-KQGRRCSCGGAEANGPGRPTPKRRSQSTPRRKL
PpDNMT3a 288 LQNLKSG-GRELVDNTINLNRKQTEBELMGLKLVNWRRTK-I TEKI IKA-VRIPEKPTVALKSPPTPSIQLRKNRTSRTFAFQ
PpDNMT3b 282 LQNLKSG-TRELVDNTINLNRKQTEBELMGLKLVNWRRTK-I TEKI IKA-VRIPEKPTVALKSPPTPSIQLRKNRTSRTFAFQ
MpDNMT3i 249 LQNLKSG-YRELVDNTINLNRKQTEBELMGLKLVNWRRTK-I TEKI IKA-VRIPEKPTVALKSPPTPSIQLRKNRTSRTFAFQ
MpDNMT3ii 252 LQNLKSG-ATRELVDNTINLNRKQTEBELMGLKLVNWRRTK-I TEKI IKA-VRIPEKPTVALKSPPTPSIQLRKNRTSRTFAFQ
SfDNMT3i 229 LQNLKSG-NRELVDNTINLNRKQTEBELMGLKLVNWRRTK-I TEKI IKA-VRIPEKPTVALKSPPTPSIQLRKNRTSRTFAFQ
SfDNMT3ii 284 LQNLKSG-SRELVDNTINLNRKQTEBELMGLKLVNWRRTK-I TEKI IKA-VRIPEKPTVALKSPPTPSIQLRKNRTSRTFAFQ
SmDNMT3i 226 LQNLKSG-FRELVDNTINLNRKQTEBELMGLKLVNWRRTK-I TEKI IKA-VRIPEKPTVALKSPPTPSIQLRKNRTSRTFAFQ
SmDNMT3ii 226 LQNLKSG-FRELVDNTINLNRKQTEBELMGLKLVNWRRTK-I TEKI IKA-VRIPEKPTVALKSPPTPSIQLRKNRTSRTFAFQ
WmDNMT3 205 LQNLKSG-KRELVDNTINLNRKQTEBELMGLKLVNWRRTK-I TEKI IKA-VRIPEKPTVALKSPPTPSIQLRKNRTSRTFAFQ
EbDNMT3 207 LQNLKSG-ARELVDNTINLNRKQTEBELMGLKLVNWRRTK-I TEKI IKA-VRIPEKPTVALKSPPTPSIQLRKNRTSRTFAFQ
PsyDNMT3 73 LQNLKSG-KRELVDNTINLNRKQTEBELMGLKLVNWRRTK-I TEKI IKA-VRIPEKPTVALKSPPTPSIQLRKNRTSRTFAFQ
McDNMT3 81 LQNLKSG-KRELVDNTINLNRKQTEBELMGLKLVNWRRTK-I TEKI IKA-VRIPEKPTVALKSPPTPSIQLRKNRTSRTFAFQ
PtaDNMT3 73 LQNLKSG-KRELVDNTINLNRKQTEBELMGLKLVNWRRTK-I TEKI IKA-VRIPEKPTVALKSPPTPSIQLRKNRTSRTFAFQ
PjDNMT3 79 LQNLKSG-KRELVDNTINLNRKQTEBELMGLKLVNWRRTK-I TEKI IKA-VRIPEKPTVALKSPPTPSIQLRKNRTSRTFAFQ
SeDNMT3_F1 205 LQNLKSG-SRELVDNTINLNRKQTEBELMGLKLVNWRRTK-I TEKI IKA-VRIPEKPTVALKSPPTPSIQLRKNRTSRTFAFQ
SeDNMT3_F2 1 -----
SaDNMT3_F1 2 LQNLKSG-FRELVDNTINLNRKQTEBELMGLKLVNWRRTK-I TEKI IKA-VRIPEKPTVALKSPPTPSIQLRKNRTSRTFAFQ
SaDNMT3_F2 1 -----

----Motif X-----
KfDNMT3 328 LSPGGSGEALFATKDRWELLGNFVSVPVIVLLSPILLSPILRAA-QRDLAIPTDVKACFKBCEWALYNEDMAPWYACI THVDVT---QP
PpDNMT3a 385 VNEENPTQRESIKDIDRWELLGNFVSVPVIVLLSPILLSPILRAE-FSG-KANIVGSRBEBLAMEPCEWALYNEDMAPWYACI THVDVT---QP
PpDNMT3b 380 VNEENPTQRESIKDIDRWELLGNFVSVPVIVLLSPILLSPILRAE-FSG-KANIVGSRBEBLAMEPCEWALYNEDMAPWYACI THVDVT---QP
MpDNMT3i 344 SVKSSPFAFGINRSARWELLGNFVSVPVIVLLSPILLSPILRAE-FSG-KANIVGSRBEBLAMEPCEWALYNEDMAPWYACI THVDVT---QP
MpDNMT3ii 322 -----DRNTRWELLGNFVSVPVIVLLSPILLSPILRAE-FSG-KANIVGSRBEBLAMEPCEWALYNEDMAPWYACI THVDVT---QP
SfDNMT3i 398 -----KDSRWELLGNFVSVPVIVLLSPILLSPILRAE-FSG-KANIVGSRBEBLAMEPCEWALYNEDMAPWYACI THVDVT---QP
SfDNMT3ii 373 TP-----ARWELLGNFVSVPVIVLLSPILLSPILRAE-FSG-KANIVGSRBEBLAMEPCEWALYNEDMAPWYACI THVDVT---QP
SmDNMT3i 260 -----LQNLKSG-FRELVDNTINLNRKQTEBELMGLKLVNWRRTK-I TEKI IKA-VRIPEKPTVALKSPPTPSIQLRKNRTSRTFAFQ
SmDNMT3ii 297 -----AKTRWELLGNFVSVPVIVLLSPILLSPILRAE-FSG-KANIVGSRBEBLAMEPCEWALYNEDMAPWYACI THVDVT---QP
WmDNMT3 281 -----IDNTRWELLGNFVSVPVIVLLSPILLSPILRAE-FSG-KANIVGSRBEBLAMEPCEWALYNEDMAPWYACI THVDVT---QP
EbDNMT3 281 TTEKVT-----KYRWELLGNFVSVPVIVLLSPILLSPILRAE-FSG-KANIVGSRBEBLAMEPCEWALYNEDMAPWYACI THVDVT---QP
PsyDNMT3 155 TEKDE-----KYRWELLGNFVSVPVIVLLSPILLSPILRAE-FSG-KANIVGSRBEBLAMEPCEWALYNEDMAPWYACI THVDVT---QP
McDNMT3 171 REDMLT-----KFSRWELLGNFVSVPVIVLLSPILLSPILRAE-FSG-KANIVGSRBEBLAMEPCEWALYNEDMAPWYACI THVDVT---QP
PtaDNMT3 155 TEKDE-----KYRWELLGNFVSVPVIVLLSPILLSPILRAE-FSG-KANIVGSRBEBLAMEPCEWALYNEDMAPWYACI THVDVT---QP
PjDNMT3 161 TEKDE-----KYRWELLGNFVSVPVIVLLSPILLSPILRAE-FSG-KANIVGSRBEBLAMEPCEWALYNEDMAPWYACI THVDVT---QP
SeDNMT3_F1 -----
SeDNMT3_F2 1 -----
SaDNMT3_F1 92 REDTIV-----KYSRWELLGNFVSVPVIVLLSPILLSPILRAE-FSG-KANIVGSRBEBLAMEPCEWALYNEDMAPWYACI THVDVT---QP
SaDNMT3_F2 -----

