

Figure S2. Multiple sequence alignment and assignment of secondary structure elements to 3-hydroxy-3-methylglutaryl-CoA synthase (HMGS) by ESPrnt 3.0, according to the *Homo sapiens* protein structure (PDB: 2P8U). The multiple alignments included genus *Dendroctonus* and other coleopteran sequences. Conserved amino acids involved in the catalytic activity (★) were manually tagged according to previous studies [109] and ExPASy-PROSITE server (<http://prosite.expasy.org/>).

HMGR_1DQ8

HMGR_1DQ8
 HMGR_D_rhizophagus
 HMGR_D_ponderosae_U5ZZ40
 HMGR_D_jeffreyi_Q9N6G8
 HMGR_D_armandi_A0A0F7LG51
 HMGR_I_paraconfusus_Q9XY99
 HMGR_I_pini_Q95WT1
 HMGR_L_decemlineata_A0A0H4ISG3
 HMGR_T_castaneum_A0A139WIA9

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MASRLFRVHGEFCTNHPWEVIVATLTTLTACMLTVEQPPPLRPTKPTIKSCLGCIQEA EYNAADLISM TIL
MASRLFRVHGEFCTNHPWEVIVATLTTLTACMLTVEQPPPLRPTKPTIKSCLGCIQEA EYNAADLISM TIL
MVSRLFLAHGEFCTNHPWEVIVATLTTLTACMLTVEQPPPLRPTKPTIKSCLGCIQEA EYNAADLISM TIL
MVSRLFLAHGEFCTNHPWEVIVATLTTLTACMLTVEQPPPLRPTKPTIKSCLGCIQEA EYNAADLISM TIL
MSARFFYAHGEFCA SHPWEVIVATLTTLTACMLTVDQHPAPPKPKVIRFCIGCLHEAEYNAADVIVMTII
MTLRLFRAHGEFCA THPWEVIVATLTTLTACMLTVDQHPAPPKPKVIRFCIGCLHEAEYNAADLIVMTII

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 HMGR_D_ponderosae_U5ZZ40
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 HMGR_D_armandi_A0A0F7LG51
 HMGR_I_paraconfusus_Q9XY99
 HMGR_I_pini_Q95WT1
 HMGR_L_decemlineata_A0A0H4ISG3
 HMGR_T_castaneum_A0A139WIA9

```

RSLAVLYCYYQFRKMHKLGSKYILGIAGLFTVFSSLVFTTTVLNLLRIKVSDDLKDAIFFFLLLDLSKAA
RSLAVLYCYYQFRKMHKLGSKYVILGIAGLFTVFSSLVFTTTVLNLLRIKVSDDLKDAIFFFLLLDLSKAA
RSLAVLYCYYQFRKMHKLGSKYVILGIAGLFTVFSSLVFTTTVLNLLRIKVSDDLKDAIFFFLLLDLSKAA
RSLAVLYCYYQFRKMHKLGSKYILGIAGVFTVFSSLVFTTTVLNLLRIKVSDDLKDAIFFFLLLDLSKAA
RSLAVLYCYYQFRKMHKLGSKYILGIAGLFTVFSSLVFTTTVLNLLRIKVSDDLKDAIFFFLLLDLSKAA
RSLAVLYCYYQFRKMHKLGSKYILGIAGLFTVFSSLVFTTTVLNLLRIKVSDDLKDAIFFFLLLDLSKAA
RCLAVLYCYYHFKLHKLKSKYILSVAGLFTVFSSLVFTTTVLNLLRMVNTDLKDAIFFFLLLDLSKAA
RCLAVLYCYYQFRKMHKLGSKYILGIAGLFTVFSSLVFTTTVLNLLRIKVSDDLKDAIFFFLLLDLSKAA

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 HMGR_I_paraconfusus_Q9XY99
 HMGR_I_pini_Q95WT1
 HMGR_L_decemlineata_A0A0H4ISG3
 HMGR_T_castaneum_A0A139WIA9

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LLAQFALNGANQAERKNTNIAKGLAELGPTITLDTLTVETLVIGVGTMSGVARLEMLSWFA CLSVLVNYIVF
LLAQFALNGANQAERKNTNIAKGLAELGPTITLDTLTVETLVIGVGTMSGVARLEMLSWFA CLSVLVNYIVF
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MLAQFALTSQNETEGKNNIAKGLAELGPTITLDTLTVETLVIGVGTMSGVARLEMLSWFA CLSVLVNYIVF
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 HMGR_L_decemlineata_A0A0H4ISG3
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MTFYFACLSLILSLSSNFCKTKDSWKILFAFKEDRKSNPVLQVRKILMSVGLMIVHVSRRWPFRRDSEV
MTFYFACLSLILSLSSNFCKTKDSWKILFAFKEDRKSNPVLQVRKILMSVGLMIVHVSRRWPFRRDSEV

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 HMGR_I_paraconfusus_Q9XY99
 HMGR_I_pini_Q95WT1
 HMGR_L_decemlineata_A0A0H4ISG3
 HMGR_T_castaneum_A0A139WIA9

