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Electronic Supporting Information

β-Amyrin synthase from *Euphorbia tirucalli* L. Functional analyses of the highly conserved aromatic residues Phe413, Tyr259 and Trp257 disclose the importance of the appropriate steric bulk, and cation- π and CH- π interactions for the efficient catalysis of the polyolefin cyclization cascade

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		*	20	*	40	*	60	*	80	*	100	
EtAS	:	MWKLKIAE	-GG-NDEYLYS	TN-NYVGR	QTWVFDPQ-P	PTPQELAQVO	QQARLNFYNNR	HVKPSSD	LWRFQFLREK	-NFKQTIPQA	KINEGE	: 87
PNY1	:	MWKLKIAE	-GNKNDPYLYS	TN-NFVGR	Q TWE FDPDYV	ASPGELEEVE	EQVRRQFWDNR	QVKPSGDI	LWRMQFLREK	-NFRQTIPQV	KVGDDE	: 89
BPY	:	MWRLKIAD	-GG-SDPYIYS	TN-NFVGR	QTWEFDPQ-A	GSPQERAEVE	SEARRNFYDNR	QVKPSGDI	LWRMQFLKEK	-NFKQTIPPV	KVEDGE	: 87
PSY	:	MWRLKIAE	-GG-NDPYLFS	TN-NFVGR	QTWEYDPE-A	GSEEERAQVE	SEARRNFYNNRF	EVKPCGDI	LWRFQVLREN	-NFKQTIGGV	KIEDEE	: 87
AtLUP1	:	MWKLKIGK	-GNGEDPHLFS	SN-NFVGR	QTWKFDHK-A	GSPEERAAVE	EEARRGFLDNRE	RVKGCSDI	LWRMQFLREK	-KFEQGIPQI	KATNIE	: 88
TRW	:	MWKLKIAE	-GG-DDEWLTT	TN-N <mark>H</mark> VGR	QHWQFDPD-A	GTEEERAEI	EKIRLNFKLNRF	QFKQSADI	LMRTQLRKEN	- PINKI PDAI	KLNETE	: 87
OEW	:	MWKLKIAD	-GTGPWLTT	TN-N <mark>H</mark> IGR	QHWEFDPE-A	GT PDE RVEVE	ERLREEFKKNRE	RTKQSADI	llmrmqlvken.	-QRVQIPPAI	KIKETE	: 86
BPW	:	MWKLKIAE	-GG-PGLVS	GN-DFIGR	QHWEFDPD-A	GT PQE RAEVI	EKVREEFTKNRF	QMKQSADI	llmrmqlrken.	-PCQPIPPPV	KVKETE	: 85
AtCAS1	:	MWKLKI-AE	GGSPWLRT	TN-N <mark>H</mark> VGR	QFWEFDPN-L	GT PEDLAAVE	EEARKSFSDNRF	VQKHSADI	LIMRLQFSREN	-LISPVLPQV	KIEDTD	: 86
PSCAS	:	MWKLKV-AE	GGT PWLRT	ln <mark>-</mark> n <mark>h</mark> vgr	QVWEFDPH-S	GS PQDLDDI B	ETARRNFHDNRF	THKHSDDI	LIMRLQFAKEN	-PMNEVLPKV	KVKDVE	: 86
PgCAS	:	MWKLKI-AE	GGN PWLRT	ln-d <mark>h</mark> vgr	QIWEFDPN-I	GSPEELAEVE	EKVRENFRNHRF	EKKHSADI	llmriqfanen [.]	-PGSVVLPQV	KVNDGE	: 86
BpCAS1	:	MWKLKIGAETARGDGG	GGGGGSETWLRS	ln-n <mark>h</mark> lgr	QIWEFHPE-L	JGTQEELQQII	DDARRRFWERRF	ERRHSSD	l <mark>mriqfaken</mark> .	-PSSANIPQV	KIKDTE	: 97
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HsLAS	:	MTE-GTCLRRRGGPYK	TEPATDLGRWR	LN-CERGR	QTWTYLQ-DE	RAGREQTGL	EAYALGLDTKNY				-FKDLP	: 68
MmLAS	:	MTE-GTCLRRRGGPYK	TEPATDLTRWR	LQ-N <mark>E</mark> LGR	Q <mark>RWT</mark> YYQAED)DPGREQTGLE	EAHSLGLDTRS				-FTDLP	: 69
SCLAS	:	MTEFYSDTI	GLPKTDPRLWR	LRTD <mark>E</mark> LGR	ESWEYL	TPQQAA	NDE	PSTFTQW	LQDPKF PQPH:	PERNKHSPDE	SAFD	: 75
SHC	:	M									А	: 2
		М		n gr	w			נ	1			
		_ *	120	*	140	*	160		180	*	200	
EtAS	:	DITYEKATTALRRA	VHFFSALQASD	-GHWPAEN.	AGPLFFLPPL	'MCLYITGHI	LDTVF PAPHRLE	ILRYIYCH	IQNE-DGGWGLI	HIE <mark>GH</mark> STMFC	TVLSYI	: 183
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BPY												. 100
PSY	•	EITYEKSTAALRRA	VHFYSALQASD	-GHWPAEN.	AGPLFFLPPL	VMCMYITGHI	INTVF PAEHQK E	ILRYIYYH	IQNE-DGGWGLI	HIE <mark>GH</mark> STMFC	TALSYI	: 183
	:	EITYEKSTAALRRA EITYEKTTTTLRRG	AVHFYSALQASD STHHLATLQTSD	-GHWPAEN. -GHWPAQI.	AGP <mark>LFF</mark> LPPL AGPLFFMPPL	VMCMYITGHI VFCVY <mark>ITG</mark> HI	LNTVF PAEHQK EDSVF PPEHRKE	ILRYIYYH ILRYIYCH	IQNE-DGGWGLI IQNE-DGGWGLI	HIEGHSTMFC HIEGHSTMFC	TALSYI TALNYI	: 183 : 183
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AtLUP1 TRW OEW BPW AtCAS1 PsCAS PgCAS BpCAS1 AtLAS1 HsLAS MmLAS		EITYEKSTAALRA EITYEKTTTILRG EITYETTTNALRG GITEEAVITTIKRA VITEEAVITTIRRA DVTEEMVETTIKRA DVTEEAVATTIRRA EVREEAVGMTIRRA ERLINEEVVNVTIRRS KAHTAFEGALNG	VHFYSALQASD THHLATLQTSD VRYFTALQASD SVRYFTALQASD SISFYSTIQAHD SLSFYSSIQAHD SLDFYSTIQAHD SLNFYSTIQSHD MSFYSTIQADD SLRFYSILQSQD SMTFYVGLQAED SVTFYAKLQAED	- GHW PAEN - GHW PAQI - GHW PAES - GHW PAES - GHW PGES - GHW PGDY - GHW PGDY - GHW PGDY - GHW PGDY - GHW PGDY - GHWTGDY - GHWTGDY	AGPLFFLPPL AGPLFFLPPL AGPLFFLPPL AGPLFFLPPL AGPLFFLPPL GGPMFLLPGL GGPMFLMPGL GGPMFLMPGL GGPLFLLPAL GGPLFLLPGL	VMCMYITGH VFCVYITGH VFCLYITGH VIALYVTGA VIALYVTGA VMALYITGD IITLSITGA VITLSITGA VITLSITGA VITLSITGT VITLSITGT LITCHVA	LNTVF PAEHQK LDSVF PPEHRKE LEEVFDAEHRKE INDILT PAHQLE INVVLSREHQKE LNTIF SPAHQKE LNTVLSEQHKQE LNAVLTDEHRKE LNAVLTDEHRKE LNAFLSKEHQCE LDGTLTAQHQIE -RIPLPAGYRE -HISLPAGYRE	ILRYIYYH ILRYIYCH MLRHIYCH IKRYIYNH ITRYIYNH IRRYLYNH MRRYLYNH ICRYLYNH ICRYLYNH IRRYLYNH IRRYLYNH IVRYLRSY	IQNE - DGGWGL IQNE - DGGWGL IQNE - DGGWGL IQNE - DGGWGL IQNE - DGGWGL IQNE - DGGWGL IQNE - DGGWGL IQNK - DGGWGL IQNK - DGGWGL IQNK - DGGWGL IQNK - DGGWGL IQNK - DGGWGL	HIEGHSTMFO HIEGHSTMFO HIEGHSTMFO HIEGHSTMFO HIEGHSTMFO HIEGPSTMFO HIEGPSTMFO HIEGPSTMFO HIEGPSTMFO HIEDKSTVFO HIEDKSTVFO	TAL SYI TALNYI SVL SYI SVL SYI SAL SYI SVL CYV SVL CYV TVL NYV TALNYI TALNYV TALNYV	: 183 : 183 : 184 : 183 : 184 : 183 : 182 : 183
AtLUP1 TRW OEW BPW AtCAS1 PsCAS PgCAS BpCAS1 AtLAS1 HsLAS MmLAS ScLAS		EITYEKSTAALRA EITYEKTTTILRG EITYETTTNALRG EVTNDAVTTTLKRA GITEEAVITTLRRA VITEEAVITTLRRA DVTEEMVETTLRG DISEDKVTVTLRRA E-VREEAVGMTLRRA ERLINEEVVNVTLRRA KAHTAFEGALNG KAQTAHEGALNG	VHFYSALQASD THHLATLQTSD VRYFTALQASD SVRYFTALQASD SSFYSTIQAHD SLSFYSSIQAHD SLSFYSTIQAHD SLSFYSTIQAHD MSFYSTIQAHD SLRFYSILQSQD SMTFYVGLQAED SASFFKLLQEPD	- GHW PAEN - GHW PAEI - GHW PAES - GHW PAES - GHW PGES - GHW PGDY - GHW PGDY - GHW PGDY - GHW PGDY - GHW PGDY - GHWTGDY - GHWTGDY - GHWAGDY SGIF PCQY	AGPLFFLPPL AGPLFFLPPL AGPLFFLPPL AGPLFFLPPL AGPLFFLPPL GGPMFLLPGL GGPMFLMPGL GGPMFLMPGL GGPLFLLPAL GGPLFLLPGL GGPLFLLPGL	VMCMYITGH VFCVYITGH IFCLYITGH VIALYVTGA VIALYVTGA VMALYITGD IITLSITGA VITLSITGA VITLSITGV VITLSITGV VITLSITGT VITLSITGT UITCHVA LITCHIS	NTVFPAEHQKE DSVFPPEHRKE NDILTPAHQLE NVVLSREHQKE NTIFSPAHQKE NTVLSEQHKQE NAVLTDEHRKE NAVLTDEHRKE NAFLSKEHQCE DGTLTAQHQIE RIPLPAGYREE - IEIPEHERIE	ILRYIYYH ILRYIYCH MLRHIYCH IKRYIYNH ITRYIYNH MRRYLYNH MRRYLYNH ICRYLYNH ICRYLYNH IRRYLYNH IVRYLRS\ LIRYIVNY	IQNE - DGGWGL IQNE - DGGWGL IQLP - DGGWGL IAHPVDGGWGL	HIEGHSTMFO HIEGHSTMFO HIEGHSTMFO HIEGHSTMFO HIEGHSTMFO HIEGPSTMFO HIEGPSTMFO HIEGPSTMFO HIEGPSTMFO HIEDKSTVFO HIEDKSTVFO HIEDKSTVFO	TAL SYI TALNYI SVL SYI SVL SYI SAL SYI SVL CYV TVL NYV TALNYI TALNYI TALNYV TALNYV TALNYV	: 183 : 183 : 184 : 184 : 183 : 182 : 183 : 184 : 183 : 182 : 160 : 161
AtLUP1 TRW OEW BPW AtCAS1 PsCAS PgCAS BpCAS1 AtLAS1 HsLAS MmLAS ScLAS SHC		EITYEKSTAALRA EITYEKTTTILRG EITYETTTNALRG GITEEAVITTLKA GITEEAVITTLRA VITEEAVITTLRA DVTEEAVATTLRG DISEDKVTVTLRG E-VREEAVGMTLRA ERLINEEVVNVTLRS KAHTAFEGALNG KAQTAHEGALNG EQLVEAPAYARTLDRA	VHFYSALQASD THHLATLQTSD VRYFTALQASD VRYFTALQASD SSFYSTIQAHD SLSFYSSIQAHD SLSFYSTIQAHD SLNFYSTIQAHD MSFYSTIQAHD SLRFYSILQSQD STFYAKLQAED SASFFKLLQEPD	- GHW PAEN - GHW PAEI - GHW PAES - GHW PAES - GHW PGES - GHW PGDY - GHW PGDY - GHW PGDY - GHW PGDY - GHW PGDY - GHWTGDY - GHWTGDY SGIF PCQY E GYWWGPL	AGPLFFLPPL AGPLFFLPPL AGPLFFLPPL AGPLFFLPPL AGPLFFLPPL GGPMFLLPGL GGPMFLMPGL GGPMFLNPGL GGPLFLLPAL GGPLFLLPGL GGPLFLLPGL KGPMFMTIGY LSNVTMEAEY	VMCMYITGH VFCVYITGH IFCLYITGH VIALYVTGA VIALYVTGA VMALYITGD IITLSITGA VITLSITGA VITLSITGV VITLSITGT VIGLYVTEV LITCHVA LITCHIS VAVNYIAG-	NTVFPAEHQKE LDSVFPPEHRKE NDILTPAHQLE NVVLSREHQKE NTIFSPAHQKE NTVLSEQHKQE NAVLTDEHRKE NVVLSKEHKRE NAFLSKEHQCE DGTLTAQHQIE RIPLPAGYREE HISLPAGYREE -IEIPEHERIE	ILRYIYY ILRYIYCH MLRHIYCH IKRYIYNH ITRYIYNH MRRYLYNH MRRYLYNH ICRYLYNH ICRYLYNH IRRYLYNH IVRYLRSV LIRYIVNI IRRYL	IQNE - DGGWGL IQNE - DGGWGL IQLP - DGGWGL CLP - DGGWGL CRE - DGTWAL	HIEGHSTMFO HIEGHSTMFO HIEGHSTMFO HIEGHSTMFO HIEGHSTMFO HIEGPSTMFO HIEGPSTMFO HIEGPSTMFO HIEGPSTMFO HIEDKSTVFO HIEDKSTVFO HIEDKSTVFO HIEDKSTVFO	TAL SYI TALNYI SVL SYI SVL SYI SAL SYI SVL CYV TVL NYV TALNYI TALNYI TALNYV TALNYV TALNYV TALNYV	: 183 : 183 : 184 : 183 : 182 : 183 : 184 : 183 : 182 : 185 : 160 : 96