DUF3444 start
KfDNMT3 420 DWDERR-LPTQFGVH---RFYEVLPSENPKSEICGV-LKAC-EYTSVDKAFSHRVNPAHLEGRI-LVPPGCEVWVYKDELRKFKGRFLHYVYVK
PpDNMT3a 484 GRSITLPLPSIEHKLNTTPAYAKDEVDENRQGGGLKRDWDQDNMQAFSHRVSVKLEDSN-LVPPGCEVWVYKDELRKFKGRFLHYVYVK
PpDNMT3b 479 GERNVLPPLPSIEHKLNTTPAYAKDEVDENRQGGGLKRDWDQDNMQAFSHRVSVKLEDSN-LVPPGCEVWVYKDELRKFKGRFLHYVYVK
MpDNMT3i 441 QLGR-KPPYIEVKELENTSAYAAEPPMDTNRGGLHRELIDKNSWAFSHRVSVKLEDSN-LVPPGCEVWVYKDELRKFKGRFLHYVYVK
MpDNMT3ii 409 GRRK-SLPRIECLFELTKFVAGDQDHWSTIRGGGLVYSEGILQSGSWAFSHRVSVKLEDSN-LVPPGCEVWVYKDELRKFKGRFLHYVYVK
SfDNMT3i 481 GAD-KNPIRIECLFELTKFVAGDQDHWSTIRGGGLVYSEGILQSGSWAFSHRVSVKLEDSN-LVPPGCEVWVYKDELRKFKGRFLHYVYVK
SfDNMT3ii 456 SYGN-KHPIRIECLFELTKFVAGDQDHWSTIRGGGLVYSEGILQSGSWAFSHRVSVKLEDSN-LVPPGCEVWVYKDELRKFKGRFLHYVYVK
SmDNMT3i 333 KKK-----QHVGFLELDTGLAANDQWSELRGGGLVYSEGILQSGSWAFSHRVSVKLEDSN-LVPPGCEVWVYKDELRKFKGRFLHYVYVK
SmDNMT3ii 384 KKK-----QHVGFLELDTGLAANDQWSELRGGGLVYSEGILQSGSWAFSHRVSVKLEDSN-LVPPGCEVWVYKDELRKFKGRFLHYVYVK
WmDNMT3 366 HNG-----NTHQHVGFLELDTGLAANDQWSELRGGGLVYSEGILQSGSWAFSHRVSVKLEDSN-LVPPGCEVWVYKDELRKFKGRFLHYVYVK
DUF3444 end <--

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Supplementary Figure 1. Alignment of plant DNMT3 protein sequences. Sequences were aligned using MUSCLE ¹. Protein accessions are listed in Supplementary Table 1. Location of MTD motifs and the DUF3444 domain are denoted. Alignment printing format was generated with Boxshade 3.2.

-----Motif I-----Motif IV-----Motif VI-----

HsDNMT1 1 D L F S G C G C L S E L H Q A G I S D T W A E W D P A A Q A F L N N P C G L G D V E M I C G G P C G F G N R K F K N L V V S L S L L E N V I L E M G Q C

NveDNMT1 1 D L F S G C G C L S E L H Q A G A E S W A E K E E P A A Q A Y L N N P C G L G D V E M I C G G P C G F G N R L F K N L V V S L S L L E N V I L E M G Q C

PpMET 1 D L F S G C G C L S E L H Q A G A T T K W A E Y E H P A S E A F N L N H P F N C V I G E V D F I N G G P C G F G N R K V Q C E I L G L S L L E N V I L E M G Q C

AtMET1 1 D L F S G C G C L S E L H Q A G I S D A K W A E Y E E P A Q A F L N N P C G L G D V E M I C G G P C G F G N R K V Q C E I L A L S L L E N V I L E M G Q C

ZmMET 1 D L F S G C G C L S E L H Q A G S E T K W A E Y E E P A G A F N K H P E A N C V I G E V D F I N G G P C G F G N R K V Q C E I L A L S L L E N V I L E M G Q C

KfDRMa 1 L S L F S G I G G A E A L H R L G I R K K V V S V E I D E H C T T D H R V V H L C G L L K Q L G F D L V I G G S P C N N L C N R G K H S L F F E P R F Y E N V I S R L Y D I

KfDRMb 1 L S L F S G I G G A E A L H R L G I R K K V V S V E I N E H C T T Q N W K K N R L C G L D V R L G G F D L V I G G S P C N L C N R G R E S R L F F E P R F L E N V I C H R A G I

BdDRM3 1 L S I Y S G I G G A E A L H R L G I R K K V V S V E S D V N R K I L K W R R T C A G E L G W L G G F D L I G G N --- Y S C R G G C M D S R L F F E P R F L E N V I S D L L N V

PhDRM3 1 L S I Y S G I G G A E V L H R L G I R K K V V S V E S D V N R K I L R W K Q T Q C G L L G W L G G F D L I G G N Y T S C K G S T I --- S N R F F E A R L L E N V I T Q L L N V

SbDRM3 1 L S I Y S G I G G A E V L H R L G I R K K V V S V E S E V N R K I L R W K S T Q C G L L G W L G G F D L I G G N Y T S C K G S N T V --- S N R F F E A R L L E N V I T Q L L N V

ZmDRM3 1 L S I Y S G I G G A E A L H R L G I R K K V V S V E S E V N R K I L R W K L K T Q C G L L G W L G G F D L I G G N Y T S C K G S T V --- S N R F F E A R L L E N V I K Q L L N V

BrDRM3a 1 L S L F S G I G G A E A L S R L G I H K K V V S V E P C G L S R S L R W K G S T Q C G L L R S L G G F D L V I G N P T P A D L S R E C F D F L N Q V V R V I G N I S S F T G I

AtDRM3 1 L S L F S G I G G A E A L D R L G I H K K V V S V E S C G L S N I L R W K Q T Q C G L L K S L G G F D V I G N C N P T P A D L S K E E F D Y L E N E A R F I G O I S G L L G I

BrDRM3b 1 L S L F S G I G G A E T N R L G I H K K V V S V E H C G L S N I L R W K Q S T Q C G L L R S L G G F D V I G N C N P P P D L S K E D F D Y L E N E A R F I G N I S G L L G I

GmDRM3a 1 L S L F S G I G G A E A L H R L I R K K V V S V E T S E T K R I L E K W R Q C G L L K L G G F D V I G N C P S Y S S R L Q L D F I S C C V R E L E N V I S Q L Y D I