```

YTIEPLVQQS...FNKTTDDSIATHVSFIRWLVLGADHIVIIILVSALLKLIFFFEIKDNLVEIKS...
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YTIEPLVQQS...FNKTTDDSIATHVSFIRWLVLGADHIVIIILVSALLKLIFFFEIKDNLVEIKS...
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YNIIEPLVQQS...FNNTESSSVHLYFERWIALGADHIVILILITALLKLIFFFEIKDNLVEIKS...
YNIIEPLVQQS...FNNTESSSVHLYFERWIALGADHIVILILITALLKLIFFFEIKDNLVEIKS...
YNIIEPLVQQS...FNNTESSSVHLYFERWIALGADHIVILILITALLKLIFFFEIKDNLVEIKS...
YNIIEPLVQQS...FNNTESSSVHLYFERWIALGADHIVILILITALLKLIFFFEIKDNLVEIKS...
YNIIEPLVQQS...FNNTESSSVHLYFERWIALGADHIVILILITALLKLIFFFEIKDNLVEIKS...
YNIIEPLVQQS...FNNTESSSVHLYFERWIALGADHIVILILITALLKLIFFFEIKDNLVEIKS...

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HMGR_1DQ8

HMGR_1DQ8
 HMGR_D_rhizophagus
 HMGR_D_ponderosae_U5ZZ40
 HMGR_D_jeffreyi_Q9N6G8
 HMGR_D_armandi_A0A0F7LG51
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 HMGR_I_pini_Q95WT1
 HMGR_L_decemlineata_A0A0H4ISG3
 HMGR_T_castaneum_A0A139WIA9

```

...GFDKETS...KPKQKQMPMINFTLGES...CESTYKDKVQOT...LITS
...GFDKETP...KPKQKQMPMINFTLGES...CESTYKDKVQOT...LATS
...GFDKETP...KPKQKQMPMINFTLGES...CESTYKDKVQOT...LATS
...GFDRETP...KPKQKQMPMINFTLGES...CESTYKDKVQOT...LITS
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EPEKREKGE...NTEKEEPKVVEVRANKRMPMSLSSEDD...CESTYKDKVQOT...QTPY
ESLEKNSSSEFCINQNLNDKFPPEIPVYKPSKFFFLGKSDIDEKSDKSSVS...EVELEDKAIQTSRYDLN.E
ESVDPGKKD...NRFK...MPLIK...QSFFLTNNTEKEDS...ACEDDKVQOTDIGRLESE

```

HMGR_1DQ8

HMGR_1DQ8
 HMGR_D_rhizophagus
 HMGR_D_ponderosae_U5ZZ40
 HMGR_D_jeffreyi_Q9N6G8
 HMGR_D_armandi_A0A0F7LG51
 HMGR_I_paraconfusus_Q9XY99
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 HMGR_L_decemlineata_A0A0H4ISG3
 HMGR_T_castaneum_A0A139WIA9