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			*	2	20	7	*	240		*	20	60		*	280)	*		300		
EtAS	:	CMRLLC	EGPNG	-GQDNAC	SRARKW	IIDHG	GATYIP	SWGK <mark>T</mark> WL	SILGV	EWSG	SNPMPPI	5 <mark>F</mark> WIL	PTFLPM	1HPAKM	W Y CRM	IVY <mark>M</mark> PM ?	SYLY <mark>G</mark>	KRF <mark>V</mark> G	PITPL	:	282
PNY1	:	CMRILO	EGPDG	-GVNNAC	ARGRKW	ILDHG	SVTAIP	SWGK <mark>T</mark> WL	SILGV	EWIG	SNPMPPI	B <mark>F</mark> WIL	PSFL <mark>P</mark> M	1HPAKM	W Y CRM	IVY <mark>M</mark> PM ?	SYLY <mark>G</mark>	KRF <mark>V</mark> G	PITPL	:	284
BPY	:	CMRILO	EGPDG	-GQDNAC	ARARKW	ILDHG	GVTHMP	SWGK <mark>T</mark> WL	SILGIE	EWIG	SNPMPPI	B <mark>F</mark> WIL	PSFLPM	1HPAKM	W Y CRM	1VYM PM :	SYLY <mark>G</mark>	KRF <mark>V</mark> G	PITPL	:	282
PSY	:	CMRILO	EGPDG	-GEDNAC	VRARNW	IRQH <mark>G</mark> (GVTHI P	SWGK <mark>T</mark> WL	SILGVE	DWLG	SNPMPPI	B <mark>F</mark> WIL	₽SFL <mark>P</mark> M	1HPAKM	WYCRI	VYM PM :	SYLY <mark>G</mark>	KRF <mark>V</mark> G	PITPL	:	282
AtLUP1	:	CLRMLC	ENP	EQDAC	KRARQW.	ILDRG	GVIFIP	SWGK <mark>F</mark> WL	SILGV	DWSG	TNPTPP	B LLML	PSFL <mark>P</mark> I	[HP <mark>G</mark> KI	LYSRM	1VSIPM:	SYLY <mark>G</mark>	KRF <mark>V</mark> G	PITPL	:	280
TRW	:	TLRLLC	EEADS	VAEDMAL	VKGRKW	ILDHG	GAVGI P	SWGK <mark>F</mark> WL	TILGV	EWGG	CNPMPP	B <mark>FWLM</mark>	PKFFPI	HP <mark>G</mark> KM	LYCRI	VYM PM ?	SYLY <mark>G</mark>	KRF <mark>V</mark> G	KITEL	:	283
OEW	:	TLRLLC	EGQED	-GEDKAV	ARGRKW	ILDHG	GAVGI P	SWGK <mark>F</mark> WL	TVLGV	EWDG	C <mark>N PM P</mark> PI	B <mark>F</mark> WLL	PNFSPI	HP <mark>G</mark> KM	LYCRI	VYM PM ?	SYLY <mark>G</mark>	KRF <mark>V</mark> G	PITGL	:	281
BPW	:	ALRILO	EGLED	-GEDGAM	AKSRKW	ILDH <mark>G</mark> (GLVAI P	SWGK <mark>F</mark> WV	TVLGL	EWSG	CNPLPPI	EFWFL	PDIFPI	HP <mark>G</mark> KM	LYCRI	VYM PM ?	SYLY <mark>G</mark>	KRF <mark>V</mark> G	PITGL	:	280
AtCAS1	:	TLRLLO	EGPND	GDGDM	EKGRDW	ILNHG	GATNIT	SWG <mark>K</mark> MWI	SVLG <mark>A</mark>	EWSG	NNPLPPI	E <mark>IWLL</mark>	PYFLPI	[HP <mark>G</mark> RM	W H CRM	IVY L PM 9	SYLY <mark>G</mark>	KRF <mark>V</mark> G	PITST	:	280
PSCAS	:	TLRLLG	EGPND	GEGDM	ERGRDW	ILEH <mark>G</mark> (GATYIT	SWG <mark>K</mark> MWI	SVLGV	EWSG	NN PM P PI	E <mark>I</mark> WLL	PYAL <mark>P</mark> V	/HP <mark>G</mark> RM	W H CRM	1VY L PM 9	SYLY <mark>G</mark>	KRF <mark>V</mark> G	PITPT	:	280
PgCAS	:	TLRLLG	EGAND	GQGAM	EKGRQW	ILDHG	SATAIT	SWG <mark>K</mark> MWL	SVLGV	EWSG	NNPLPPI	E <mark>T</mark> WLL	PYILPI	[HP <mark>G</mark> RM	W HRR	IVY L PM 9	SYLY <mark>G</mark>	KRF <mark>V</mark> G	PITPT	:	280
BpCAS1	:	TLRLLG	E-PED	GMGAV	EKARKW	ILDHG	GATAIT	SWG <mark>K</mark> MWL	SVLGV	EWSG	NNPLPPI	e <mark>v</mark> wlc	PYLLPC	CHPGRM	W H CRM	IVY L PM 9	SYLY <mark>G</mark>	KRF <mark>V</mark> G	PITST	:	290
AtLAS1	:	ALRLMG	EELDG	GDGAM	ESARSW	IHHHG	GATFIP	SWGK <mark>F</mark> WL	SVLG <mark>A</mark> S	EWSG	NNPLPPI	E <mark>L</mark> WLL	PYSLPE	hp <mark>grm</mark>	W H CRM	IVY L PM :	SYLY <mark>G</mark>	RREVO	RTNGT	:	280
HsLAS	:	SLRILG	VGPD	DPDL	VRARNI	LHKKG	GAVAI P	SWGK <mark>F</mark> WL	AVLNV3	SWEG	LNTLFP	EMWLF	PDWA <mark>P</mark> A	AHPSTI	W H CRÇ	DVYLPM:	sycya	VRLSA	AEDPL	:	255
MmLAS	:	ALRILO	IGPD-	DPDL	VRARNV	LHKKG	GAVAI P	SWGK <mark>F</mark> WL	AVLNV3	SWEG	LNTLFPI	EMWLF	PEWVPA	AHPSTI	W H CRÇ	DVYLPM:	sycya	TRLSA	SEDPL	:	256
SCLAS	:	ILRLLG	LPKD-	HPVC	AKARST	LLRLG	G <mark>aigsp</mark>	HWGKIWL	SALNL	KWEG	VN P <mark>A</mark> P PI	E <mark>TWL</mark> L	PYSLPM	1 H P G R W	WYH FRG	VYI PV:	SYLSI	VKFSC	PMTPL	:	257
SHC	:	ALKYIG	MSRD-	EEPM	QKALRF	IQSQG	G <mark>IESSR</mark>	VETRMWL	ALVGEY	PWEK	VPMVPPI	EIMFL	GKRM <mark>P</mark> I	LNIYEF	G IW ARA	ATV <mark>V</mark> ALS	S <mark>IV</mark> MS	RQ	PVFPL	:	189
		CA CC	-			6 01	~	E 4 TT	: 6a 4	S M a		F 1.1	n D			5n69	9	f			
		64 60	7		Ľ	o Gi	9	soge wo	, og s	, w A	пр ры	E 10	р Р	D) 17 74	110 11	ppo,	эу у	L			
		64 66	7		Ľ	o Gi	g	sog4 we	, og .	, A	пр ры	E 00	р ғ	PNY1	Y261	opo.	эу у	L			
		64 6G	, *	3	20	, , ,	9 *	34 <u>0</u>	, og .	*	np pP	60 _	р <u>г</u>	PNY1	Y261	,	•y y *		400		
EtAS	:	ILQLR-	-Q <mark>EL</mark> HT	3 Qpy <mark>hh</mark> in	20 MTKT <mark>R</mark> H:	LCAHEI	9 * DVYYPH	340 PLIQDLM	WDS <mark>I</mark> YI	* FTEP	np pP 3 LLTRWP	60 FNKII	p p r <mark>k</mark> kale	PNY1	Y261 Sou	INSRYI	∍y y * IIGC <mark>V</mark>	EKV	400 LCMLA	:	379
EtAS PNY1	:	ILQLR- ILQLR-	-Q <mark>EL</mark> HT -E <mark>EL</mark> YG	3 QPYHHIN QPY <mark>NE</mark> IN	r 20 wtktrh: wrktrr	LCAHEI VCAKEI	9 * DVYYPH DIYYPH	340 PLIQDLM PLIQDLI	WDSLYI	, w g * FTEP /LTEP	np pP 3 LLTRWP LLTRWP	60 FNKII FNKL-	p p r <mark>k</mark> kale r <mark>e</mark> kalç	PNY1	Y261 JOL HYEDE HYEDE	SNSRYI SNSRYI	°y y * IIGC <mark>V</mark> IIGCV	EKV EKV	400 ICM LA ICMLV	:	379 380
EtAS PNY1 BPY	: : :	ILQLR- ILQLR- ILQLR-	-QELHT -EELYG -EELYT	3 Qpyhhin Qpynein Qpy <mark>hQ</mark> vn	L 20 WTKTRH: WRKTRR' WKKVRH:	LCAHEI VCAKEI LCAKEI	9 TVYYPH DIYYPH DIYYPH	340 9LIQDLM PLIQDLI PLIQDLI	WDSLY WDSLY	, w g * IFTEP /LTEP IFTEP	np pP 3 LLTRWP LLTRWP LLTRWP	60 FNKII FNKL- FNKLV	P P RKKALE REKALÇ R <mark>E</mark> KALÇ	PNY1 SVTMKH 2TTMKH 2VTMKH	Y261 I HYEDE I HYEDE I HYEDE	SNSRYI SNSRYI SNSRYI	°y y * IIGCV IIGCV IIGCV	EKV EKV EKV	400 LCMLA LCMLV LCMLA	: :	379 380 379
EtAS PNY1 BPY PSY	: : : : :	ILQLR- ILQLR- ILQLR- ILQLR-	-QELHT -EELYG -EELYT -EELYT	3 QPYHHIN QPYNEIN QPYHQVN EPY <mark>EK</mark> IN	L 20 WTKTRH: WRKTRR WRKVRH: WTKTRH:	LCAHEI VCAKEI LCAKEI LCAKEI	9 TAAL TAAL TAAL TAAL TAAL TAAL TAAL TAA	340 PLIQDLM PLIQDLI PLIQDLI PLIQDLI PLIQDLI	WDSLYI WDSLYI WDSLYI WDSLYI	* FTEP /LTEP FTEP	np pP 3 LLTRWP LLTRWP LLTRWP LLTRWP	60 FNKII FNKL- FNKLV FNKLV	P P R <mark>k</mark> kale REkalç REkalç	PNY1 SVTMKH 2TTMKH 2VTMKH SVTMKH	Y261	SNSRYI SNSRYI SNSRYI SNSRYI	*y y tigcv figcv figcv figcv	EKV EKV EKV EKV	400 LCMLA LCMLV LCMLA LCMLA	::	379 380 379 379
EtAS PNY1 BPY PSY AtLUP1	: : : : :	ILQLR- ILQLR- ILQLR- ILQLR- ILQLR- ILLLR-	- QELHT - EELYG - EELYG - EELHT - EELHT	3 Qpy <mark>hhin</mark> Qpy <mark>ne</mark> in QpyhQvn epyekin epy <mark>ee</mark> in	20 WTKTRH: WRKTRR WKKVRH: WTKTRH:	LCAHEI VCAKEI LCAKEI LCAKEI LYAKEI	9 * DVYYPH DIYYPH DIYYPH DIYYPH DMYY <mark>A</mark> H	340 PLTQDLM PLIQDLI PLIQDLI PLIQDLI PLIQDLI PLIQDLI	WDSLYI WDSLYI WDSLYI WDSLYI SDTLQI	* FTEP /LTEP FTEP FTEP IFTEP	np pP S LLTRWP LLTRWP LLTRWP LLTRWP LLTRWP	60 FNKII FNKL- FNKLV FNKLV LNKLV	P F R <mark>k</mark> kale REkalç REkalç Rkrale R <mark>E</mark> kalç	PNY1	Y261 IHYEDE IHYEDE IHYEDE IHYEDE	SNSRYI SNSRYI SNSRYI SNSRYI SNSRYI SNSRYI	* FIGCV FIGCV FIGCV FIGCV FIGCV	EKV EKV EKV EKV EKV	400 LCMLA LCMLV LCMLA LCMLA LCMLA	::	379 380 379 379 377
EtAS PNY1 BPY PSY AtLUP1 TRW		ILQLR- ILQLR- ILQLR- ILQLR- ILLR- VRDLR-	* -QELHT -EELYG- -EELYT -EELHT: -EELYL. -QELYT:	3 QPYHHIN QPYNEIN QPYHQVN EPYEEIN DPY <mark>DE</mark> IN	20 MTKTRH: WRKTRR' WKKVRH: WKKSRR: WNKARN'	LCAHEI VCAKEI LCAKEI LCAKEI LYAKEI TCAKEI	9 * DVYYPH DIYYPH DIYYPH DMYY <mark>A</mark> H DLYYPH	340 PLTQDLM PLTQDLI PLTQDLI PLTQDLI PLTQDLI PLVQDLI PFVQDMV	WDSLYI WDSLYI WDSLYI WDSLYI SDTLQI SDTLQI	* FTEP IFTEP FTEP IFTEP IFVEP IVVEP	np pP 3 LLTRWP LLTRWP LLTRWP LLTRWP LLTRWP	60 FNKII FNKL- FNKLV FNKLV LNKLV ISTL-	P F RKKALE REKALÇ RKRALE REKALÇ REKALF	PNY1 SVTMKH 2TTMKH 2VTMKH SVTMKH 2LTMKH SVAMDH	Y261 IHYEDE IHYEDE IHYEDE IHYEDE IHYEDE VHYEDE	SPS SNSRYI SNSRYI SNSRYI SNSRYI SNSRYI SSRYI	°y y FIGCV FIGCV FIGCV FIGCV FIGCV CIGCV	EKV EKV EKV EKV EKV EKV	400 LCMLA LCMLV LCMLA LCMLA LCMLA LCLLA	:::::::::::::::::::::::::::::::::::::::	379 380 379 379 377 377
EtAS PNY1 BPY PSY AtLUP1 TRW OEW		ILQLR- ILQLR- ILQLR- ILQLR- ILLLR- VRDLR- VLSLR-	* -QELHT -EELYG- -EELYT -EELHT: -EELYL: -QELYT: -QELYT:	3 QPYHHIN QPYNEIN QPYHQVN EPYEEIN DPYDEIN EPYHGIN	20 MTKTRH: MRKTRR' MKKVRH: MKKSRR: MKKSRR' MNKARN' MNRARN'	LCAHEI VCAKEI LCAKEI LCAKEI LCAKEI TCAKEI TCAKEI	9 * DVYYPH DIYYPH DIYYPH DMYY <mark>A</mark> H DLYYPH DLYYPH	340 PLIQDIM PLIQDII PLIQDII PLIQDII PLVQDII PFVQDMV PLAQDMI	WDSLYJ WDSLYJ WDSLYJ WDSLYJ SDTLQI WGVLHI WGFLHI	* FTEP /LTEP FTEP FTEP IFVEP IVVEP IVVEP	np pP 3 LLTRWP LLTRWP LLTRWP LLTRWP VLTRRP VLTSRP	60 FNKII FNKL- FNKLV FNKLV LNKLV ISTL- FSKL-	P F REKALS REKALS REKALS REKALS REKALS REKALS	PNY1	Y261 IHYEDE IHYEDE IHYEDE IHYEDE VHYEDE VHYEDE VHYEDE	ENSRYI ENSRYI ENSRYI ENSRYI ENSRYI ENSHYI CSSRYI MNSRYI	*y y FIGCV FIGCV FIGCV FIGCV FIGCV CIGCV	EKV EKV EKV EKV EKV EKV	400 LCMLA LCMLA LCMLA LCMLA LCMLA LCLIA	:::::::::::::::::::::::::::::::::::::::	379 380 379 379 377 377 379 377
EtAS PNY1 BPY PSY AtLUP1 TRW OEW BPW		ILQLR- ILQLR- ILQLR- ILQLR- ILLLR- VRDLR- VLSLR- IQSLR-	- QELHT - EELYG - EELYT - EELHT - EELHT - QELYT - QELYT - QELYN	3 QPYHHIN QPYNEIN QPYHQVN EPYEEIN DPYDEIN EPYHGIN EPYHQIN	20 MTKTRH: WRKTRR WKKVRH: MKKSRR: MKKSRR: WNKARN WNRARN	LCAHEI VCAKEI LCAKEI LCAKEI LYAKEI TCAKEI TCAKEI TVAKEI	9 * DVYYPH DIYYPH DIYYPH DIYYPH DLYYPH DLYYPH DLYYPH	340 PLIQDIM PLIQDII PLIQDII PLIQDII PLVQDII PFVQDMV PLAQDMI PLAQDII	WDSLYI WDSLYI WDSLYI WDSLYI SDTLQI WGYLHI WGFLHI WGFLHI	* /LTEP /LTEP FTEP FTEP IFVEP IVVEP IVVEP IVAEP	np pP S LLTRWP LLTRWP LLTRWP LLTRWP VLTRWP VLTRWP VLTRWP	60 FNKII FNKU- FNKUV FNKUV LNKUV ISTU- FSKU- FSKU-	P F REKALS REKALS REKALS REKALS REKALS REKALS REKALS	PNY1 SVTMKH 2TTMKH 2VTMKH 2LTMKH 2LTMKH CVAMDH CVAMEH CAALGH	Y261	SPS SNSRYI SNSRYI SNSRYI SNSRYI SNSRYI SNSRYI SNSRYI SNSRYI SNSKYI	*y y FIGCV FIGCV FIGCV FIGCV FIGCV CIGCV CIGCV CIGSV	EKV EKV EKV EKV EKV EKV EKV	400 LCMLA LCMLA LCMLA LCMLA LCLIA LCLIA	:::::::::::::::::::::::::::::::::::::::	379 380 379 379 377 379 377 379