GmDRM3b 1 L S L F S G I G G A E A L H R L G I R K K V V S V E T S E T K R I L E F W R Q C G L L K L G G F D V I G N C P S N L S R L L L E F I S C C V R E L E N V I S Q L Y D I

MeDRM3 1 L S F S G I G G A E A L D R L G I R K K V V S V E T S E M R R L R W K Q T Q C G L L K L G G F D V I G N C P S N L S R L L L E F I S C C H C A R S P C F D F I L D C I V R F I G N I S Q L Y D I

PrpDRM3 1 L S F S G I G G A E A L H R L G I R K K V V S V E T N A T R K I L R W K E N T Q C G L D V H K L G G F D L I C H Q C P D S I S K I S C F D F I L D C I V R F I G N I S Q L Y D I

AtDRM3 1 L S I C S G I G G A E L S H L G I Q N C I V S V E S S D I N R L I N W N K K T Q C G L D V E K L G G F D V I G G N S K A S V S S C L D Q P F F E I R L L E N V I T Q L L G T

SmDRMa 1 L S L F S G I G G E V A L H R L G I R K K V V S V E T S A D C H R L S M W H R T Q C T H D V T E L G G F D L V I G G S P C N N F C N R G K S L F F E P R F Y E N V I S R L Y D I

SmDRMb 1 L S L F S G I G G A E A L H R L G I R K K V V S V E S N V D N R I L E R K W S T Q C G H D V L L G G F D L V I G G S P C N N L C N R G H S L F F E P R F Y E N V I S R L Y D I

MpDRMii 1 L S L F S G I G G A E A L H L G I R K K V V S V E I D P I V R R I E H M Q I T Q C G L D V I L G G F D L V I G G S P C N L C N R G K S V A F F E A R F Y E N V I S R L Y D I

MpDRMi 1 L S L F S G I G G A E A L H L G I R K K V V S V E I D E K A R S L D S M K S T Q C G L D V K L F K G F D L V I G G S P C N N L C N R G T S V A F F E P R F Y E N V I S R L Y D I

SfDRMb 1 L S L F S I G G A E A L H L G I R K K V V S V E I D E I N A C E A W R A Q C I L I N M S L G G F D L I G G S P C N F C N R G V T S I F F E A R F Y E N V I S R L Y D I

PrpDRM2 1 L S L F S G I G G A E A L H L G I R K K V V S V E I L E F P R C Q I W K S V I Q C G L D V R H L G G F D L I G G S P C N N F A C S N R G H S L F F E P R F Y E N V I T Q L L G I

SfDRMc 1 L S L F S G I G G A E A T L C K R Q V V S V E I N E G T R C A A W R E A Q C G L D V A L G G F D L I G G S P C N N L C N R G K S L F F E P R F Y E N V I S R L Y D I

FpDRM1 1 L S L F S G I G G A E A L H R L G I R K K V V S V E I D D G T R C E A W R A T Q C G L N R K L G G F D L I G G S P C N N L C N R G T Q S A F F E P R F Y E N V I S R L Y D I

SfDRMa 1 L S L F S G I G G A E A L H R L G I R K K V V S V E I L E G S R C E A M A A T Q C G L D V A L G G F D L I G G S P C N N L C N R G P C S N F F E P R F Y E N V I S R L Y D I

FpDRMa 1 L S L F S G I G G A E A L H R L G I R K K V V S V E I C K E N R L I L S M W E K T Q C G L D V N L G G F D L I G G S P C N N L C N R G K H S L F F E P R F Y E N V I S R L Y D I

PtaDRMc 1 L S L F S G I G G A E A L H R L G I R K K V V S V E I C K E N R L I L S M W E K T Q C G L D V N L G G F D L I G G S P C N N L C N R G K H S L F F E P R F Y E N V I S R L Y D I

FpDRMc 1 L S L F S G I G G A E A L D R L G I R K K V V S V E I C K E N R L I L S M W E K T Q C G L D V N L G G F D L I G G S P C N N L C N R G K H S L F F E P R F Y E N V I S R L Y D I

PsyDRMd 1 L S L F S G I G G A E A L D R L G I R K K V V S V E I C K V N R L I L S M W E K T Q C G L D V N L G G F D L I G G S P C N N L C N R G K H S L F F E P R F Y E N V I S R L Y D I

PtaDRMe 1 L S L F S G I G G A E A L D R L G I R K K V V S V E I C K V N R L I L S M W E K T Q C G L D V N L G G F D L I G G S P C N N L C N R G K H S L F F E P R F Y E N V I S R L Y D I

PabDRMe 1 L S L F S G I G G A E A L H R L G I R K K V V S V E I C K E N R L I L S M W E K T Q C G L D V N L G G F D L I G G S P C N N L C N R G K H S L F F E P R F Y E N V I S R L Y D I

FpDRMb 1 L S L F S G I G G A E A L H R L G I R K K V V S V E I C K E N R L I L S M W E K T Q C G L D V N L G G F D L I G G S P C N N L C N R G K H S L F F E P R F Y E N V I S R L Y D I

PsyDRMa 1 L S L F S G I G G A E A L H R L G I R K K V V S V E I C K E N R L I L S M W E K T Q C G L D V N L G G F D L I G G S P C N N L C N R G K H S L F F E P R F Y E N V I S R L Y D I

PtaDRMa 1 L S L F S G I G G A E A L H R L G I R K K V V S V E I C K E N R L I L S M W E K T Q C G L D V N L G G F D L I G G S P C N N L C N R G K H S L F F E P R F Y E N V I S R L Y D I

GblDRM 1 L S L F S G I G G A E A L N R I S I C K V V S V E I C A R N R L I L S M W K K T Q C G L D V H L G G F D L I G G S P C N N L C N R G Q S L F F E P R F Y E N V I S R H F G G I

PsyDRMb 1 L S L F S G I G G A E A L H R L G I R K K V V S V E I C P K N R L I L S S M W I T Q C G L D V H L G G F D L V I G G S P C N N F C N N R K R S L F F E P R F Y E R V I R H F G G I

PtaDRMb 1 L S L F S G I G G A E A L H R L G I R K K V V S V E I C P K N R L I L S S M W I T Q C G L D V H L G G F D L V I G G S P C N N F C N N R K R S L F F E P R F Y E R V I R H F G G I