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SVLVITQEPETELPREPRNNEECLOITGNAEKCAFLSDAEIIOIVNAKHFPAYKLETLIEIHERGVSI RR
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NSDVDSSSDDVPKQCRSLKDCVKIFKNIDIGATALDDDEIILTKNKNIAAYQIEKEVDDPERGVGIRR
NSDVDSSSDDVPKQCRSLKDCVKIFKNIDIGATALDDDEIILTKNKNIAAYQIEKEVDDPERGVGIRR
NSDVDSSSDDVPKQCRSLKDCVKIFKNIDIGATALDDDEIILTKNKNIAAYQIEKEVDDPERGVGIRR
NSEAHSSSEDDIPKVKCTLEDCLKIYNNVDMGATALDDDEIILTKNKNIAAYQIEKEVDDPERGVGIRR
NPDAHSSSEDDIPKVKCTLEDCLKIYNNVDMGATALDDDEIILTKNKNIAAYQIEKEVDDPERGVGIRR
QNLLSENNEENVKNSCRTLEECLATYNDFDGAVALNDEEVIILVKKKHIAAYQIEKEVDDPERGVGIRR
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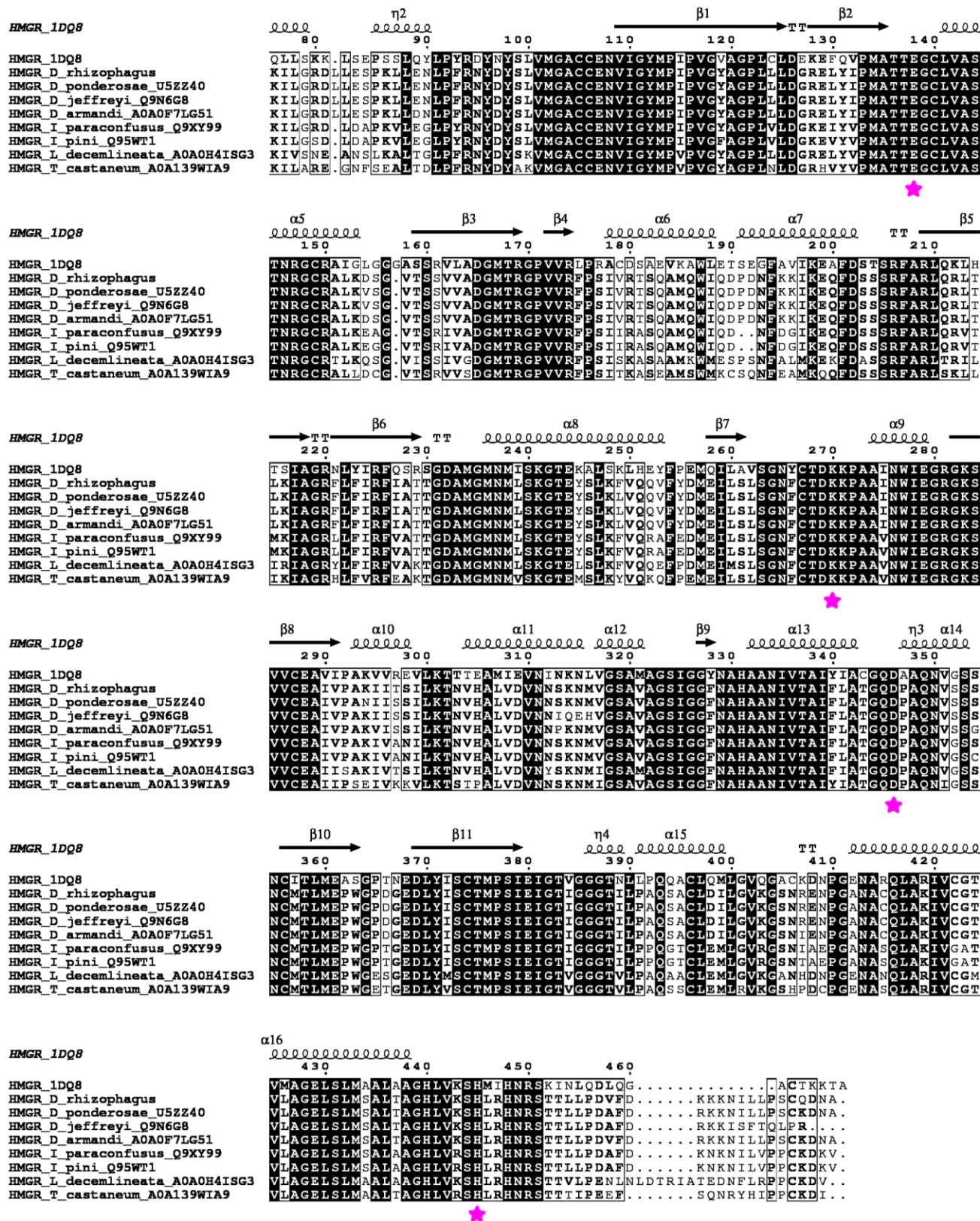