EtAS PNY1 BPY PSY AtLUP1 TRW OEW BPW AtCAS1		ILQLR- ILQLR- ILQLR- ILQLR- ILLLR- VRDLR- VLSLR- VLSLR- VLSLR-	-QELHT -EELYG -EELYT -EELHT -QELYT -QELYT -QELYN -QELYN -KELFT	3 QPYHHIN QPYNEIN QPYHQVN EPYEEIN EPYEEIN EPYHGIN EPYHQIN VPYHEVN	20 MTKTRH: MRKTRR' MKKVRH: MKKSRR: MKKSRR! MNKARN' MNKARS' MNKARS'	LCAHEI VCAKEI LCAKEI LCAKEI LCAKEI TCAKEI TCAKEI TVAKEI LCAKEI	9 * DVYYPH DIYYPH DIYYPH DLYYPH DLYYPH DLYYPH DLYYPH DLYYPH	340 PLIQDLM PLIQDLI PLIQDLI PLIQDLI PLVQDLI PFVQDMU PLAQDMI PLIQDLI PLVQDII	WDSLYI WDSLYI WDSLYI WDSLYI SDTLQI WGVLHI WGFLHI WGFLHI WASLHI	* FTEP ITTEP FTEP IFVEP IVVEP IVVEP IVAEP IVAEP	np pP 3 LLTRWP LLTRWP LLTRWP LLTRWP VLTRWP VLTRWP VLTRWP VLTRWP	60 FNKI FNKL FNKLV FNKLV LNKLV ISTL FSKL FSKL GANL	P F REKALS REKALS REKALS REKALS REKALS REKALS REKALS REKALS	PNY1 SVTMKH 2TTMKH 2VTMKH 2UTMKH 2UTMKH 2UTMKH 2UTMKH 2UTMKH 2UTMEH 2UTMEH 2UTMEH 2UTMEH	Y261	SPS SNSRYI SNSRYI SNSRYI SNSRYI SNSRYI SNSRYI SNSRYI SNSRYI SNSRYI SNSRYI SNSRYI	*y y FIGCV FIGCV FIGCV FIGCV CIGCV CIGCV CIGCV CIGCV CIGPV	EKV EKV EKV EKV EKV EKV EKV NKV	400 LCMLA LCMLA LCMLA LCMLA LCLIA LCLIA LCLIA LCLIA		379 380 379 377 377 377 377 376 376
EtAS PNY1 BPY PSY AtLUP1 TRW OEW BPW AtCAS1 PSCAS		ILQLR- ILQLR- ILQLR- ILQLR- ILLLR- VRDLR- VLSLR- VLSLR- VLSLR- VLSLR-	- QELHT - EELYG - EELYT - EELHT - EELYL - QELYT - QELYT - QELYN - KELFT	3 QPYHHIN QPYNEIN QPYHQVN EPYEEIN EPYEEIN EPYHGIN VPYHEVN VPYHEVN VPYHDID	20 MTKTRH: MRKTRR' MKKVRH: MKKSRR: MNKARN' MNKARN' MNKARN' MNKARS' MNEARN: MNEARN:	LCAHEI VCAKEI LCAKEI LCAKEI TCAKEI TCAKEI TVAKEI LCAKEI LCAKEI	9 * DVYYPH DIYYPH DIYYPH DLYYPH DLYYPH DLYYPH DLYYPH DLYYPH DLYYPH	340 PLIQDLM PLIQDLI PLIQDLI PLIQDLI PLVQDLI PLVQDMI PLAQDMI PLIQDLI PLVQDIL PLVQDIL	MDSLYI MDSLYI MDSLYI MDSLYI MDSLYI SDTLQI MGVLHI MGVLHI MGFLHI MGFLHI MASLHI MATLHI	* FTE P /LTE P FTE P FTE P IFVE P IVVE P IVAE P IVAE P (IVE P (IVE P	np pP 3 LLTRWP LLTRWP LLTRWP LLTRWP VLTSRP VLTRWP VLTRWP VLTRWP VLMRWP VLMRWP	60 FNKII FNKU- FNKUV FNKUV LNKUV ISTU- FSKU- GANU- GANU- GKKU-	P F REKALS REKALS REKALS REKALS REKALS REKALS REKALS REKALS	PNY1 SVTMKH 2TTMKH 2VTMKH 2VTMKH 2LTMKH 3VAMDH 3VAMDH 3VAMEH 3AAIGH 3TAIEH 3TAIEH	Y261	SPS SNSRYI SNSRYI SNSRYI SNSRYI SNSRYI SNSRYI SNSRYI SNSRYI SNSRYI SNTRYI SNTRYI	*y y FIGCV FIGCV FIGCV FIGCV FIGCV CIGCV CIGCV CIGCV CIGPV CIGPV	EKV EKV EKV EKV EKV EKV EKV NKV NKV	400 LCMLA LCMLA LCMLA LCMLA LCLIA LCLIA LCLIA LNMLC LNMLC		379 380 379 377 377 377 376 376 376
EtAS PNY1 BPY PSY AtLUP1 TRW OEW BPW AtCAS1 PSCAS PgCAS		ILQLR- ILQLR- ILQLR- ILLLR- VRDLR- VLSLR- VLSLR- VLSLR- VLSLR- VLSLR-	- QELHT - EELYG - EELYT - EELHT - EELYL - QELYT - QELYT - QELYN - KELFT - KELFT	3 QPYHHIN QPYNEIN QPYHQVN EPYEKIN EPYELIN EPYHGIN VPYHEVN VPYHDID VPYHEID	20 MTKTRH: MRKTRR' MKKVRH: MKKSRR: MNKARN' MNRARN' MNRARN' MNEARN: MNQARN: MNQARN:	LCAHEI VCAKEI LCAKEI LCAKEI TCAKEI TCAKEI TVAKEI LCAKEI LCAKEI LCAKEI	9 * DVYYPH DIYYPH DIYYPH DLYYPH DLYYPH DLYYPH DLYYPH DLYYPH DLYYPH DLYYPH	340 PLIQDLM PLIQDLI PLIQDLI PLVQDLI PLVQDLI PLVQDMU PLIQDII PLVQDII PLVQDII PLVQDII	MDSLYI MDSLYI MDSLYI MDSLYI SDTLQI MGVLHI MGFLHI MGFLHI MASLHI MASLHI MASLHI	* FTE P /LTE P FTE P FTE P IFVE P IVVE P IVAE P (IVAE P (IVAE P (IVAE P (VWE P	np pP 3 LLTRWP LLTRWP LLTRWP LLTRWP VLTSRP VLTRWP VLTRWP VLTRWP VLTRWP VLTRWP IFMHWP	60 FNKII FNKL- FNKLV FNKLV INKLV ISTL- FSKL- FSKL- GANL- GKKL- AKKL-	P F RKKALE REKALC REKALC REKALF REKALF REKALF REKALF REKALF REKALF	PNY1	Y261	SPS SNSRYI SNSRYI SNSRYI SNSRYI SSSRYI SSSRYI SNSRYI SNSRYI SNTRYI SNTRYI SNTRYI SNTRYI	*y y FIGCV FIGCV FIGCV FIGCV FIGCV CIGCV CIGCV CIGCV CIGCV CIGPV CIGPV	EKV EKV EKV EKV EKV EKV EKV NKV NKV NKV	400 LCMLA LCMLA LCMLA LCMLA LCLIA LCLIA LCLIA LNMLC LNMLC LNMLC		379 380 379 377 377 377 376 376 376 376
EtAS PNY1 BPY PSY AtLUP1 TRW OEW BPW AtCAS1 PSCAS PgCAS BpCAS1		ILQLR- ILQLR- ILQLR- ILLLR- VRDLR- VLSLR- VLSLR- VLSLR- VLSLR- VLSLR- IQSLR-	* -QELHT -EELYG -EELYT -EELYT -QELYT -QELYT -QELYN -KELFT -KELFT -KEVFS -KELYT	3 QPYHHIN QPYNEIN QPYHQVN EPYEKIN EPYELIN CPYHGIN VPYHGIN VPYHEID VPYHEID VPYHEID	20 MTKTRH: MRKTRN MKKVRH: MKKSRR: MNKARN' MNKARN' MNEARN: MNQARN: MNQARN: MNQARN: MNQARN:	LCAHEI VCAKEI LCAKEI LCAKEI TCAKEI TCAKEI LCAKEI LCAKEI LCAKEI DCAKEI	S	340 PLIQDIM PLIQDII PLIQDII PLVQDII PLVQDII PLVQDII PLVQDII PLVQDII PLVQDII PLVQDII PLVQDII	MDSLYI MDSLYI MDSLYI MDSLYI MDSLYI MSTLQI MGFLHI MGFLHI MGFLHI MASLHI MASLDI MASLDI MASL	* FTE P /LTE P FTE P FTE P IFVE P IVVE P IVAE P IVAE P IVAE P IVAE P XVWE P AYE P	np pP 3 LLTRWP LLTRWP LLTRWP LLTRWP VLTRWP VLTRWP VLTRWP VLTRWP VLTRWP IFMHWP IFMHWP	60 FNKII FNKL- FNKLV FNKLV ISTL- FSKL- FSKL- GANL- GANL- AKKL- AKKL-	RKKALE REKALQ REKALQ REKALQ REKALQ REKALP REKALP REKALP REKALP REKALP	PNY1	Y261	SPS SNSRYI SNSRYI SNSRYI SNSRYI SNSRYI SNSRYI SNSRYI SNSRYI SNTRYI SNTRYI SNTRYI SNTRYI SNTRYI	*y y FIGCV FIGCV FIGCV FIGCV FIGCV CIGCV CIGCV CIGCV CIGPV CIGPV CIGPV CIGPV	EKV EKV EKV EKV EKV EKV EKV NKV NKV NKV	400 LCMLA LCMLA LCMLA LCMLA LCLIA LCLIA LCLIA LNMLC LNMLC LNMLC		379 380 379 379 377 376 376 376 376 376 376
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EtAS PNY1 BPY PSY AtLUP1 TRW OEW BPW AtCAS1 PSCAS PgCAS BpCAS1 AtLAS1 HSLAS		ILQLR- ILQLR- ILQLR- ILQLR- VRDLR- VLSLR- VLSLR- VLSLR- VLSLR- VLSLR- VLSLR- VLSLR- VLSLR- VLSLR- VLSLR- VLSLR-	* -QELHT -EELYG -EELYT -EELHT: -QELYT: -QELYN: -KELFT -KELFT -KELFT -KELYT -RELYT -QELYV	3 QPYHHIN QPYNEIN QPYHQVN EPYEEIN DPYDEIN EPYHGIN VPYHEID VPYHEID VPYHEID IPYHHID EDFASID	2 0 TKTRH: MRKTRN KKVRH: MKKSRR: MNKARN' MNKARN' MNKARN' MNQARN: MNQARN: MNKARN MNKARN MNKARN MNKARN MNKARN MNKARN	LCAHEI VCAKEI LCAKEI LCAKEI TCAKEI TCAKEI LCAKEI LCAKEI LCAKEI DCAKEI QCAKEI	9	340 PLIQDIM PLIQDII PLIQDII PLVQDII PLVQDII PLVQDII PLVQDII PLVQDII PLVQDII PLVQDII PLVQDII PLVQDII SWLLRVV	WDSLYI WDSLYI WDSLYI WDSLYI SDTLQI WGVLHI WGFLHI WGFLHI WGFLHI WASLHI WASLHI WASLHI WASLHI WASLU WSCLNI	* FTE P FTE P FTE P IFVE P IVVE P IVVE P IVAE P IVAE P IVE P IVE P IVE P IVE P	np pP 3 LLTRWP LLTRWP LLTRWP LLTRWP VLTRWP VLTRWP VLTRWP VLTRWP VLMRWP VFMNWP IFMHWP LFMYWP LLERWP	60 FNKII FNKL- FNKLV FNKLV ISTL- FSKL- GKKL- GKKL- AKKL- AKKL- SAHL-	P P RKKALS REKALS REKALS REKALS REKALS REKALS REKALS REKALS REKALS REKALS REKALS	PNY1 SVTMKH DTTMKH DVTMKH SVTMKH SVTMKH SVTMKH SVAMEH SVAMEH STAIEH STAIEH STAIEH STAIEH STAIEH STAIEH STAIEH STAIEH STAIEH STAIEH	Y261	SPS, SNSRYI SNSRYI SNSRYI SNSRYI SNSRYI SNSRYI SNSRYI SNSKYI SNTRYI SNS SNSRYI SNSRY SNSRYI SNSRY SNSRY SNS SNSRY SNSRY SNSRY SNSRY SNS	*y y FIGCV FIGCV FIGCV FIGCV FIGCV CIGCV CIGCV CIGCV CIGPV CIGPV CIGPV CIGPV SIGPI	EKV EKV EKV EKV EKV EKV EKV EKV NKV NKV NKV SKT	400 LCMLA LCMLA LCMLA LCMLA LCMLA LCLIA LCLIA LCLIA LNMLC LNMLC LNMLC LNMLC LNMLC		379 380 379 377 377 377 376 376 376 376 376 376
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EtAS PNY1 BPY PSY AtLUP1 TRW OEW BPW AtCAS1 PSCAS PGCAS1 AtLAS1 HSLAS MmLAS SCLAS		ILQLR- ILQLR- ILQLR- ILQLR- ILLLR- VRDLR- VLSLR- VLSLR- VLSLR- VLSLR- VLSLR- VLSLR- VLSLR- VLSLR- VQSLR- VQSLR- VQSLR- VQSLR- VQSLR-	* -QELHT -EELYG -EELYT -EELHT: -QELYT: -QELYN: -KELFT -KELFT -KELFT -KELYT -RELYT -QELYV -QELYV -NEIYT	3 QPYHHIN QPYNEIN QPYHQVN EPYEKIN EPYEEIN CPYDEIN EPYHGIN VPYHEID VPYHEID VPYHEID IPYHHID EDFASID QDYASID KPEDKIN	2 0 TKTRH: MRKTRN KKVRH: MKKSRR: MNKARN MNKARN MNKARN MNKARN MNCARN: MNCAR	LCAHEI VCAKEI LCAKEI LCAKEI TCAKEI TCAKEI LCAKEI LCAKEI DCAKEI QCAKEI NVAPDI NVSPDI	S	340 PLIQDIM PLIQDII PLIQDII PLIQDII PLVQDII PLVQDII PLVQDII PLVQDII PLVQDII PLVQDII PLVQDII SWILRVV SWILRVV	WDSLYI WDSLYI WDSLYI WDSLYI SDTLQI WGVLHI WGFLHI WGFLHI WGFLHI WASLHI WASLHI WASLHI WASLUI WASLUI WASLYI YALLN- YGLLN-	* FTE P FTE P FTE P IFTE P IFTE P IFVE P IVVE P IVVE P IVAE P IVAE P IVAE P IVE P IVE P IVE P IVAE	np pP 3 LLTRWP LLTRWP LLTRWP LLTRWP VLTRWP VLTRWP VLTRWP VLTRWP VLTRWP LTRWP LTRWP LFMYWP LERWP LYERFH YLRNRF	60 FNKII FNKLV FNKLV FNKLV ISTL- FSKL- FSKL- GANL- GANL- GKKL- AKKL- STSL- STSL- IYSLS	RKKALE REKALQ REKALQ REKALQ REKALQ REKALQ REKALQ REKALQ REKALQ REKALQ RNHALQ RNHALQ RKWAVQ	PNY1 SVTMKH DTTMKH DVTMKH SVTMKH SVTMKH SVTMKH SVTMKH SVTMKH SVAMDH SVAMDH SVAMEH STAIEH STAIEH STAIEH STAIEH STAIEH DTVMQH DVMQH DLYEH DL	Y261	SUSRYI SUSRYI SUSRYI SUSRYI SUSRYI SUSRYI SUSRYI SUSRYI SUSRYI SUTRYI SUTRYI SUTRYI SUSRYI SU	*y y FIGCV FIGCV FIGCV FIGCV FIGCV CIGCV CIGCV CIGCV CIGPV CIGPV CIGPV CIGPV CIGPV CIGPT SIGPI	EK - V $EK - V$ $K - V$ $NK - V$ $NK - V$ $NK - V$ $SK - T$ $AV - V$	400 LCMLA LCMLA LCMLA LCMLA LCMLA LCLIA LCLIA LCLIA LCLIA LNMLC LNMLC LNMLC INMLC INMLV INMLV		379 379 379 377 377 377 376 376 376 376 376 376 376
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EtAS F413