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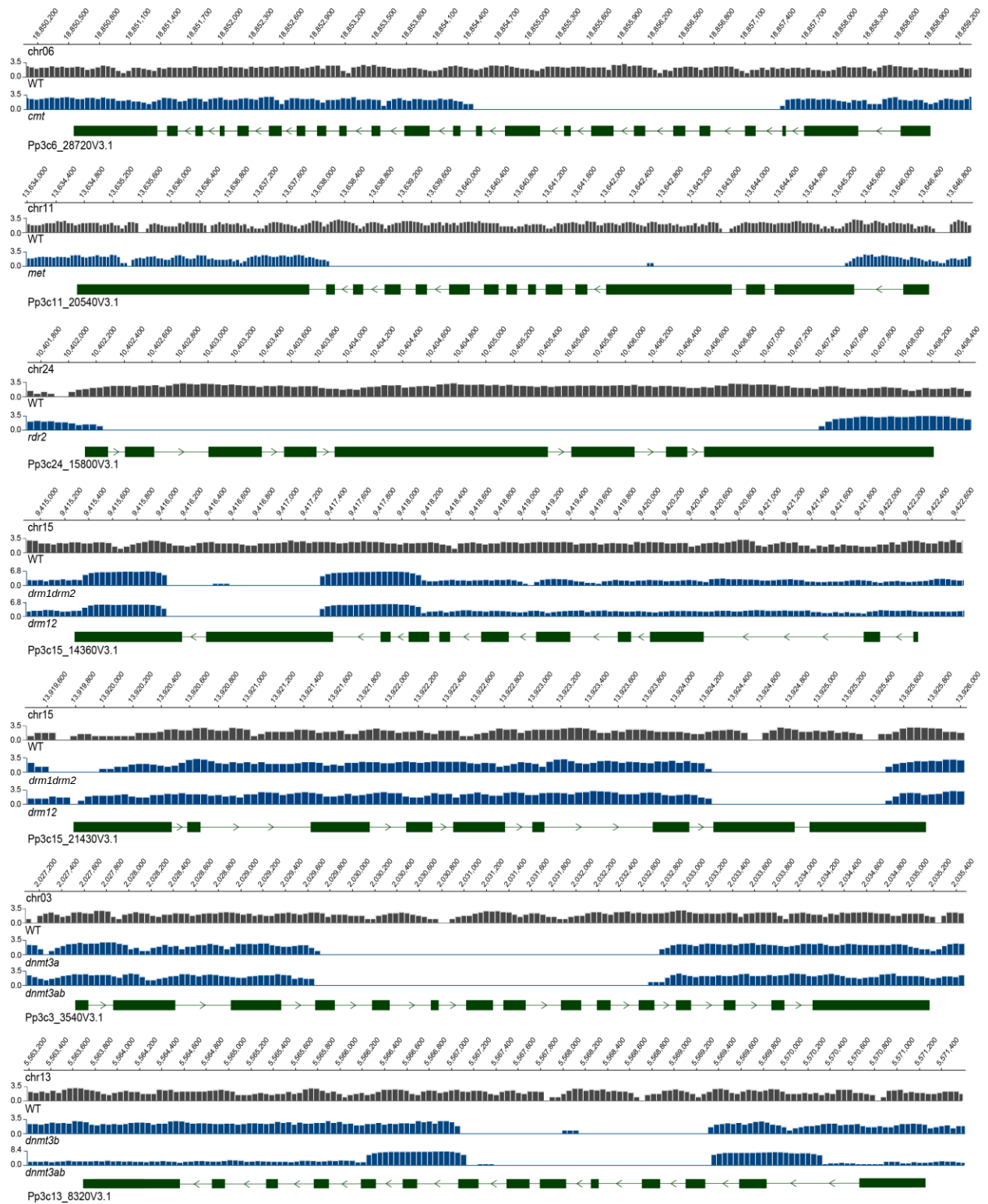
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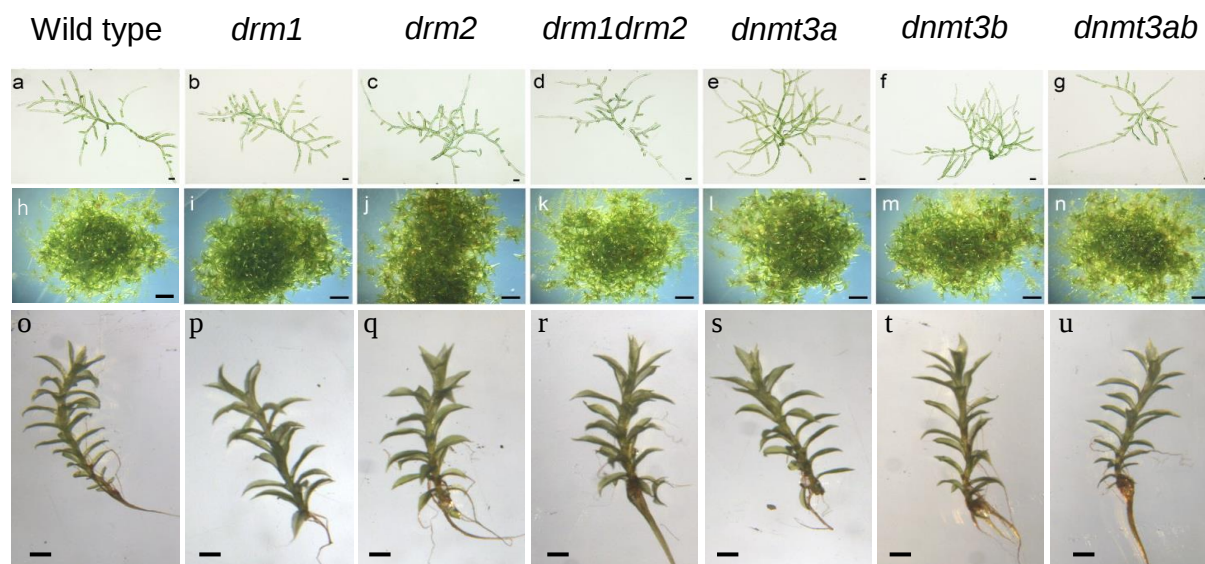
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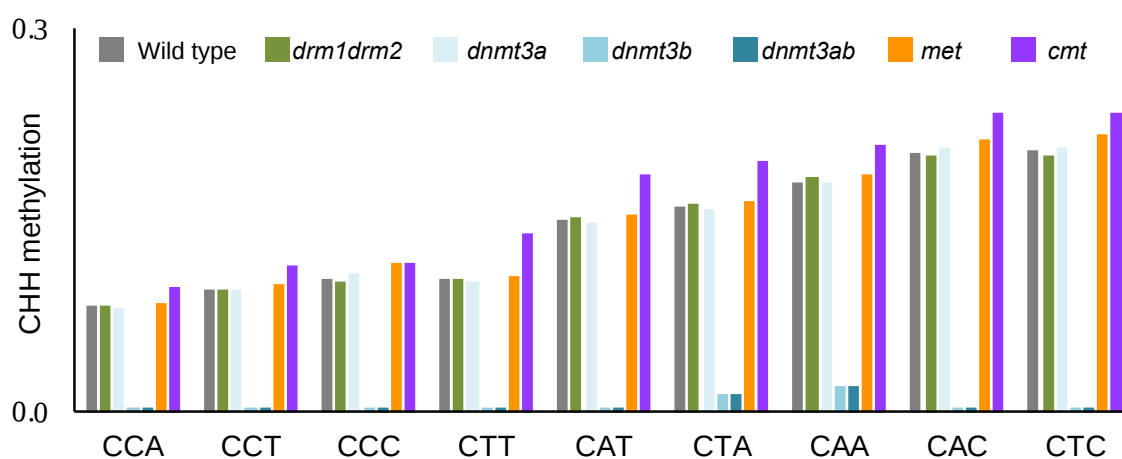
Supplementary Figure 2. Alignment of plant DNMT3 and DRM MTD motifs. Alignment of selected DNMT3, DRM and DNMT1 MTD protein sequences was performed using MUSCLE¹. The motif order was rearranged in DRM sequences to match the linear organization of canonical DNMTs. For clear presentation, non-conserved blocks of alignment were filtered by Gblocks². Protein accessions are listed in Supplementary Table 1. MTD motifs are denoted. Alignment printing format was generated with Boxshade 3.2.