Figure S3. Multiple sequence alignment and assignment of secondary structure elements to 3-hydroxy-3-methylglutaryl-CoA reductase (HMGR) by ESPrnt 3.0, according to the *Homo sapiens* protein structure (PDB: 1DQ8). The multiple alignments included genus *Dendroctonus* and other coleopteran sequences. TMHMM Server v. 2.0 predicted five transmembrane helices (blue boxes). Conserved amino acids involved in the catalytic activity (★) were manually tagged according to previous studies [110] and ExPASy-PROSITE server (<http://prosite.expasy.org/>).

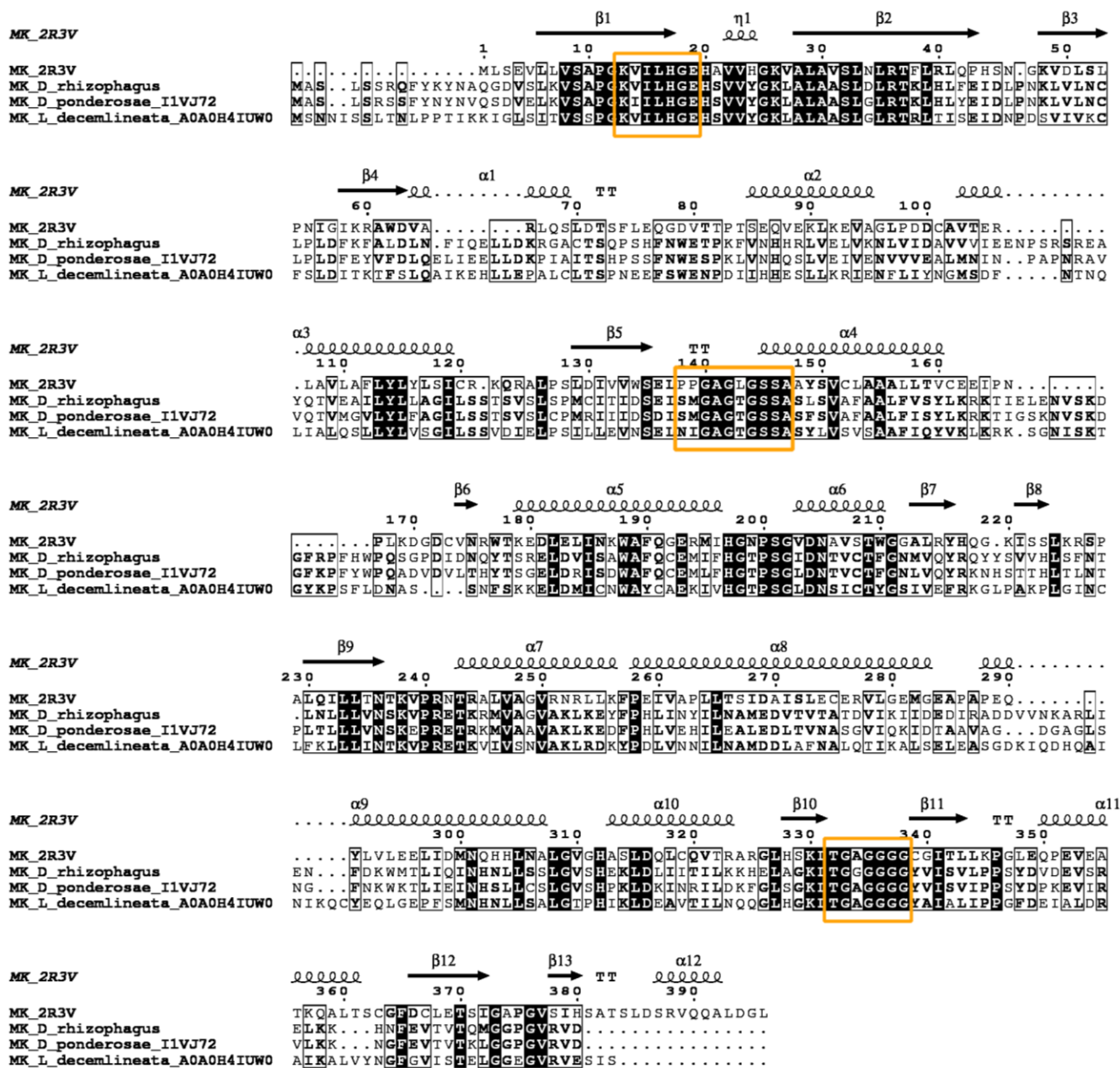