EtAS F474



D485C486TAE involved in EtAS β-amyrin synthase

S4

			*	620	*	640	*	660	*	680	*	700		
EtAS	:	HALIMEKKI	LYPGHRKE	KEIENFITI	VAVKYLEDVO	TADGGWYGNWG	VCFTY <mark>G</mark> TWFA	VGGLAAAG	KNYNNCA	AMRKAVDELLR	TQKQDGGWGES	YLSCPH	: 6	566
PNY1	:	OALVLEKKI	LYPGHRKE	KEIDNFITI	NAVRYLEDTO	MPDGSWYGNWG	VCFTY <mark>G</mark> SWFA	LGGI AAAG	KTYYNCA	AVRKAVEFLLK	SOMDDGGWGES	YLSCPK	: 6	567
BPY	:	OTLVLEKKI	LYEGHRKE	KEIENFIKI	VAAOFLOVIO	MPDGSWYGNWG	VCFTY <mark>G</mark> TWFA	I GGI AAVG	KTYNNCL	AVRRAVDELLR	AORDNGGNGES	YLSCPK	: 6	566
PSY	•	OALVLEKKI	LY PGHRKI	KETENETEI	NAVRELEDTO	TEDGSWYGNMG	VCFTYGSMFA	LGGLAAAG	KTYTNCA	ATRKGVKFLLT	TOREDGGNGES	YLSSPK	: 6	566
At LUP1		OALDLERKI	YEDHEKI	KETNRSTEI	XAVOF TODNO	TPDGSMYGNMG	VCETYATMEA	TIGGUAAAG	ETYNDCL	AMRNGVHETTT	TORDDGGMGES	YLSCSE	: 6	564
 Т R M		OGLTLEKKI	НРСНВТИ	KETEHCISI	RAVENTO	ESDGSMYGCMG	TCYTY <mark>G</mark> TMF A	VDAT VACG	KNYHNCP	ALOKACKETTS	KOLPDGGNGES	YLSSN	: 6	566
OEM		OALKLEKOI	HEGHER	KETASCISI	KATOYTEATON	NPDGSMDGSMG	TCFTYGTMFA	VEGUVACG	KNYHNSP	TERRACEFTES	KOLPDGGMSES	YLSSN	: 6	564
BPW		HGLALERKE	YPRHRG	FETDSSTY	RGTOYTEDVO	EPDGSWYGHMG	TCYTYGTMEA		RNYKNCP	ALRKSCEFTTS	KOLPNGGNGES	YLSSON		563
AtCAS1	÷	OALTSERKI	YEGHEKI	KEVDECTEI	KAVKETESTO	AADGSMYGSMA	VCETYGTMEG	VKGLVAVG	KTLKNSP	HVAKACEFTTS	KOOPSGGMGES	YLSCOD	. 6	564
PSCAS		OALATEGE	YPGHERI	RETOCCIEN	KAVAFTEKTO	ASDGSWYGSWG	VCETYGTMEG	TKGLTAAG	KNESNCL	STRKACEFTTS	KOLPSGGMAES	YLSCON	: 6	564
Pacas	÷	OALTAFKKI	FPGHRR	RETOHSTE	KAALFTEKTO	SSDGSWYGSWG	VCETYGTMEG	TKGLVTAG	RTFSSCA	STREACDELLS	KOVASGGNGES	YLSCON		564
BpCAS1	:	OALTLEKKI	HPGHERI	RETENCTAL	KAAEFTENTO/	ASDGSMYGSMG	VCETYAGMEG	TKGTVAAG	RTYKNCS	STHKACDYLLS	KELASGGMGES	YLSCOD		574
At LAS1		OGLVLETT	NSSYKR	KETVGSTNI	SAVEFTEKTOI	LPDGSWYGSWG	VCETYATMEG	TKGMLASC	KTYESSL	CTREACGETTS	KOLCCGGWGES	YLSCON		564
HSLAS	:	OALKYFHKE	REBEHRAN	AETRETITO	OGTEFCEROOI	RADGSMEGSMG	VCETYGTMEG	LEAFACMG	OTYRDGTACA	EVERACDELLS	ROMADGGNGEL	FESCEE	 	538
MmLAS	:	OALKHEHEE	IF PDYRA <i>i</i>	AEVRETING	DGUDECRRKOU	RADGSMEGSMG	VCETYGTMEG	TEAFACMG	HTYODGAACA	EVACACNETIS		DEESCEO	 	539
SCLAS	:	LGLTYFHKY	(F-DYRK)	ZETRTRTR	ZOLDF CKKROI LATEFTKKSOI	LPDGSMYGSMG	TCETYAGMEA	ТЕАТНТУС	ETYENSS	TWRKGCDELVS	KOMKDGGWGES	MKSSEL		541
SHC	:	ECECSE	GYI	DAMKVTRI 104	PAVENT KREOK	K DDCSMFCRMC	VNYLYCTCAV	WSAT KAVC		YTOKALDWWEO	HONDDCCWCEL	CREVED		542
DIIC	•		n .	- 6	a 5 O	DCeW C Wa	665tY wf	6 C	IDIKE P	6 56	2 CCWare	e g	• •	12
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			*	720	*	740	*	760 🔽	*	780	*	800		
EtAS		KKYVPLEDN	* JRSNLVH	720 Ismaim <mark>g</mark> i	* SAGOMDRDP:	740 Tethraakl <mark>i</mark> ti	* NSOLEDGDFP	760 Oortr gv	* MKNOMTHYA	780 Ayrntypimai	* AEYRNRVPLPS	800 	: 7	762
EtAS PNY1	:	KK <mark>Y</mark> VPLEDN KVYVPLEGN	* JRSNLVH JRSNLVH	720 Iswalmgli Igwalmgli	* ISAGQMDRDP: IHSEOAERDP:	740 TPLHRAAKLLII TPLHRAAKLLII	* N <mark>SQLEDGDF</mark> P NSOMEDGDFP	760 QQEITGV OOEISGV	* E MKNCMLHYA E MKNCMLHYA	780 Ayrniyplwal Ayrniyplwal	* AEYRNRVPLPS AEYRRRVPLPS	800 TTL LGT	: 7 : 7	762 763
EtAS PNY1 BPY	:	K <mark>K</mark> YVPLEDM KVYVPLEGM KEYVPLEGM	* JRS <mark>NLV</mark> H JRSNLVH JKSNLVH	720 ISWALMGLI IGWALMGLI IAWAMMGLI	* I SAGQMDRDP' I HSEQAERDP' I HAGOAERDP'	740 TPLHRAAKLLI TPLHRAAKLLI TPLHRAAKLII	* NSQLEDGDFP NSQMEDGDFP NSOLEDGDFP	760 QQEITGV QQEISGV OOEITGV	* E MKNCMLHYA E MKNCMLHYA E MKNCMLHYA	780 Ayrniyplwal Ayrniyplwal Aykniyplwal	* AEYRNRVPLPS AEYRRRVPLPS AEYRKHVPLP-	800 STTL SLGT LGKNLN	: 7 : 7 : 7	762 763 764
EtAS PNY1 BPY PSY	:	KKYVPLEDI KVYVPLEGI KEYVPLEGI KIYVPLEGI	* JRSNLVH JRSNLVH JKSNLVH JRSNVVH	720 ISWALMGLI IGWALMGLI IAWAMMGLI IAWALMGLI	* I SAGQMDRD P' I HSEQAERD P' I HAGQAERD P' I HAGOSERD P'	740 TPLHRAAKLLT TPLHRAAKLLT TPLHRAAKLTT TPLHRAAKLLT	* NSQLEDGDFP NSQMEDGDFP NSQLEDGDFP NSQLEOGDMP	760 QQEITGV QQEISGV QQEITGV QQEITGV	* E MKNOMLHYA E MKNOMLHYA E MKNOMLHYA E MKNOMLHYP	780 Ayrniyplwal Ayrniyplwal Aykniyplwal Myrdiyplwal	* AEYRNRVPLPS AEYRKHVPLP- AEYRRRVPLP-	800 TTL LGT LGKNLN	: 7 : 7 : 7 : 7	762 763 764 758
EtAS PNY1 BPY PSY AtLUP1	: : : :	KKYVPLED KVYVPLEG KEYVPLEG KIYVPLEG ORYTPSEG	* JRSNLVH JRSNLVH JKSNLVH JRSNVVH ZRSNLVO	720 PSWALMGLI PGWALMGLI PAWAMMGLI PAWALMGLI PSWAMMALI	* I SAGQMDRDP I HSEQAERDP I HAGQAERDP I HAGQSERDP I HTGOAERDL	740 TPLHRAAKLLI TPLHRAAKLLI TPLHRAAKLII TPLHRAAKLLII TPLHRAAKLII	* NSQLEDGDFP NSQLEDGDFP NSQLEDGDFP NSQLEQGDWP NSQLENGDFP	760 QQEITGV QQEISGV QQEITGV QQEITGV	* E MKNOMLHYA E MKNOMLHYA E MKNOMLHYA E MKNOMLHYP E MNTOMLHYA	780 AYRNIYPLWAL AYRNIYPLWAL AYKNIYPLWAL MYRDIYPLWAL TYRNTFPLWAL	* AEYRRRVPLPS AEYRRRVPLP- AEYRRRVPLP- AEYRRRVPLP-	800 TTL LGT LGKNLN	::: ::: ::: ::: :::	762 763 764 758 755
EtAS PNY1 BPY PSY AtLUP1 TRW		KKYVPLED KVYVPLEG KEYVPLEG KIYVPLEG QRYIPSEG KVYTNLEG	* VRSNLVH VRSNLVH VRSNVVH VRSNVVH SRSNLVQ VRSNLVQ	720 FSWALMGLI FGWALMGLI FAWAMMGLI FAWALMGLI FSWAMMALI FSWATTSLI	* ISAGQMDRDP' IHSEQAERDP' IHAGQAERDP' IHAGQSERDP' IHTGQAERDLI IKAGQAETDP'	740 TPLHRAAKLLII TPLHRAAKLLII TPLHRAAKLIII TPLHRAAKLLII IPLHRAAKLIII TPTSNGVRLII	* NSQLEDGDFP NSQLEDGDFP NSQLEDGDFP NSQLEQGDWP NSQLENGDFP NSQLENGDFP	760 QQEITGV QQEISGV QQEITGV QQEITGV QQEIVGA	* E MKNOMLHYA E MKNOMLHYA E MKNOMLHYA E MKNOMLHY P E MNTOMLHYA E MKNONLHYS	780 AYRNIYPLWAL AYRNIYPLWAL AYKNIYPLWAL MYRDIYPLWAL TYRNTFPLWAL SFRNIFPIWAL	* AEYRNRVPLPS AEYRRRVPLP AEYRRRVPLP- AEYRRVVFI GEYRRVVFI	800 TTL LGT LGKNLN	::::::::::::::::::::::::::::::::::::::	762 763 764 758 755
EtAS PNY1 BPY PSY AtLUP1 TRW OEW		KKYVPLED KVYVPLEG KEYVPLEG KIYVPLEG QRYIPSEG KVYTNLEG KVYTNLEG	* 1RSNLVH 1RSNLVH 1RSNVVH 1RSNVVH 2RSNLVQ 1RSNLVH 1RSNLVH	720 ISWALMGLI IGWALMGLI IAWALMGLI ISWALMGLI ISWALMALI ISWALISLI	* I SAGQMDRD P' I HSEQAERD P' I HAGQAERD P' I HAGQSERD P' I HTGQAERD L' I KAGQAEID P' I KAGQVEID PO	740 TPLHRAAKLLT TPLHRAAKLLT TPLHRAAKLTT TPLHRAAKLLT IPLHRAAKLTT TPISNGVRLLT GPTHRGTKLTV	* NSQLEDGDFP NSQLEDGDFP NSQLEDGDFP NSQLENGDFP NSQLENGDFP NSQMEEGDFP NSQMEDGDFP	760 QQEITGV QQEITGV QQEITGV QQEITGV QQEITGV QQEITGV	* E MKNOMLHYA E MKNOMLHYA E MKNOMLHYA E MKNOMLHYA E MKNONLHYS E MKNONLNYS E MKNONLNYS	780 AYRNIYPLWAL AYRNIYPLWAL MYRDIYPLWAL TYRNTFPLWAL SFRNIFPIWAL SYRNIFPIWAL	* AEYRNRVPLPS AEYRRRVPLP- AEYRRRVPLP- AEYRRVVFI GEYRRIV GEYRRIV	800 STTL LGT LGKNLN		762 763 764 758 755 755
EtAS PNY1 BPY PSY AtLUP1 TRW OEW BPW		KKYVPLED KVYVPLEG KEYVPLEG KIYVPLEG QRYIPSEG KVYTNLEG KVYTNLEG KVYTNLEG	* JRSNLVH JRSNLVH JRSNVVH JRSNVVH SRSNLVQ JRSNLVQ JRSNLVQ JRSNLVQ	720 ISWALMGL IGWALMGL IAWAMMGL ISWALMGL ISWALMGL ISWALISL ISWALISL ISWALLSL	* ISAGQMDRDP' IHSEQAERDP' IHAGQAERDP' IHAGQSERDP' IHTGQAERDL' IKAGQAEIDP' IKAGQVEIDP(IDAROAETDP'	740 TPLHRAAKLLI TPLHRAAKLLI TPLHRAAKLII TPLHRAAKLII IPLHRAAKLII TPISNGVRLLI GPIHRGIKLLV TPTHRGVRVI	* NSQLEDGDFP NSQLEDGDFP NSQLEDGDFP NSQLENGDFP NSQMEEGDFP NSQMEDGDFP NSQMEDGDFP	760 QQEITGV QQEITGV QQEITGV QQEITGV QQEITGV QEITGV	* E MKNOMLHYA E MKNOMLHYA E MKNOMLHYA E MKNOMLHYA E MKNONLHYS E MKNONLNYS E MKNOTLNYS	780 AYRNIYPLWAL AYRNIYPLWAL MYRDIYPLWAL TYRNTFPLWAL SFRNIFPIWAL SYRNIFPIWAL SYRNIFPIWAL	* AEYRNRVPLPS AEYRKHVPLP- AEYRRRVPLP- AEYRKVVFI GEYRRIV GEYRRIV GEYRRIV	800 STTL LGT LGKNLN		762 763 764 758 755 755 753
EtAS PNY1 BPY PSY AtLUP1 TRW OEW BPW AtCAS1		KKYVPLED KVYVPLEG KEYVPLEG KIYVPLEG QRYIPSEG KVYTNLEG KVYTNLEG KVYTNLEG KVYSNLDG	* JRSNLVH JRSNLVH JRSNLVH JRSNLVH JRSNLVQ JRSNLVQ JRSNLVQ JRSNLVQ JRSNLVQ	720 ISWALMGL IGWALMGL IAWAMMGL ISWALMGL ISWALLSL ISWALLSL IAWALLSL IAWALLSL	* ISAGQMDRDP IHSEQAERDP IHAGQAERDP IHAGQSERDP IHTGQAERDL IKAGQAEIDP IKAGQVEIDP IDARQAEIDP	740 TPLHRAAKLLI TPLHRAAKLII TPLHRAAKLII TPLHRAAKLII IPLHRAAKLII TPISNGVRLLI GPIHRGIKLLVI TPIHRGVRVLII	* NSQLEDGDFP NSQLEDGDFP NSQLEQGDWP NSQLENGDFP NSQMEEGDFP NSQMEDGDFP NSQMEDGDFP	760 QQEITGV QQEITGV QQEITGV QQEITGV QQEITGV QEITGV QEITGV	* F MKNCMLHYA F MKNCMLHYA F MKNCMLHYA F MNTCMLHYA F MNTCMLHYA F MKNCNLNYS F MKNCTLNYS F MKNCTLNYS	780 AYRNIYPLWAL AYRNIYPLWAL MYRDIYPLWAL IYRNIFPLWAL SFRNIFPIWAL SYRNIFPIWAL SYRNIFPIWAL AYRNIFPIWAL	* AEYRNRVPLPS AEYRRRVPLP- AEYRRRVPLP- AEYRKVVFI GEYRRIV GEYRRIV GEYRRRV GEYRRRV	800 STTL LGT LGKNLN 		762 763 764 758 755 755 753 752
EtAS PNY1 BPY PSY AtLUP1 TRW OEW BPW AtCAS1 PSCAS		KKYVPLED KVYVPLEG KEYVPLEG KIYVPLEG QRYIPSEG KVYTNLEG KVYTNLEG KVYTNLEG KVYSNLDG KVYSNLEG	* 1RSNLVH 1RSNLVH 1RSNLVH 1RSNLVQ 1RSNLVQ 1RSNLVQ 1RSNLVQ 1RSNLVQ 1RSHVVN	720 SWALMGL GWALMGL FAWAMMGL FAWALMGL SWALMGL SWALLSL SWALLSL FAWALLSL FAWAMLAL	* ISAGQMDRDP IHSEQAERDP IHAGQAERDP IHAGQSERDP IHTGQAERDL IKAGQAEIDP IKAGQVEIDP IGAGQAEVDRI IGAGQAEVDRI	740 TPLHRAAKLLI TPLHRAAKLII TPLHRAAKLII TPLHRAAKLII IPLHRAAKLII GPIHRGIKLLVI TPIHRGVRVLII KPLHRAARYLII	* NSQLEDGDFP NSQLEDGDFP NSQLEQGDWP NSQLENGDFP NSQMEEGDFP NSQMEDGDFP NSQMEDGDFP NSQMEDGDFP	760 QQEITGV QQEITGV QQEITGV QQEITGV QQEITGV QQEITGV QQEITGV QQEITGV	* F MKNCMLHYA F MKNOMLHYA F MKNOMLHYA F MKNOMLHYA F MKNONLHYA F MKNONLNYS F MKNOTLNYS F MRNOTLNYS F NRNOMLTYA	780 AYRNIYPLWAL AYRNIYPLWAL MYRDIYPLWAL SFRNIFPLWAL SYRNIFPIWAL SYRNIFPIWAL AYRNIFPIWAL	* AEYRNRVPLPS AEYRRRVPLP- AEYRRRVPLP- AEYRRVVFI GEYRRIV GEYRRIV GEYRRRI GEYRRRV GEYRRRV	800 STTL LGT LGKNLN	······································	762 763 764 758 755 755 753 752 752