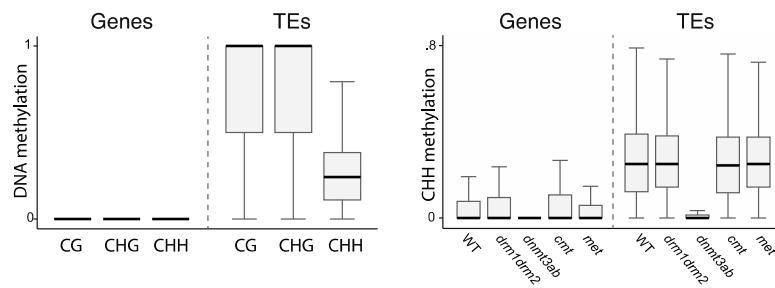
Supplementary Figure 3. Genotyping of PpDNMT mutants. Coverage of BS-seq reads at *PpDNMT* genes in WT and *dnmt* mutants.



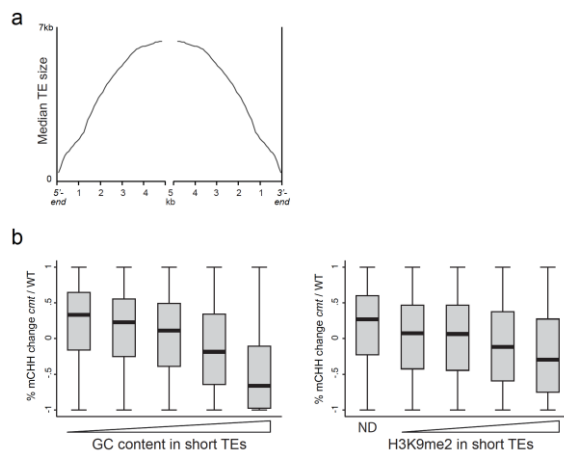
Supplementary Figure 4. Mutagenesis of PpDNMT3 and PpDRM does not disrupt *P. patens* development. Morphological analysis of protonema and gametophore development in WT and PpDNMT3 and DRM deletion mutants. **a-g**, Seven days old protonemata of WT (**a**) and mutants (**b-g**). Scale bar: 50 μ m. **h-n**, Three weeks old plants bearing gametophores of WT (**h**) and mutants (**i-n**). Scale bar: 250 μ m. **o-u**, Six weeks old gametophores of WT (**o**) and mutants (**p-u**). Scale bar: 1 mm.



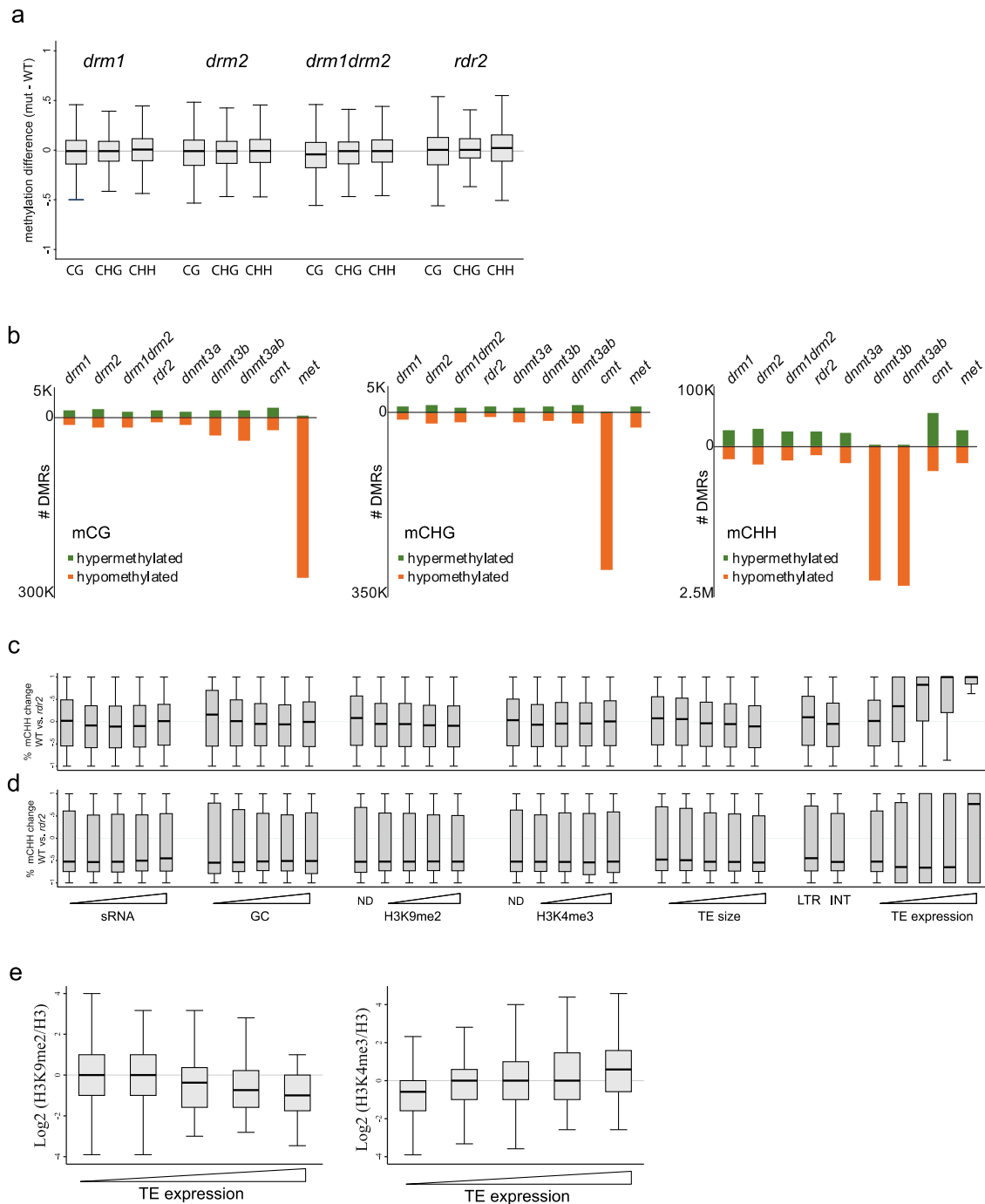
Supplementary Figure 5. Preferences in CHH methylation subcontexts. Averaged genomic CHH methylation level, in wild type and DNMT mutants, separated to its subcontexts.