Figure S4. Multiple sequence alignment and assignment of secondary structure elements to mevalonate kinase (MK) by ESPrict 3.0, according to the *Homo sapiens* protein structure (PDB: 2R3V). The multiple alignments included genus *Dendroctonus* and other coleopteran sequences. Conserved motifs (orange boxes) were manually tagged according to previous studies [111–113].

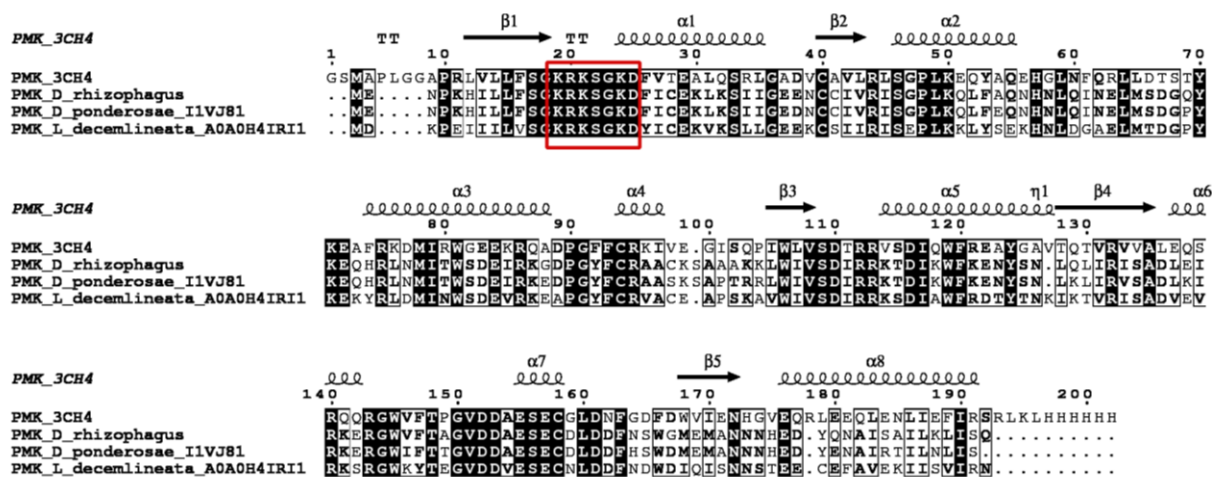


Figure S5. Multiple sequence alignment and assignment of secondary structure elements to phosphomevalonate kinase (PMK) by ESPript 3.0, according to the *Homo sapiens* protein structure (PDB: 3CH4). The multiple alignments included genus *Dendroctonus* and other coleopteran sequences. Conserved motif (red box) was manually tagged according to previous studies [114,115].