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EtAS PNY1 BPY PSY AtLUP1 TRW OEW BPW AtCAS1 PSCAS PgCAS BpCAS1 AtLAS1		KKYVPLED KVYVPLEG KEYVPLEG KIYVPLEG KVYTNLEG KVYTNLEG KVYTNLEG KVYSNLDG KVYSNLEG KVYTNLEG KVYTNLEG	* JRSNLVH JRSNLVH JRSNVVH SRSNLVQ JRSNLVQ JRSNLVQ JRSNLVQ JRSNVVN JRSHVVN JRSHVVN JRSHVVN JRSHVVN	720 SWALMGL GWALMGL FAWALMGL SWALMGL SWALLSL SWALLSL FAWALLSL GWAMLAL GWAMLAL GWAMLAL	* ISAGQMDRDP IHSEQAERDP IHAGQAERDP IHAGQSERDP IHAGQAERDI IHAGQAEIDP IKAGQVEIDP IGAGQAEVDRI IGAGQAEVDRI IEAEQAKRDP IDAGQAERDP IDAGQAERDP	740 TPLHRAAKLII TPLHRAAKLII TPLHRAAKLII TPLHRAAKLII TPLHRAAKLII GPIHRGIKLIV TPIHRGVRVLI KPLHRAARVLII TPLHRAAKLII TPLHRAAKLII TPLHRAARILII	* NSQLEDGDFP NSQLEDGDFP NSQLEQGDWP NSQLENGDFP NSQMEEGDFP NSQMEDGDFP NSQMEDGDFP NSQMENGDFP NSQLENGDFP NSQMENGDFP NSQMENGDFP	760 QQEITGV QQEITGV QQEITGV QQEITGV QQEITGV QQEITGV QQEITGV QQEITGV QEEIMGV QEEIMGV QEEIMGV	* F MKNCMLHYA F MKNCMLHYA F MKNCMLHYA F MKNCMLHYA F MKNCMLHYA F MKNCTLNYS F MKNCTLNYS F MRNCTLNYS F NRNCMITYA F NKNCMITYA F NKNCMITYA	780 AYRNIYPLWAL AYRNIYPLWAL AYKNIYPLWAL TYRNTFPLWAL SYRNIFPIWAL SYRNIFPIWAL AYRNIFPIWAL AYRNIFPIWAL AYRNIFPIWAL AYRNIFPIWAL AYRNIFPIWAL	* AEYRNRVPLPS AEYRRRVPLP- AEYRRRVPLP- GEYRRIV GEYRRIV GEYRRI GEYRRI GEYRRRV GEYRCQV GEYRCRV GEYRCRV GEYRCRV	800 STTL SLGT 	······································	762 763 764 755 755 753 752 753 753 753
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EtAS PNY1 BPY PSY AtLUP1 TRW OEW BPW AtCAS1 PSCAS PgCAS BpCAS1 AtLAS1 HSLAS MmLAS		KKYVPLEG KVYVPLEG KIYVPLEG KIYVPLEG KVYTNLEG KVYTNLEG KVYSNLDG KVYSNLEG KVYSNLEG KVYTNLEG KVYTNLEG KVYTNLEG KVYTNLEG KVYTNLPG RYLQSJ	* JRSNLVH JRSNLVH JRSNLVH JRSNLVH JRSNLVH JRSNLVQ JRSNLVQ JRSNLVQ JRSNVVN JRSHVVN JRSHVVN JRSHVVN JRSHVVN JRSHVVN JRSHVVN	720 SWALMGLI GWALMGLI FAWALMGLI SWALMGLI SWALLSLI SWALLSLI FAWALLSLI FAWALLSLI GWAMLALI GWAMLALI GWAMLALI SWALLALI CWAMMGLI CWAMMGLI	* ISAGQMDRDP IHSEQAERDP IHAGQAERDP IHAGQAERDP IHTGQAERDL IHTGQAERDP IHTGQAEIDP IGAGQAEIDP IGAGQAEVDRI IEAEQAKRDP IDAGQAERDP IEAGQAERDP IEAGQASRDPI IAVRHPDII	740 TPLHRAAKLII TPLHRAAKLII TPLHRAAKLII TPLHRAAKLII TPLHRAAKLII GPIHRGIKLIV TPIHRGVRVII TPIHRGVRVII TPLHRAARVII TPLHRAAKLII TPLHRAAKLII TPLHRAARIII TPLHRAARIII	* NSQLEDGDFP NSQLEDGDFP NSQLEQGDWP NSQLENGDFP NSQMEDGDFP NSQMEDGDFP NSQMEDGDFP NSQLENGDFP NSQLENGDFP NSQMENGDFP NSQMENGDFP NSQMENGDFP SQMEDGDYP SQMEDGDYP	760 QQEITGV QQEITGV QQEITGV QQEITGV QQEITGV QQEITGV QQEITGV QQEIMGV QEEIMGV QEEIMGV QEEIMGV QEEIMGV	* E MKNCMLHYA E MKNCMLHYA E MKNCMLHYA E MKNCMLHYA E MKNCMLHYA E MKNCTLNYS E MKNCTLNYS E NRNCTLNYS E NRNCMITYA E NKNCMITYA E NKNCMISYS E NRNCMISYS	780 AYRNIYPLWAL AYRNIYPLWAL AYKNIYPLWAL TYRNTFPLWAL SYRNIFPIWAL SYRNIFPIWAL AYRNIFPIWAL AYRNIFPIWAL AYRNIFPIWAL AYRNIFPIWAL SYRNIFPIWAL SYRNIFPIWAL	* AEYRNRVPLPS AEYRRRVPLP- AEYRRVVFI GEYRRIV GEYRRRV GEYRRRV GEYRCQV GEYRCQV GEYRCRV GEYRCRV GEYRCRV GEYRCRV GEYRCRV GEYRCRV	800 TTL LGT LGKNLN 	******************	762 763 764 755 755 752 753 752 753 753 753 753 753
EtAS PNY1 BPY PSY AtLUP1 TRW OEW BPW AtCAS1 PSCAS PgCAS BpCAS1 AtLAS1 HSLAS MmLAS ScLAS		KKYVPLEG KVYVPLEG KIYVPLEG KIYVPLEG QRYIPSEG KVYTNLEG KVYTNLEG KVYSNLDG KVYSNLEG KVYSNLEG KVYTNLEG KVYTNLEG KVYTNLEG RYLQSJ RRYVQSJ	* JRSNLVH JRSNLVH JRSNLVH JRSNLVH JRSNLVQ JRSNLVQ JRSNLVQ JRSNLVQ JRSNVVN JRSHVVN JRSHVVN JRSHVVN JRSHVVN JRSHVVN JRSHVN JRSHIVN JRSHIVN	720 SWALMGLI GWALMGLI FAWAMMGLI SWALISLI SWALISLI SWALLSLI FAWALLSLI FAWAMLALI GWAMLALI GWAMLALI GWAMLALI SWALLALI CWAMMGLI CWALMGLI FAWATTALI	* ISAGQMDRDP IHSEQAERDP IHAGQAERDP IHAGQAERDP IHTGQAERDD IHTGQAERDD IHTGQAERDP IKAGQVEIDP IGAGQAEVDRI IEAEQAKRDP IDAGQAERDP IDAGQAERDP IEAGQASRDPI IAVRHPDII IAVRHPDII	740 TPLHRAAKLII TPLHRAAKLII TPLHRAAKLII TPLHRAAKLII TPLHRAAKLII GPIHRGIKLIV TPIHRGVRVII TPLHRAARVII TPLHRAAKLII TPLHRAAKLII TPLHRAAKIII MPLHRGAKSII EAQERGVRCIL	* NSQLEDGDFP NSQLEQGDFP NSQLEQGDFP NSQLENGDFP NSQMEDGDFP NSQMEDGDFP NSQMEDGDFP NSQMENGDFP NSQMENGDFP NSQMENGDFP NSQMENGDFP NSQMENGDFP NSQMENGDFP NSQMENGDFP NSQMENGDFP	760 QQEITGV QQEITGV QQEITGV QQEITGV QQEITGV QQEITGV QQEITGV QQEITGV QQEIMGV QEEIMGV QEEIMGV QEEIMGV QEEIMGV QEEILGV QENISGV	* F MKNCMLHYA F MKNCMLHYA F MKNCMLHYA F MKNCMLHYA F MKNCMLHYA F MKNCTLNYS F MKNCTLNYS F MKNCTLNYS F NKNCMITYA F NKNCMITYA F NKNCMISYS F NKNCMISYS F NKNCMISYS	780 AYRNIYPLWAL AYRNIYPLWAL AYKNIYPLWAL TYRNTFPLWAL SYRNIFPIWAL SYRNIFPIWAL AYRNIFPIWAL AYRNIFPIWAL AYRNIFPIWAL AYRNIFPIWAL SYRNIFPIWAL SYRNIFPIWAL	* AEYRNRVPLPS AEYRRNVPLP- AEYRRVVPLP- AEYRRVVFI GEYRRRV GEYRRRV GEYRRRV GEYRCV GEYRCRV GEYRCRV GEYRCRV GEYRCRV GEYRCRV GEYRCRV GEYRCRV GRFSQLYPERA	800 TTL LGT LGT 	······································	762 763 764 755 755 755 753 753 753 753 753 753 753
EtAS PNY1 BPY PSY AtLUP1 TRW OEW BPW AtCAS1 PSCAS PgCAS BpCAS1 AtLAS1 HSLAS MmLAS ScLAS SHC		KKYVPLEG KVYVPLEG KEYVPLEG KIYVPLEG QRYIPSEG KVYTNLEG KVYTNLEG KVYSNLEG KVYSNLEG KVYSNLEG KVYTNLEG KVYTNLEG KVYTNLEG KVYTNLEG RYLQSJ RRYVQSJ HSYVDSI	* JRSNLVH JRSNLVH JRSNLVH JRSNLVH JRSNLVQ JRSNLVQ JRSNLVQ JRSHVVN JRSHVVN JRSHVVN JRSHVVN JRSHVVN JRSHVVN JRSHVVN JRSHIVN JRSHIVN JRSHIVN JRSHIVN JRSHIVN JRSHIVN	720 SWALMGL GWALMGL FAWAMMGL SWALMGL SWALSL SWALSL SWALSL FAWALSL GWAMLAL GWAMLAL GWAMLAL SWALLAL CWAMMGL CWALMGL FAWALIAL	* ISAGQMDRDP IHSEQAERDP IHAGQAERDP IHAGQAERDD IHTGQAERDD IHTGQAERDD IHTGQAERDP IAGQAETDP IGAGQAEVDRI IGAGQAERDP IDAGQAERDP IDAGQAERDP IAVRHPDII IAVRHPDII IAVRHPDII	740 TPLHRAAKLII TPLHRAAKLII TPLHRAAKLII TPLHRAAKLII TPLHRAAKLII GPIHRGIKLIV TPIHRGVRVII TPLHRAARVII TPLHRAARVII TPLHRAAKLII TPLHRAAKLII TPLHRAAKLII TPLHRAAKIII TPLHRAAKIII A RRGVOVIV	* NSQLEDGDFP NSQLEDGDFP NSQLEQGDWP NSQLENGDFP NSQMEDGDFP NSQMEDGDFP NSQMEDGDFP NSQMENGDFP NSQMENGDFP NSQMENGDFP NSQMENGDFP NSQMENGDFP NSQMENGDFP NSQMENGDFP NSQMEDGDYP EKQLPNGDWP CKQLPNGDWP	760 QQEITGV QQEITGV QQEITGV QQEITGV QQEITGV QEITGV QEITGV QEITGV QEITGV QEITGV QEIMGV QEIMGV QEIMGV QEILGV QEILGV QEILGV QENISGV	* F MKNCMLHYA F MKNCMLHYA F MKNCMLHYA F MKNCMLHYA F MKNCMLHYA F MKNCTLNYS F MKNCTLNYS F MKNCTLNYS F NKNCMITYA F NKNCMITYA F NKNCMITYA F NKNCMISYS F NKSCAISYT F NKSCAISYT F NKSCAISYT	780 AYRNIYPLWAL AYRNIYPLWAL AYRNIYPLWAL TYRNTFPLWAL SFRNIFPIWAL SYRNIFPIWAL AYRNIFPIWAL AYRNIFPIWAL AYRNIFPIWAL AYRNIFPIWAL SYRNIFPIWAL SYRNIFPIWAL SYRNIFPIWAL	* AEYRNRVPLPS AEYRRNVPLP- AEYRRVVPLP- AEYRRVVFI GEYRRRV GEYRRRV GEYRRRV GEYRCV GEYRCV GEYRCRV GEYRCRV GEYRCRV GEYRCRV GEYRCRV GEYRCRV GEYRCRV GEYRCRV GEYRCRV GEYRCRV GEYRCRV GEYRCRV GEYRCRV GEYRCRV GEYRCRV	800 TTL LGT LGT 		762 763 764 755 755 755 753 752 753 753 753 753 753 753
EtAS PNY1 BPY PSY AtLUP1 TRW OEW BPW AtCAS1 PSCAS PgCAS BpCAS1 AtLAS1 HSLAS MmLAS ScLAS SHC		KKYVPLEG KVYVPLEG KEYVPLEG KIYVPLEG KVYTNLEG KVYTNLEG KVYSNLEG KVYSNLEG KVYSNLEG KVYTNLEG KVYSN KVYSN KYSN KYSN KYSN KYSN KYSN KYSN KYSN K	* JRSNLVH JRSNLVH JRSNLVH JRSNLVH JRSNLVQ JRSNLVQ JRSNLVQ JRSHVVN JRSHVVN JRSHVVN JRSHVVN JRSHVVN JRSHVVN JRSHVVN JRSHVVN JRSHVVN JRSHVVN JRSHVVN JRSHVVN JRSHVVN JRSHVVN JRSHVVN	720 SWALMGL GWALMGL FAWAMMGL SWALMGL SWALS SWALS SWALS FAWALS GWAMLAL GWAMLAL GWAMLAL SWALLAL CWAMMGL CWALMGL FAWALAL	* ISAGQMDRDP IHSEQAERDP IHAGQAERDP IHAGQAERDP IHTGQAERDD IHTGQAERDD IAGQAEIDP IGAGQAEVDRI IGAGQAEVDRI IEAEQAKRDP IDAGQAERDP IDAGQAERDP IDAGQAERDP IAVRHPDII IAVRHPDII IAGGRAESEAJ	740 TPLHRAAKLII TPLHRAAKLII TPLHRAAKLII TPLHRAAKLII TPLHRAAKLII TPISNGVRLII GPIHRGIKLIV TPTHRGVRVII KPLHRAARVII TPLHRAAKLII TPLHRAAKLII TPLHRAAKLII TPLHRAAKIII TPLHRAAKIII TAQERGVRCII TAQERGIRCII ARRGVQYLV	* NSQLEDGDFP NSQLEDGDFP NSQLEQGDWP NSQLENGDFP NSQMEDGDFP NSQMEDGDFP NSQMEDGDFP NSQMENGDFP	760 QQEITGV QQEITGV QQEITGV QQEITGV QQEITGV QEITGV QEITGV QEITGV QEITGV QEIMGV QEIMGV QEIMGV QEILGV QEILGV QENISGV QENISGV	* EMKNCMLHYA EMKNCMLHYA EMKNCMLHYA EMKNCMLHYA EMKNCMLHYA EMKNCMLHYS EMKNCTLNYS EMKNCTLNYS EMKNCMITYA ENKNCMITYA ENKNCMITYA ENKNCMISYS ENKSCAISYT ENKSCAISYT ENKSCAISYT ENKSCAISYT	780 AYRNIYPLWAL AYRNIYPLWAL AYRNIYPLWAL TYRNTFPLWAL SFRNIFPIWAL SYRNIFPIWAL AYRNIFPIWAL AYRNIFPIWAL AYRNIFPIWAL AYRNIFPIWAL SYRNIFPIWAL SYRNIFPIWAL SYRNIFPIWAL SYRNIFPIWAL SYRNIFPIWAL SYRNIFPIWAL	* AEYRNRVPLPS AEYRRVVPLP- AEYRRVVFI GEYRRIV GEYRRRV GEYRRRV GEYRCQV GEYRCQV GEYRCRV	800 TTL LGT LGKNLN 	***************************************	762 763 758 755 753 753 753 753 753 753 753 753 753