Supplementary Figure 6. DNA methylation in genes and transposons. Distribution of DNA methylation per 50 bp windows that either overlap with genes or with TEs. Left panel shows CG, CHG, and CHH methylation in wild type. Right panel shows CHH methylation in wild type and *dnmt* mutants within 50 bp windows that have at least 10% methylation in either of the samples.



Supplementary Figure 7. Regulation of CHH methylation by PpCMT and PpDNMT3. **a.** Pattern of average TE size along the aligned TEs in Figures 2a, d, and 3e. *P. patens* TEs were aligned at the 5' or 3' ends and average TE size within each 100 bp interval is plotted. **b.** Box plots showing the distribution of percent-methylation-change per 50 bp windows between wild type and *cmt* mutant over H3K9me2, GC content within TEs shorter than 500 bp long.



Supplementary Figure 8. DNA methylation in *drm* and *rdr2* mutants. **a.** DNA methylation difference between WT and indicated mutants. **b.** Number of hypo- and hyper-methylated CG, CHG, and CHH DMRs in each of the mutants. **c-d.** Percent-methylation-change between WT and *rdr2* mutant within *rdr2*-CHH-DMRs (c) or *drm12*-CHH-DMRs (d) over five centiles of indicated genomic or chromatin attributes. The WT plant is genetically unrelated to the *rdr2* one, thus comparison between these two plants could contribute to a noise level that could mask a weak hypo-methylation signal. Therefore, we analyzed the CHH methylation change in *rdr2* within *drm12*-CHH-DMRs (d). Note the change from global hypermethylation in *rdr2* in (c) to a slight hypo-methylation at low GC regions, short TEs, LTRs, and expressed TEs in (d).

Supplementary Table 1. DNMT gene model ID and source.