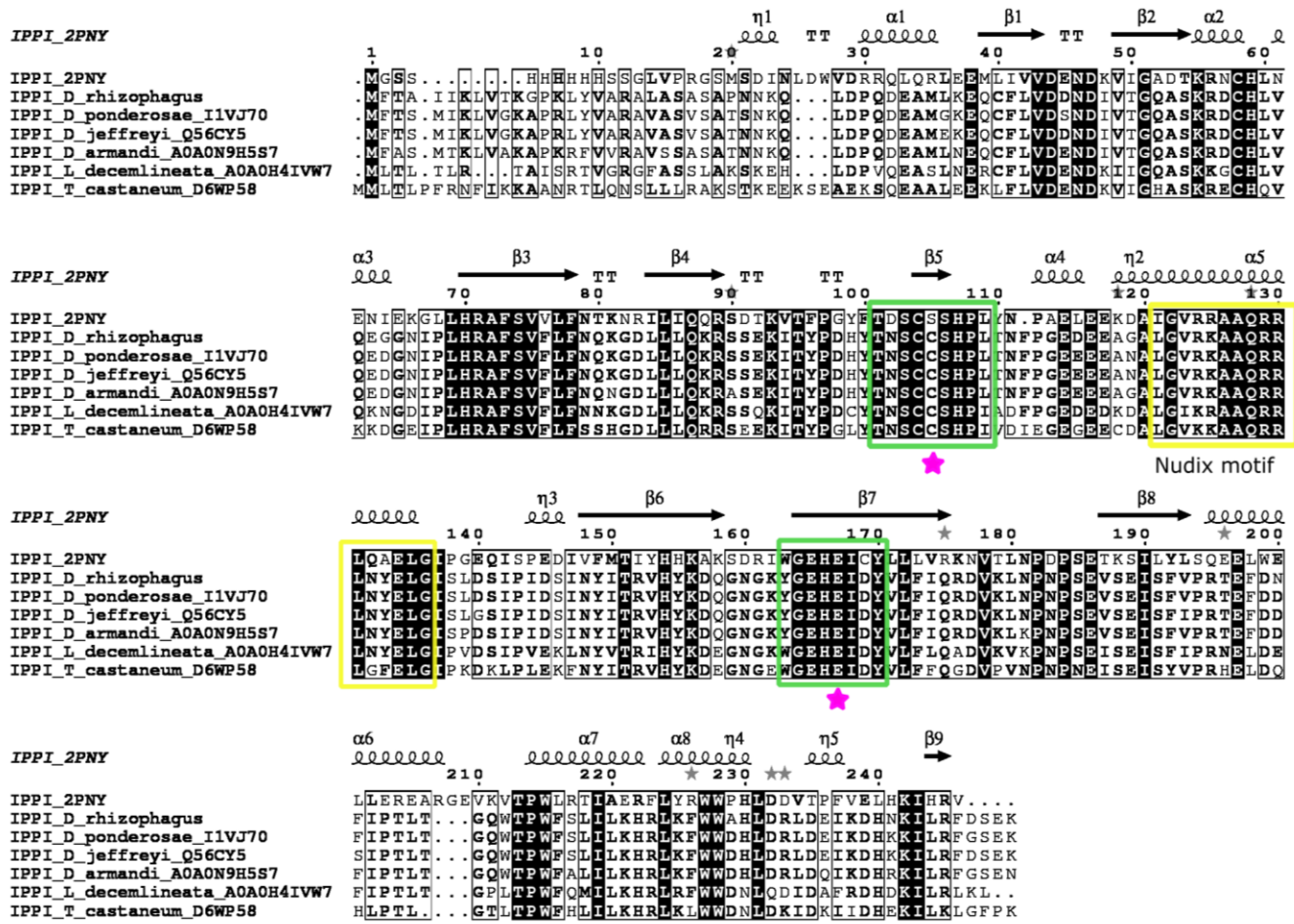


Figure S7. Multiple sequence alignment and assignment of secondary structure elements to isopentenyl diphosphate isomerase (IPPI) by ESPrnt 3.0, according to the *Homo sapiens* protein structure (PDB: 2PNY). The multiple alignments included genus *Dendroctonus* and other coleopteran sequences. Conserved motifs (green and yellow boxes) and amino acids involved in the catalytic activity (★) were manually tagged according to previous studies [118,119] and ExPASy-PROSITE server (<http://prosite.expasy.org/>).

MFS.MKMCNNRNSCREFFLEARRTTISKTS.TDKNSDAISRQDEKLN.VESDSNGSYSRWKQMHNN
MFS.MKLCNNRNSCREFFLEARRTTISKTS.TDKNSDAISRQDEKLN.VESDSTGSYSRWKQMHNN
MFS.MKLCNNRNSCREFFLEARRTTISKTS.TDKNSDAISRQDEKLN.VESDSTGSYSRWKQMHNN
MFS.MKVCNNRNSCREFFLEARRTTISKTS.TDKNSDAISRQDEKLN.VESDSTGSYSRWKQMHNN
MFS.MKACNNRNSCTRWLEFFRRNISKTS.TDKNSDAISRQDKMQHASKTHEVAFENKLSYTRWQKMQHN
MFS.SKKLAINRNTSREILREIRRHISKTT.GVTNSDAISRQESKLGG.NLDLNGSDYGESRNKWKISKQO