		*		
EtAS	:		:	-
PNY1	:		:	-
BPY	:	QVVNCIGQSLYKKYK	:	779
PSY	:		:	-
AtLUP1	:	VN	:	757
TRW	:	QNI	:	758
OEW	:	LHAQT	:	758
BPW	:	LFA	:	755
AtCAS1	:	LLQQGE	:	759
PsCAS	:	LQAC	:	756
PgCAS	:	L-QGPS	:	758
BpCAS1	:	LKAL	:	767
AtLAS1	:	L $$ SL	:	756
HsLAS	:		:	-
MmLAS	:		:	-
SCLAS	:		:	-
SHC	:	ERR	:	631

The triterpene cyclases amino acids sequences were aligned using Clustal W, as implemented in the (CLC Sequence Viewer (CLC bio), and the figure was made by GenDoc (http://www.nrbsc.org/gfx/genedoc/). EtAS: *Euphorbia tirucalli* β-amyrin synthase (AB206469), PNY1: *Panax ginseng* β-amyrin synthase (AB009030), BPY: *Betula platyphylla* β-amyrin synthase (AB055512), PSY: *Pisum sativum* β-amyrin synthase (AB034802), AtLUP1: *Arabidopsis thaliana* multifunctional triterpene cyclase (At1g78970), TRW: *Taraxacum officinale* lupeol synthase (AB025345), OEW: *Olea europaea* lupeol synthase (AB025343), BPW: *Betula platyphylla* lupeol synthase (AB055511), AtCAS1: *Arabidopsis thaliana* cycloartenol synthase (At2g07050), PsCAS: *Pisum sativum* cycloartenol synthase (D89619), PgCAS: *Panax ginseng* cycloartenol synthase (AB009029), BpCAS1: *Betula platyphylla* cycloartenol synthase (AB055509), AtLAS1: *Arabidopsis thaliana* lanosterol synthase (At3g45130), HsLAS: *Homo sapiens* lanosterol synthase (P48449), MmLAS: *Mus musculus* lanosterol synthase (AK044016), ScLAS: *Saccharomyces cerevisiae* lanosterol synthase (P38604), SHC: *Alicyclobacillus acidocaldarius* squalene-hopene cyclase

Fig. S2. EIMS and NMR spectra of Product 10-acetate

Fig. S2-1. EIMS spectrum of Product 10 acetate



Fig. S2-2. ¹H-NMR spectrum of product **10**-Ac in CDCl₃ (600 MHz).