DNMT_group	Name	Gene Model	Taxonomic Group1	Taxonomic Group2	Organism	Protein Length (AA)	Source
DNMT1	NveDNMT1	125496	Animals	Cnidaria	Nematostella vectensis	1263	Metazome
DNMT1	HsDNMT1	ENS00000130816	Animals	Mammals	Homo sapiens	1632	Metazome
DNMT1	PpMET	Pp3c11_20540	Bryophytes	Mosses	Physcomitrella patens	1579	Phytozome
DNMT1	ZmMET	GRMZM2G333916_T01	Angiosperms	Monocots	Zea mays	1536	Phytozome
DNMT1	AtMET1	AT5G49160	Angiosperms	Eudicots	Arabidopsis thaliana	1535	Phytozome
DNMT3	NveDNMT3	127267	Animals	Cnidaria	Nematostella vectensis	624	Metazome
DNMT3	CIDNMT3	270939	Animals	Tunicata	Ciona intestinalis	618	Metazome
DNMT3	MmDNMT3a	ENS0000000020991	Animals	Mammals	Mus musculus	910	Metazome
DNMT3	MmDNMT3b	ENS0000000051830	Animals	Mammals	Mus musculus	860	Metazome
DNMT3	HsDNMT3a	ENS00000011972	Animals	Mammals	Homo sapiens	914	Metazome
DNMT3	HsDNMT3b	ENS000000088305	Animals	Mammals	Homo sapiens	853	Metazome
DNMT3	KfDNMT3	kfi00080_0350_v1.1	Charophytes		Klebsormidium flaccidum	893	K. nitens genome project
DNMT3	MpDNMT3i	Mapoly0043s0021.1	Bryophytes	Liverworts	Marchantia polymorpha	654	Phytozome
DNMT3	MpDNMT3ii	Mapoly0095s0030.1	Bryophytes	Liverworts	Marchantia polymorpha	687	Phytozome
DNMT3	PpDNMT3a	Pp3c3_3540V3.1	Bryophytes	Mosses	Physcomitrella patens	736	Phytozome
DNMT3	PpDNMT3b	Pp3c13_8320V3.1	Bryophytes	Mosses	Physcomitrella patens	711	Phytozome
DNMT3	SfDNMT3i	Sphfalx0068s0040.1	Bryophytes	Mosses	Sphagnum fallax	739	Phytozome
DNMT3	SfDNMT3ii	Sphfalx0127s0004.1	Bryophytes	Mosses	Sphagnum fallax	767	Phytozome
DNMT3	SmDNMT3i	fgenes2_pg_C_scaffold_6000551	Lycophytes		Selaginella moellendorffii	630	Phytozome
DNMT3	SmDNMT3ii	fgenes2_pg_C_scaffold_17000071	Lycophytes		Selaginella moellendorffii	685	Phytozome
DNMT3	EbDNMT3	GNQG-2005968	Gymnosperms	Cycadales	Encephalartos barteri	551	1KP
DNMT3	SeDNMT3_F1	KAWQ-2009204	Gymnosperms	Cycadales	Stangeria eriopus	248	1KP
DNMT3	SeDNMT3_F2	KAWQ-2054998	Gymnosperms	Cycadales	Stangeria eriopus	244	1KP
DNMT3	WmDNMT3	TOXE-2012823	Gymnosperms	Gnetales	Welwitschia mirabilis	562	1KP
DNMT3	PtaDNMT3	PTA00084430	Gymnosperms	Conifers	Pinus taeda	426	PLAZA
DNMT3	PsyDNMT3	PSY00011178	Gymnosperms	Conifers	Pinus sylvestris	426	PLAZA
DNMT3	McDNMT3	CDFR-2008757	Gymnosperms	Conifers	Manoao colensoi	405	1KP
DNMT3	SaDNMT3_F1	KLGF-2012241	Gymnosperms	Conifers	Sundacarpus amarus	344	1KP
DNMT3	SaDNMT3_F2	KLGF-2078876	Gymnosperms	Conifers	Sundacarpus amarus	105	1KP
DNMT3	PjDNMT3	MFTM-2078885	Gymnosperms	Conifers	Pinus jeffreyi	298	1KP
DRM	KfDRMa	kfi00018_0570_v1.1	Charophytes		Klebsormidium flaccidum	697	K. nitens genome project
DRM	KfDRMb	kfi00253_0110_v1.1	Charophytes		Klebsormidium flaccidum	1395	K. nitens genome project
DRM	MpDRMa	Mapoly0103s0053.3	Bryophytes	Liverworts	Marchantia polymorpha	723	Phytozome
DRM	MpDRMb	Mapoly0109s0015.2	Bryophytes	Liverworts	Marchantia polymorpha	758	Phytozome
DRM	PpDRM1	Pp3c15_14362	Bryophytes	Mosses	Physcomitrella patens	1036	Phytozome
DRM	PpDRM2	Pp3c15_21430	Bryophytes	Mosses	Physcomitrella patens	842	Phytozome
DRM	SfDRMa	Sphfalx0006s0094	Bryophytes	Mosses	Sphagnum fallax	551	Phytozome
DRM	SfDRMb	Sphfalx0011s0183	Bryophytes	Mosses	Sphagnum fallax	836	Phytozome
DRM	SfDRMc	Sphfalx0209s0004	Bryophytes	Mosses	Sphagnum fallax	790	Phytozome
DRM	SmDRMa	411110	Lycophytes		Selaginella moellendorffii	566	Phytozome
DRM	SmDRMb	fgenes2_pg_C_scaffold_5000240	Lycophytes		Selaginella moellendorffii	551	Phytozome
DRM	GbiDRM	GBI00021934	Gymnosperms	Ginkgoales	Ginkgo biloba	655	PLAZA
DRM	PabDRMa	PAB00006266	Gymnosperms	Conifers	Picea abies	356	PLAZA
DRM	PabDRMb	PAB00012689	Gymnosperms	Conifers	Picea abies	482	PLAZA
DRM	PabDRMc	PAB00046707	Gymnosperms	Conifers	Picea abies	596	PLAZA
DRM	PabDRMd	PAB00048154	Gymnosperms	Conifers	Picea abies	532	PLAZA
DRM	PabDRRe	PAB00049465	Gymnosperms	Conifers	Picea abies	398	PLAZA
DRM	PpiDRMa	PII00065449	Gymnosperms	Conifers	Pinus pinaster	747	PLAZA
DRM	PpiDRMb	PII00073543	Gymnosperms	Conifers	Pinus pinaster	423	PLAZA
DRM	PsyDRMa	PSY00004978	Gymnosperms	Conifers	Pinus sylvestris	747	PLAZA
DRM	PsyDRMb	PSY0005220	Gymnosperms	Conifers	Pinus sylvestris	473	PLAZA
DRM	PsyDRMc	PSY0006869	Gymnosperms	Conifers	Pinus sylvestris	662	PLAZA
DRM	PsyDRMd	PSY0008531	Gymnosperms	Conifers	Pinus sylvestris	645	PLAZA
DRM	PtaDRMa	PTA00004821	Gymnosperms	Conifers	Pinus taeda	687	PLAZA
DRM	PtaDRMb	PTA00013841	Gymnosperms	Conifers	Pinus taeda	581	PLAZA
DRM	PtaDRMc	PTA00015283	Gymnosperms	Conifers	Pinus taeda	367	PLAZA
DRM	PtaDRMd	PTA00023209	Gymnosperms	Conifers	Pinus taeda	461	PLAZA
DRM	PtaDRMe	PTA00046027	Gymnosperms	Conifers	Pinus taeda	435	PLAZA
DRM	PtaDRMf	PTA00067039	Gymnosperms	Conifers	Pinus taeda	349	PLAZA
DRM	AtrDRM3	evm_27.TU.AmTr_v1.0_scaffold00003.192	Angiosperms	Basel Angiosperms	Amborella trichopoda	719	Phytozome
DRM	AtrDRM2	evm_27.TU.AmTr_v1.0_scaffold00096.44	Angiosperms	Basel Angiosperms	Amborella trichopoda	503	Phytozome
DRM	BdDRM2a	Brad1g11420	Angiosperms	Monocots	Brachypodium distachyon	518	Phytozome
DRM	BdDRM2b	Brad1g77873	Angiosperms	Monocots	Brachypodium distachyon	610	Phytozome
DRM	BdDRM3	Brad2g38577	Angiosperms	Monocots	Brachypodium distachyon	706	Phytozome
DRM	BdDRM2c	Brad4g05680	Angiosperms	Monocots	Brachypodium distachyon	588	Phytozome
DRM	PhDRM3	Pahal.C01225	Angiosperms	Monocots	Panicum hallii	660	Phytozome
DRM	PhDRM2a	Pahal.I00079	Angiosperms	Monocots	Panicum hallii	603	Phytozome
DRM	PhDRM2b	Pahal.I00969	Angiosperms	Monocots	Panicum hallii	588	Phytozome
DRM	SbDRM2a	Sobic.001G458100	Angiosperms	Monocots	Sorghum bicolor	577	Phytozome
DRM	SbDRM2b	Sobic.001G535800	Angiosperms	Monocots	Sorghum bicolor	608	Phytozome
DRM	SbDRM2c	Sobic.003G124000	Angiosperms	Monocots	Sorghum bicolor	609	Phytozome
DRM	SbDRM3	Sobic.009G032200	Angiosperms	Monocots	Sorghum bicolor	657	Phytozome
DRM	ZmDRM3	GRMZM2G065599	Angiosperms	Monocots	Zea mays	461	Phytozome
DRM	ZmDRM2a	GRMZM2G092497	Angiosperms	Monocots	Zea mays	604	Phytozome
DRM	ZmDRM2b	GRMZM2G137366	Angiosperms	Monocots	Zea mays	610	Phytozome
DRM	ZorDRM3	Zosma21g00360.1	Angiosperms	Monocots	Zostera marina	597	Phytozome
DRM	ZorDRM2	Zosma67g00380.1	Angiosperms	Monocots	Zostera marina	570	Phytozome
DRM	AtDRM3	AT3G17310	Angiosperms	Eudicots	Arabidopsis thaliana	711	Phytozome
DRM	AtDRM2	AT5G14620	Angiosperms	Eudicots	Arabidopsis thaliana	627	Phytozome
DRM	AtDRM1	AT5G15380	Angiosperms	Eudicots	Arabidopsis thaliana	625	Phytozome
DRM	BrDRM2a	Brara.B00561	Angiosperms	Eudicots	Brassica rapa	406	Phytozome
DRM	BrDRM3b	Brara.E02454	Angiosperms	Eudicots	Brassica rapa	703	Phytozome
DRM	BrDRM2b	Brara.G02881	Angiosperms	Eudicots	Brassica rapa	599	Phytozome
DRM	BrDRM3a	Brara.I04643	Angiosperms	Eudicots	Brassica rapa	502	Phytozome
DRM	BrDRM2c	Brara.J02008	Angiosperms	Eudicots	Brassica rapa	602	Phytozome
DRM	GmDRM2a	Glyma.02G035700	Angiosperms	Eudicots	Glycine max	538	Phytozome
DRM	GmDRM2b	Glyma.05G005600	Angiosperms	Eudicots	Glycine max	591	Phytozome
DRM	GmDRM3a	Glyma.07G233200	Angiosperms	Eudicots	Glycine max	695	Phytozome
DRM	GmDRM3b	Glyma.17G038300	Angiosperms	Eudicots	Glycine max	730	Phytozome
DRM	GmDRM2c	Glyma.19G006100	Angiosperms	Eudicots	Glycine max	581	Phytozome
DRM	MeDRM3	Manes.03G210200	Angiosperms	Eudicots	Manihot esculenta	780	Phytozome
DRM	MeDRM2a	Manes.15G149300	Angiosperms	Eudicots	Manihot esculenta	639	Phytozome
DRM	MeDRM2b	Manes.17G113600	Angiosperms	Eudicots	Manihot esculenta	638	Phytozome
DRM	PrpDRM3	Prupe.1G109800	Angiosperms	Eudicots	Prunus persica	718	Phytozome
DRM	PrpDRM2a	Prupe.3G287400	Angiosperms	Eudicots	Prunus persica	585	Phytozome
DRM	PrpDRM2b	Prupe.8G038800	Angiosperms	Eudicots	Prunus persica	583	Phytozome

Supplementary Table 2. Primers used in this study.