RxxS
 α1
α2
α3

1 10 20 30 40 50

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

[illegible]

$\alpha 6$ $\alpha 7$ $\alpha 8$
00000000000000000000 00000000000000000000 TTT 00000000
130 140 150 160 170 180 190
AINDSFLLESVYRVLKKYCQRQPYVHHLELFLQTAYQTETGOMLDLITAP.VSKVDLSHFSEERKAI
AINDALMVENAVYLLKKRHLKDHMPVPLMELEFHDGNLKTTLGQSLDLMCLDNTNGKPKLDMFTMSRYTSI
AVNDAMVIMENAVYLLKKRHLKDHMPVPLMELEFHEGNLKTTLGQSLDLMCLDNTNGKPKLDMFTMSRYTSI
AVNDAMVIMENAVYLLKKRHLKDHMPVPLMELEFHEGNLKTTLGQSLDLMCLDNTNGKPKLDMFTMSRYTSI
AINDAIMMENAVYLLKKRHLKDHMPVPMMELEFHEGTIKTTLGQSLDLMCLDNTNGKPKLDMFTMSRYTSI
AVYDAMVMENGVYLLKKRHLKDHMPVMTNIELEFHEDMALKTSLGQSLDLMCLDNDGKPKLDIHNE.QDTSI
AFNDAILLEHGYILLKKRHFQHHCVYPTIMELEFHDVTLKTSMGQALDCLCNK.DGKPNLELFTMNKYSI
AVIDGTLLESSTIYILRKRYFDHPSVPIELEFHDVTLKCSMGKSLDGYIMN.NAGSDLSRFTMKNYNL

$\alpha 9$ $\alpha 10$ $\alpha 11$
00000 0000 0000000000 000000000000000000000000
 200 210 220 230 240 250 260
 VKYKTAFFYSFYIPVAAAMMYMVGIDSKREEHENAKAILLEMGEYFOIODDVLDFCFGDPATTKGVGTDITQDNK
 VKYKTAFFYSQMPVAIAMYLAGMSDEEEOHROAKTILMEMGFFFOIODDVLDFCFGDPVTGKVGTDITQDGK
 VKYKTAFFYSQMPVAIAMYLAGMSDEEEOHROAKTILMEMGFFFOIODDVLDFCFGDPVTGKVGTDITQDGK
 VKYKTAFFYSQMPVAIAMYLAGMSDEEEOHROAKTILMEMGFFFOIODDVLDFCFGDPVTGKVGTDITQDGK
 VNYKTSYYSPFYIPVAAAMMYLLGMDPEEOHROAKTILLDMGFFFOIODDVLDFCFGDPNVTGKLGTDITQDGK
 VKYKTAFFYSQMPVAIAMMYANLYDPEEMHROAKTILMEMGLFFFOIODDVLDFCFGDPVEVTGKKGNDIREGK
 MKYRTGYHSEQLFVGAAMYLAQMYPDEEOHROAKTILLLELGOFYOIKQDELNCFGDSQVTKWKLGSHTINEG

$\alpha 12$ $\alpha 13$ $\alpha 14$ $\alpha 15$
00000000 0000000000 00000000000000 0000000000000000
270 280 290 300 310 320 330
CSWLIVVQGLORVTFEQRQLLEDN YCRKKEPEKVAKVKEYL EAVGMRRAAFQQYEEESYRRLQEL IEKHSNRI
CSWLAVVALQORASPAQRKIMEEH YGRSEPESSVARIKNLYVDLC LPNTYAYIYEEESFNIIKTH IQQISKGL
CSWLAVVALQORASPAQRKIMEEH YGRPEPESIARIKNLYVDLC LPNTYAYIYEEESFNIIKTH IQQISKGL
CSWLAVVALQORASPAQRKIMEEH YGRPEPESIARIKNLYVDLC LPNTYAYIYEEESFNIIKTH IQQISKGL
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CSWLAVMALQORSTPAQRKIMEEH YGRPEPESSVAIIKQLYEDLT LPNTYAYIYEEESFNIIKTH IQQISKDC
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α16

oooooooo

340

PKEIFLGLAQKIYKRQ
RHDLFKIMEKIYKREC
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VTIFSKHYGEAFKRES
PHKLFKIMEKIYRRD
PHKLFLLDLKLFENQ