Fig. S2-3. ¹³C-NMR spectrum of product **10** Ac (150 MHz)



Fig. S2-4. ¹H-¹H COSY 90 of product **10** Ac







Fig. S2-6. NOESY spectrum of product 10 Ac



S9



Fig. S2-7. HSQC spectrum of product 10 Ac

Fig. S2-8. HMBC spectrum of product 10 Ac



Fig. S2-9. NMR data analyses for proposing structure of 10-Ac, optical rotation and HRMS data.

								The dete	stereoch rmined	nemistry at C(20) ha	as yet tobe
32	$\begin{array}{c} 29 \\ 29 \\ 10 \\ 11 \\ 12 \\ 13 \\ 10 \\ 14 \\ 14 \\ 14 \\ 15 \\ 16 \\ 26 \\ 16 \\ 1$									c=0.017, CHCl ₃) 0bsd. 468.39641	
e t	600 MHz in C ₆ D ₆ he solvent peak ¹ H: 7.2	28 ppm; ¹³ 6	C:128.0	NOE: COSY		► A —	HMBC:				
e t NC	500 MHz in C ₆ D ₆ he solvent peak ¹ H: 7.2 . ¹ H	²⁸ ppm; ¹³	C:128.0	^o ppm ^{NOE:} COSY	, HOHAH	► A NO.	нмвс: ¹ н	¹³ C	NO.		¹³ C
e t <u>NC</u> 1	500 MHz in C ₆ D ₆ he solvent peak ¹ H: 7.2 0. ¹H 0.88(m);1.57(m)	28 ppm; ¹³ 1 1 ³ C 38.75	C:128.0 NO.	NOE: COSY 1 H 1.456 (bd,	 ◄ · · · · · · · · · · · · · · · · · · ·	► A NO.	нмвс:	¹³ C 150.9	NO.	1H	¹³ C
6 t NC 1 2	500 MHz in C ₆ D ₆ he solvent peak ¹ H: 7.2). ¹H 0.88(m);1.57(m) 1.75(m);1.86(m)	28 ppm; ¹³ (1 ³ C 38.75 24.13 20.40	C:128.0 NO. 9 10	NOE: COSY 1H 1.456 (bd, J=12.5 Hz)	 ◄ HOHAH ¹³C 51.05 37.39 	NO.	HMBC:	¹³ C 150.9	NO. 25 26	¹ H 1.827(3H, s)	¹³ C 131.1 25.84
e t NC 1 2 3	600 MHz in C ₆ D ₆ he solvent peak ¹ H: 7.2). ¹H 0.88(m);1.57(m) 1.75(m);1.86(m) 4.81 (dd, J=11.7, 4.6Hz)	²⁸ ppm; ¹³ ¹³ C 38.75 24.13 80.49	C:128.0 NO. 9 10 11	NOE: COSY 1H 1.456 (bd, J=12.5 Hz) 1.24(m);1.58(m)	 ✓ HOHAH ¹³C 51.05 37.39 22.08 	► A NO. 17 18 19	HMBC:	¹³ C 150.9 18.34 16.33	NO. 25 26 27	¹ H 1.827(3H, s) 1.744(3H,s)	¹³ C 131.1 25.84 17.71
e t NC 1 2 3 4	600 MHz in C ₆ D ₆ he solvent peak ¹ H: 7.2 D. 1.7 0.88(m);1.57(m) 1.75(m);1.86(m) 4.81 (dd, J=11.7, 4.6Hz)	¹³ C 1 ³ C 38.75 24.13 80.49 38.13	C:128.0 NO. 9 10 11 12	NOE: COSY 1H 1.456 (bd, J=12.5 Hz) 1.24(m);1.58(m) 1.57(m);1.89(m)	 HOHAH ¹³C 51.05 37.39 22.08 23.60 	NO. 17 18 19 20	HMBC:	¹³ C 150.9 18.34 16.33	NO. 25 26 27 28	¹ H 1.827(3H, s) 1.744(3H,s) 1.024(3H, s)	¹³ C 131.1 25.84 17.71 28.09
e t NC 1 2 3 4 5	500 MHz in C ₆ D ₆ he solvent peak ¹ H: 7.2). ¹H 0.88(m);1.57(m) 1.75(m);1.86(m) 4.81 (dd, J=11.7, 4.6Hz) 0.844 (bd, J=10.1 Hz)	¹³ C ¹³ C 38.75 24.13 80.49 38.13 56.33	C:128.0 NO. 9 10 11 12 13	NOE: COSY 1H 1.456 (bd, J=12.5 Hz) 1.24(m);1.58(m) 1.57(m);1.89(m) 2.875(bd, J=10.9Hz)	 HOHAH ¹³C 51.05 37.39 22.08 23.60 48.84 	NO. 17 18 19 20 21	HMBC:	¹³ C 150.9 18.34 16.33 33.81	NO. 25 26 27 28 29	¹ H 1.827(3H, s) 1.744(3H,s) 1.024(3H, s) 1.044(3H, s)	¹³ C 131.1 25.84 17.71 28.09 16.76
e t NC 1 2 3 4 5 6	500 MHz in C ₆ D ₆ he solvent peak ¹ H: 7.2). 1 H 0.88(m);1.57(m) 1.75(m);1.86(m) 4.81 (dd, J=11.7, 4.6Hz) 0.844 (bd, J=10.1 Hz) 1.46(m);1.58(m)	²⁸ ppm; ¹³ ¹³ C 38.75 24.13 80.49 38.13 56.33 18.50	C:128.0 NO. 9 10 11 12 13 14	NOE: COSY 1H 1.456 (bd, J=12.5 Hz) 1.24(m);1.58(m) 1.57(m);1.89(m) 2.875(bd, J=10.9Hz)	, HOHAH ¹³ C 51.05 37.39 22.08 23.60 48.84 53.30	NO. 17 18 19 20 21 22	HMBC:	¹³ C 150.9 18.34 16.33 33.81 19.01 26.12	NO. 25 26 27 28 29 30	¹ H 1.827(3H, s) 1.744(3H,s) 1.024(3H, s) 1.044(3H, s) 1.241(3H, s)	¹³ C 131.1 25.84 17.71 28.09 16.76 17.96
e t 1 2 3 4 5 6 7	500 MHz in C ₆ D ₆ he solvent peak ¹ H; 7.2 1 H 0.88(m);1.57(m) 1.75(m);1.86(m) 4.81 (dd, J=11.7, 4.6Hz)	¹³ C 38.75 24.13 80.49 38.13 56.33 18.50 35.62	C:128.0 NO. 9 10 11 12 13 14 15	NOE: COSY 1H 1.456 (bd, J=12.5 Hz) 1.24(m);1.58(m) 1.57(m);1.89(m) 2.875(bd, J=10.9Hz) 1.81(m);2.52(bd,	, HOHAH ¹³ C 51.05 37.39 22.08 23.60 48.84 53.30 38.86	NO. 17 18 19 20 21 22 23	HMBC:	¹³ C 150.9 18.34 16.33 33.81 19.01 36.12 26.36	NO. 25 26 27 28 29 30 31	1 <u>н</u> 1.827(3H, s) 1.744(3H,s) 1.024(3H, s) 1.04(3H, s) 1.241(3H, s) 1.241(3H, s)	¹³ C 131.1 25.84 17.71 28.09 16.76 17.96 169.9

The stereoisomer of **10**, described below, was isolated by Wu's group from the mutants of S. cerevisiae lanosterol synthase, which was reported in the following references.



- Wu, Tung-Kung; Chang, Yi-Chun; Liu, Yuan-Ting; Chang, Cheng-Hsiang; Wen, Hao-Yu; Li, Wen-Hsuan; Shie, Wen-Shiang, Organic & Biomolecular Chemistry (2011), 9(4), 1092-1097.
- 2. Liu, Yuan-Ting; Hu, Tain-Chang; Chang, Cheng-Hsiang; Shie, Wen-Shiang; Wu, Tung-Kung, Organic Letters (2012), 14(20), 5222-5225.

Fig. S3. EIMS and NMR spectra of Product 12-acetate.

Fig. S3-1. EIMS spectrum of product 12-Ac



Fig. S3-2. ¹H-NMR spectrum of product **12**-Ac in C_6D_6 (400 MHz).



Fig. S3-3. ¹³C-NMR spectrum of product **12**-Ac in C_6D_6 (100 MHz).



Fig. S3-4. 1 H- 1 H COSY spectrum of product 12-Ac in C₆D₆.



Fig. S3-5. HOHAHA spectrum of product 12-Ac in C₆D₆.



Fig. S3-6. NOESY spectrum of product 12-Ac in C_6D_6 (400 MHz).



Fig. S3-7. NOESY spectrum of product **12**-Ac in C_6D_6 (600 MHz)-Expanded Region)



Fig. S3-8. HSQC spectrum of product 12-Ac in C₆D₆



Fig. S3-9. HMBC spectrum of product 12-Ac in C₆D₆



Fig. S3-10. NMR data analyses for proposing structure of 12-Ac, optical rotation and HRMS data.



HMBC:

NOE: <-----> COSY: _____ [α]_D²⁰= -17.1 (c=0.0354, CHCl3) HREIMS M+: Obsd. 468.39641; Calcd. 468.39673

400 MHz in C_6D_6 the solvent peak ¹H: 7.28 ppm; ¹³C:128.0 ppm

NC). ¹ Н	¹³ C	NO.	¹ H	¹³ C	NC). ¹ Н	¹³ C	NO.	¹ H	¹³ C
1	0.92(m);1.63(m)	38.54(t)	9	1.47 (m)	50.80(d)	17		34.87(s)	25	0.920(3H,s)	16.58(q)
2	1.73(m);1.88(m)	24.07(t)	10		37.32(s)	18		133.4(s)	26	1.008(3H,s)	17.90(q)
3	4.85(dd, 11.6,	80.53 (d)	11	1.31(m);1.47(m)	22.00(t)	19	1.84 (m);2.46 (bd,	39.04 (t)	27	1.328(3H,s)	21.63 (q)
4	4.8 HZ)	37.95(s)	12	1.95(m):2.78(m)	25.36(t)		J=15.6 Hz)	33 45(c)	28	1.225(3H, s)	23.83 (q)
5) 855 (bd .l=11.6 Hz)	55.64(d)	13		134.9(s)	20	1 21(m):1 62(m)	35 74 (t)	29	0.959 (3H, s)	32.52(q)
6	1.35(m);1.54(m)	18 59(t)	14		44.96 (s)	21	1.51(11), 1.03(11)	30.80 (+)	30	1.125(3H, s)	24.34 (q)
	1.49(011 m)	25.00(4)	45			22	1.51 (2H, III)	33.00 (l)	31		169.9(s)
1	1.40(20.111)	35.08(t)	15	1.21(m);1.90 (m)	26.92 (t)	23	1.045(3H, s)	28.18(q)	32	1.889 (3H, s)	20.86 (q)
8		41.29 (s)	16	1.51(m); 1.63(m)	37.06(t)	24	1.035(3H,s)	16.95(q)			

Fig. S4. EIMS and NMR spectra of product 15 acetate.

Fig. S4-1. EIMS spectrum of 15-Ac.



Fig. S4-2. ¹H-NMR spectrum of 15-Ac in CDCl₃ (400 MHz).



Fig. S4-3. ¹³C NMR spectrum of 15-Ac in CDCl₃ (100 MHz).



Fig. S4-4. ¹H-¹H COSY spectrum of 15-Ac in CDCl₃.



Fig. S4-5. HOHAHA spectrum of 15-Ac in CDCl₃.



Fig. S4-6. NOESY spectrum of 15-Ac in CDCl₃.



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Fig. S4-7. HSQC spectrum of 15-Ac in CDCl₃.



Fig. S4-8. HMBC spectrum of 15-Ac in CDCl₃.



Fig. S4-9. NMR data analyses for proposing structure of 15-Ac, optical rotation and HRMS data.





400 MHz in CDCl₃ the solvent peak ¹H: 7.26 ppm; ¹³C:77.0 ppm

NO.	¹ H	¹³ C	NO.	¹ H	¹³ C	NO.	¹ H	¹³ C	NO.	¹ H	¹³ C
1	1.05 (m);1.71(m)	38.77	9	1.34 (m)	50.88	17	2.73 (1H, m)	41.17	25	_	131.0
2	1.64 (2H, m)	23.71	10		37.14	18	0.962 (3H, s)	15.59	26	1.681 (3H,s)	25.72
3 4.4	l8 (dd, J=10.3, 6.4 Hz)	80.93	11	1.17 (m); 1.52(m)	21.47	19	0.868 (3H, s)	16.27	27	1.618 (3H_s)	17.71
4		37.90	12	1.06 (m);1.47(m)	24.88	20		136.9	28	0.856 (3H, s)	27.97
5	0.84 (1H, m)	55.96	13	1.63(1H, m)	44.44	21	1.604 (3H,s)	19.02	29	0.850 (3H, s)	16.50
6	1.50 (2H, m)	18.16	14		49.32	22	5.15 (t, J=7.2 Hz)	124.8	30	0.900 (3H,s)	15.95
7	1.28(m); 1.58(m)	35.38	15	1.12(m); 1.58(m)	31.81	23	2.66 (2H, m)	26.38	31		171.0
8		40.53	16	1.45 (m);1.73 (m)	26.55	24	5.06 (t, J=7.2 Hz)	123.8	32	2.044(3H, s)	21.33

Fig. S5. EIMS and NMR spectra (400 MHz, C₆D₆) of product **17**-acetate **Fig. S5-1**. EIMS spectrum of product **17**-Ac.