	Primer Name	Sequence (5' -> 3')
Cloning	Ppdrm1 5'UTR BamHI Fw	GGATCCTGGAACGCAAAACAAGACCG
	Ppdrm1 5'UTR BamHI Rv	GGAGGTGGATCCAATTGTTCTTTC
	Ppdrm1 3'UTR SphI Fw	GCATGCTTCCCTGGCAGAAATTGG
	Ppdrm1 3'UTR NotI SphI Rv	GCATGCGGCCGCGAGCATCAAATTAGAGCTTCAGGG
	Ppdrm2 5'UTR BamHI Fw	GGATCCGTGGTGAACCTAGTTGTCCATTGG
	Ppdrm2 5'UTR BamHI Rv	GGATCCTGGCGTGTAAAGCTCACACTAA
	Ppdrm2 3'UTR SphI Fw	GCATGCGTTTGCTTGCCTTGTTCCTTC
	Ppdrm2 3'UTR NotI SphI Rv	GCATGCGGCCGCCATCCTTTTGCAACAATCCTCC
	Ppndmt3a HindIII 5'KO Fw	AAGCTTGTCGTGCTGAGTATCAGATAATCGTAGC
	Ppndmt3a HindIII 5'KO Rv	AAGCTTAATCCAAGTGTTCGAATCCGC
	Ppndmt3a SphI 3'KO Fw	GCATGCTAGCTCTCTGAAGTATCCG
	Ppndmt3a 3'KO Rv	AATCGTGCCTTCTACACATACATGCC
	Ppndmt3b HindIII 5'KO Fw	AAGCTTCGGGTTTCGGAGTCTGGGTT
	Ppndmt3b HindIII 5'KO Rv	AAGCTTGCAGGCCAGAGGAAAGAGCG
	Ppndmt3b SphI 3'KO Fw	GCATGCCCATGTTCGAATCTTTGACTTGCC
	Ppndmt3b 3'KO Rv	ACATTCCGTTTACCAGTAGCATCTGG
	KpnI Zeo Fw	GGTACCGTCAACATGGTGGAGCACGACA
	SphI Zeo Rv	GCATGCCAGGTCAGTGGATTGTGTTTAGG
Deletion mutant screening		
	Ppdrm1 2240 5' Fw	GGAACACGGTGGATGTATTCCTTCT
	Ppdrm1 5550 3' Rv	AGGCGGTATGGTTGTGCCACC
	Ppdrm1 3209 e1 Fw	GGTCAAGGTCGAATCATCTCAACG
	Ppdrm1 3779 e1 Rv	GCGTTGGGATGTTTGGAGCA
	Ppdrm2 2292 5' Fw	GACAATTTCATTTCATGCGAGTTGTC
	Ppdrm2 5324 3' Rv	CAAGCCATGCCTATTGTTATCATCTGTTT
	Ppdrm2 3202 e1 Fw	ATTGGCTTGGTCTTCTGTTCA
	Ppdrm2 3581 e1 Rv	TGTGGGAATTGCAGTGGCGT
	Ppndmt3a 5046 Fw	GCTGCAAGCGTGAGCGATTC
	Ppndmt3a 10651 Rv	GGGTGGATATCACTAAGCTCCACC
	Ppndmt3a 6377 Fw	GCTGACCAATCTAGGCATCCCG
	Ppndmt3a 8427 Rv	TGGAGGGCTTGATTAGGCAGAG
	Ppndmt3b 5678 Fw	GCTGATGACTGCTTGAGCCTTCG
	Ppndmt3b 10445 Rv	TCCACTCGTCTACTTCTTCTTTGAGATAGG
	Ppndmt3b 7159 Fw	GGTCGGGTGAACGGCTGG
	Ppndmt3b e11 Rv	AAGGCTATCCTGTGAGTTGGCTT
	35S Rv	TGGGACCACTGTCGGCAGAG
	35S-Ter-R-Fw	GCCCCGCTTAAAAATTGGT
Validation of RPS insertion	RPS-top-R new	AAGTAGAGAAAGGAAAGAGAAAGGGG
	35S Rv	TGGGACCACTGTCGGCAGAG
Bisulfite sequencing (Sanger)	RPS-top-R new	AAGTAGAGAAAGGAAAGAGAAAGGGG
	RPS-top-F	CTGTATTTTCTCCCTTCA
BS-seq	bs-seq-adapter-fwd	GATCGGAAGAGCGGTTCAGCAGGAATGCCGA*G
	bs-seq-adapter-rv	ACACTCTTTCCTACACGACGCTCTTCCGATC*T
	bs-seq-primer fwd	AATGATACGCGACACCAGAGATCTACACTCTTCCCTACACGACGCTCTTCCGATC*T
	bs-seq-primer-rv	CAAGCAGAAGACGGCATACGAGATCGGTCTCGGCATTCCTGCTGAACCGCTCTTCCGATC*T
		*= phosphorothioate bond, C= methylated cytosine

Supplementary Table 3. BS-seq stats summary.

Genetic background	Mapping			Median site coverage	Average genomic methylation levels				Average organelle methylation levels	
	Total reads	Mapped reads	Ratio		CG	CWG	CCG	CHH	Mitochondria	Chloroplast
wild type	41145982	34088890	83%	3	19.56%	21.12%	8.44%	15%	0.17%	0.17%
<i>drm1</i>	41372443	33415124	81%	3	20.9%	22.26%	9.57%	16.24%	0.17%	0.17%
<i>drm2</i>	52331188	42380753	81%	3	19.79%	21.25%	8.87%	15.29%	0.17%	0.17%
<i>drm12</i>	39059321	31104455	80%	3	19.43%	21.18%	8.84%	15.38%	0.17%	0.16%
<i>dnmt3a</i>	46395247	34361843	74%	3	20.14%	21.4%	8.83%	14.88%	0.17%	0.17%
<i>dnmt3b</i>	46037700	34325065	75%	3	19.94%	22.79%	10.68%	0.84%	0.18%	0.17%
<i>dnmt3ab</i>	51456246	40940817	80%	3	19.62%	22.59%	10.57%	0.83%	0.17%	0.16%
<i>met</i>	48204209	37218804	77%	3	1.28%	21.74%	0.65%	15.35%	0.17%	0.17%
<i>cmt</i>	47855012	37225542	78%	3	20.68%	0.49%	0.39%	15.5%	0.17%	0.17%
<i>rdr2</i>	51728794	40797730	79%	3	24.8%	25.83%	13.2%	17.82%	0.53%	0.59%

Median coverage and averaged methylation levels in wild type and PpDNMT mutant genomes. Substantial losses in methylation (>90%) are marked in red.

Supplementary References

1. Edgar, R. C. MUSCLE: multiple sequence alignment with high accuracy and high throughput. *Nucleic Acids Res* **32**, 1792–1797 (2004).
2. Castresana, J. Selection of conserved blocks from multiple alignments for their use in phylogenetic analysis. *Mol. Biol. Evol.* **17**, 540–552 (2000).