Fig. S5-2. ¹H-NMR spectrum of product 17-Ac (400 MHz, C_6D_6).



Fig. S5-3. ¹³C-NMR spectrum of product 17-Ac (100 MHz, C_6D_6).



Fig. S5-4. ¹H-¹H COSY spectrum of product **17**-Ac.



S23





Fig. S5-6. NOESY spectrum of product 17-Ac.



S24

Fig. S5-7. HSQC spectrum of product 17-Ac.



Fig. S5-8. HMBC spectrum of product 17-Ac.



Fig. S5-9. NMR data analyses for proposing structure of **17**-Ac and HREIMS data. Reliable optical rotation was not obtained due to the sample loss during isolation and the instrumental analyses.







HREIMS M+: Obsd. 466.38168 Calcd. 466.38108

400 MHz in $\rm C_6D_6$ the solvent peak $^1\rm H:$ 7.28 ppm; $^{13}\rm C:128.0$ ppm

NOE: <----> COSY: HMBC:

			-								
NO	. ¹ H	¹³ C	NO.	¹ H	¹³ C	NO.	¹ H	¹³ C	NO.	¹ H	¹³ C
1	0.82 (m);1.52 (m)	38.58	9	1.43 (bd, 12.0 Hz)	50.56	17	—	146.2	25	—	131.3
2	1.71 (m); 1.84(m)	24.09 [″]	10	—	37.23	18	1.038 (3H, s)	18.26 ^b	26	1.822 (3H, s)	25.85
3 4	.80 (dd, J=11.6, 4.8 Hz)	80.44	11	1.22 (m); 1.56(m)	21.96	19	0.876 (3H, s)	16.29	27	1.713 (3H,s)	17.80
4	—	38.09	12	Hz)	24.03 <i>a</i>	20		145.7	28	1.019 (3H, s)	28.08
5	0.83 (m)	56.24	13	3.05 (1H,dd, J=13.0, 3.2 Hz)	48.37	21	5.23 (s); 5.14 (s)	110.5	29	1.038 (3H, s)	16.76 ^b
6	1.46 (m); 1.56(m)	18.47	14	· <u> </u>	53.45	22	2.47 (m); 2.57(m)	35.44	30	1.247 (3H,s)	16.12
7	1.31(bd, J=12.5Hz); 1.58(m)	35.46	15	1.84 (m); 2.49 (m)	39.00	23	2.45 (2H, m)	28.02	31		170.0
8		40.10	16	5.84 (bs)	127.1	24	5.42 (Very broad s)	124.9	32	1.882 (3H, s)	20.86

a and *b*: The assignments are exchangeable between the same letters.

Fig. S6. GCMS spectrum of the acetate of the hexane-extract obtained from the Y259H mutant. **19** acetate. The EIMS of **19** acetate was almost identical to that of dammara-(E)-20(22),(E)24(25)dien-3 β -ol acetate that was isolated from F728H mutant (Ito, R.; Hashimoto I.; Masukawa Y.; Hoshino, T. *Chem.-Eur. J.* **2013**, *19*, 17150-17158, see Supporting Information, Fig. S36, EIMS) and is quite similar as that of EIMS of **15**-acetate.





Fig. S7.1. Homology modeling of β-amyrin synthase prepared with Pymol (http://www.pymol.org). This model was constructed by ESyPred3D (http://www.unamur.be/sciences/ biologie/urbm/ bioinfo/esypred/), based on on the X-ray crystal structure of human lanosterol cyclase (pdb ID: 1w6k, *Nature* **432**, 118-122, 2004). Lambert C, Leonard N, De Bolle X & Depiereux E (2002) ESyPred3D: Prediction of proteins 3D structures *Bioinformatics*. **18**, 1250-1256.



Lanosterol molecule is shown with green color. We have reported the detailed functional analysis of F728 in the previous paper (R. Ito, I. Hashimoto, Y. Masukawa and T. Hoshino, Chem. Eur. J. 2013, 19, 17150-17158). The site-directed mutagenesis experiments have demonstrated that the function of cation/ π interaction was assigned to the F728 residue. On the other hand, the steric bulk at 474 position is critical to the accurate folding of oxidosqualene to complete the polycyclization reaction (Ito, R.; Masukawa, Y.; Nakada, C.; Amari, K.; Nakano, C.; Hoshino, T. Org. Biomol. Chem. 2014, 12, 3836-3846). By the mutagenesis experiments, we found that D⁴⁸⁵C⁴⁸⁶TA motif triggers the polycyclization reaction and the C564 is involved in hydrogen bond formation with the carboxyl residue of D485, resulting in enhancement of the acidity (R. Ito, Y. Masukawa and T. Hoshino, FEBS J., 2013;280:1267-1280). F474 is situated in the vicinity to B-ring formation site. F413 residue is located in approximate to the C/D ring. Y259 and W257 that correspond to Y261 and to W259, respectively, of *P. ginseng* PNY β -amyrin synthase, are also marked in this model. It was reported that the Y261H mutant of PNY gave the teracyclic products (see the Text and the ref. T. Kushiro, M. Shibuya, K. Masuda, Y. Ebizuka, J. Am. Chem. Soc., 2000, 122, 6816-6824. The hydrogen bonding may occur between OH of the polar amino acids (Ser, Thr or Tyr mutants) and the phenolic OH of Y259, because of the proximal distance between them (see Fig. S7.2), which would have brought about the inappropriate placement of Y259, resulting in the decreased activities of the polar amino acid-substituted mutants (see Figure 3 in Text).

Fig. S7.2. Distances between OH of Y259 and OH of polar amino acids (Ser and Thr), OH of Tyr and NH or N of His, which were estimated from the modeling constructed by the methods of ESyPred3D. Lanosterol molecule is shown with green color.



Hydrogen bonding is presumed between OH of Y259 and the polar group of Ser, Thr, His and Tyr, and water molecule(s) is also likely to intervene between the OH of Y259 and the polar groups of the substituted amino acids.

Fig. S8. GC traces of the lipophilic acetylated materials produced by various mutants targeted for F413. A 100 mL culture of each mutants were subjected to centrifugation. The cell pellets were subjected to saponification with 15% KOH/MeOH under reflux condition, followed by the extraction of the lipophilic materials with hexane extract (3 x 10 mL). The triterpene fraction including products was obtained by partial purification with a SiO₂ column to remove oxidosqualene, dioxidosqualene and nontriterpene impurities (hexane/EtOAc=100:1), followed by acetylation with Ac₂O/Py. The acetate mixture was dissolved in 1.0 mL of hexane. A 0.5 μ L of the hexane was injected to the GC apparatus. The GC conditions were as follows: J & W, DB-1 capillary column (Length 30 m, I.D. 0.32 mm, Film Thickness 0.25 mm); column injection temp., 300°C; column temperature, 245-270°C (0.35 °C/min).



Fig. S9. Estimation of the EtAS enzymatic activities for the wild-type and the F413X mutants.



<Expression level of β–amyrin synthase (EtAS)>

Figure S9.1. Expression level (mg/L) of the EtAS enzymes of the wild-type and the site-directed mutant. The yeast cells grown in 1L-medium were collected and the protein amounts (mg) were quantified by Western blot analysis.



<GC analyses for the quantities of oleanane-type triterpenes>

Fig. S9.2. The quantities of products **2** and **12** (oleanane skeleton) produced by 1Lculture of each of the mutant strains that were determined by GC analyses using GGOH (geranylgeraniol) as an internal standard.

<Enzyme activities for the production of oleanane-type triterpenes>



Fig. S9.3. Enzyme activities of the mutants relative to that of the wild-type for the production of oleanane skeleton. The wild-type activity (100%) indicates the sum of the relative activities shown in Figs. S9.3, Fig. S9.5 and S9.7. These enzyme activities were estimated by dividing the amounts of oleanane-type products (**2** and **12**) by the expressed quantities of EtAS enzymes. This means that the values of Fig. S9.2 were divided by those of Fig. S9.1. The wild-type did not show 100% activity, i.e., 96.3 \pm 0.7 %, because the wild-type produced the tetracycles **13** and **14** in a small amount (see Figs. S9.5 and S9.7).



< GC analyses for the quantities of Dammarane-types>

Fig. S9.4. The quantities of products **10**, **11**, **13** (dammarane skeleton) produced by 1L-culture of each of the mutant strains that were determined by GC analyses using GGOH (geranylgeraniol) as an internal standard. Product **10** is tentatively categorized as Dammarane skeleton, but not 17-epi-dammaraen skeleton. To make sense, the stereochemistry of C-20 must be determined.

< Enzyme activities for the production of Dammarane-types>



Figure S9.5. Enzyme activities of the mutants relative to that of the wild-type. These enzyme activities were estimated by dividing the amounts of dammarane-type products (**10**, **11**, **13**) by the expressed quantities of EtAS enzymes, that is, the values of Fig. S9.4 were divided by those of Fig. S9.1. The activity of the wild-type for the production of **13** and **14** was very low, i.e., $1.53\pm0.61\%$, thus, the relative activity does not correspond to 100%. The total values of Fig.S9.3 and Fig. S9.5 for the wild-type corresponds to 100%.



< GC analyses for the quantities of 17-epi-Dammarane-type>

Fig. S9.6. The quantities of products **14** (17*-epi*-dammarane skeleton) produced by 1L-culture of each of the mutant strains, which were determined by GC analyses using GGOH (geranylgeraniol) as an internal standard.



< Enzyme activities for the production of 17-epi-Dammarane-types>

Figure S9.7. Enzyme activities of the mutants relative to that of the wild-type. These enzyme activities were estimated by dividing the amounts of 17-ep-dammarane-type product **14** by the expressed quantities of EtAS enzymes (%).

< GC analyses for the quantities of bicyclic product >



Fig. S9.8. The quantities of products **9** produced by 1L-culture of each of the mutant strains, which were determined by GC analyses using GGOH (geranylgeraniol) as an internal standard.



Figure S9.9. Enzyme activities of the mutants relative to that of the wild-type. These enzyme activities were estimated by dividing the amounts of bicyclic product **9** by the expressed quantities of EtAS enzymes (%).

Fig. S10. Estimation of the EtAS enzyme activities for the Y259X mutants.



<Expression level of β -amyrin synthase (EtAS)>

Fig. S10.1. Expression level (mg/L) of the EtAS enzymes of the wild-type and the site-directed mutant. The yeast cells grown in 1L-medium were collected and the protein amounts (mg) were quantified by Western blot analysis.

<GC analyses for the quantities of oleanane-type triterpenes>



Fig. S10.2. The quantities of products **2**, **16** and **18** (oleanane skeleton) produced by 1L-culture of each of the mutant strains that were determined by GC analyses using GGOH (geranylgeraniol) as an internal standard.



<Enzyme activities for the production of oleanane-type triterpenes>

Fig. S10.3. Enzyme activities of the mutants relative to that of the wild-type for the production of oleanane skeleton. See the legend to Fig. S9.3 for the calculation method.

<GC analyses for the quantities of lupanyl-type triterpene, lupeol>



Fig. S10.4. The quantities of product **20** (lupeol, 6/6/6/5-fused pentacycle) produced by 1L-culture of each of the mutant strains that were determined by GC analyses using GGOH (geranylgeraniol) as an internal standard.



<Enzyme activities for the production of lupeol>

Fig. S10.5. Enzyme activities of the mutants relative to that of the wild-type. These enzyme activities were estimated by dividing the amounts of lupanyl-type product **20** by the expressed quantities of EtAS enzymes.



<GC analyses for the quantities of tetracyclic triterpenes>

Fig. S10.6. The total quantities of products **11**, **13**, **14**, **15**, **17** and **19** produced by 1L-culture of each of the mutant strains that were determined by GC analyses using GGOH (geranylgeraniol) as an internal standard.



< Enzyme activities for the production of dammarenyl skeleton>

Fig. S10.7. Enzyme activities of the mutants relative to that of the wild-type. These enzyme activities were estimated by dividing the amounts of tetracyclic products 11, 13, 14, 15, 17 and 19 by the expressed quantities of EtAS enzymes.

Fig. S11. Estimation of the EtAS enzyme activities for the W257X mutants.

<Expression level of β -amyrin synthase (EtAS)>



Fig. S11.1. Expression level of β -amyrin synthase (EtAS) for the wild-type and the mutants. The protein amounts (mg) were quantified by Western blot analysis.



<GC analyses for the quantities of oleanane-type triterpenes>

Fig. S11.2. The quantities of oleanyl products (2 and 16) for wild-type and the variants, which were determined by GC analyses.



<Enzyme activities for the production of oleanane-type triterpenes>

Fig. S11.3. Enzyme activities of the mutants relative to that of the wild-type. These enzyme activities were estimated by dividing the amounts of oleany products 2 and 16 by the expressed quantities of EtAS enzymes.

<GC analyses for the quantities of lupanyl-type triterpene, lupeol>



Fig. S11.4. The quantities of lupane skeleton (**20**, lupeol) for wild-type and the variants, which were determined by GC analyses.



<Enzyme activities for the production of lupeol>

Fig. 11.5. Enzyme activities of the mutants relative to that of the wild-type. These enzyme activities were estimated by dividing the amounts of lupeol 20 by the expressed quantities of EtAS enzymes.





Fig. S11.6.The quantities of dammarenyl skeleton (13 and 14) for wild-type and the variants, which were determined by GC analyses.

<Enzyme activities for the production of dammarenyl skeleton>



Fig. S11.7. Enzyme activities of the mutants relative to that of the wild-type. These enzyme activities were estimated by dividing the amounts of dammarenyl skeleton (**13** and **14**) by the expressed quantities of EtAS enzymes.