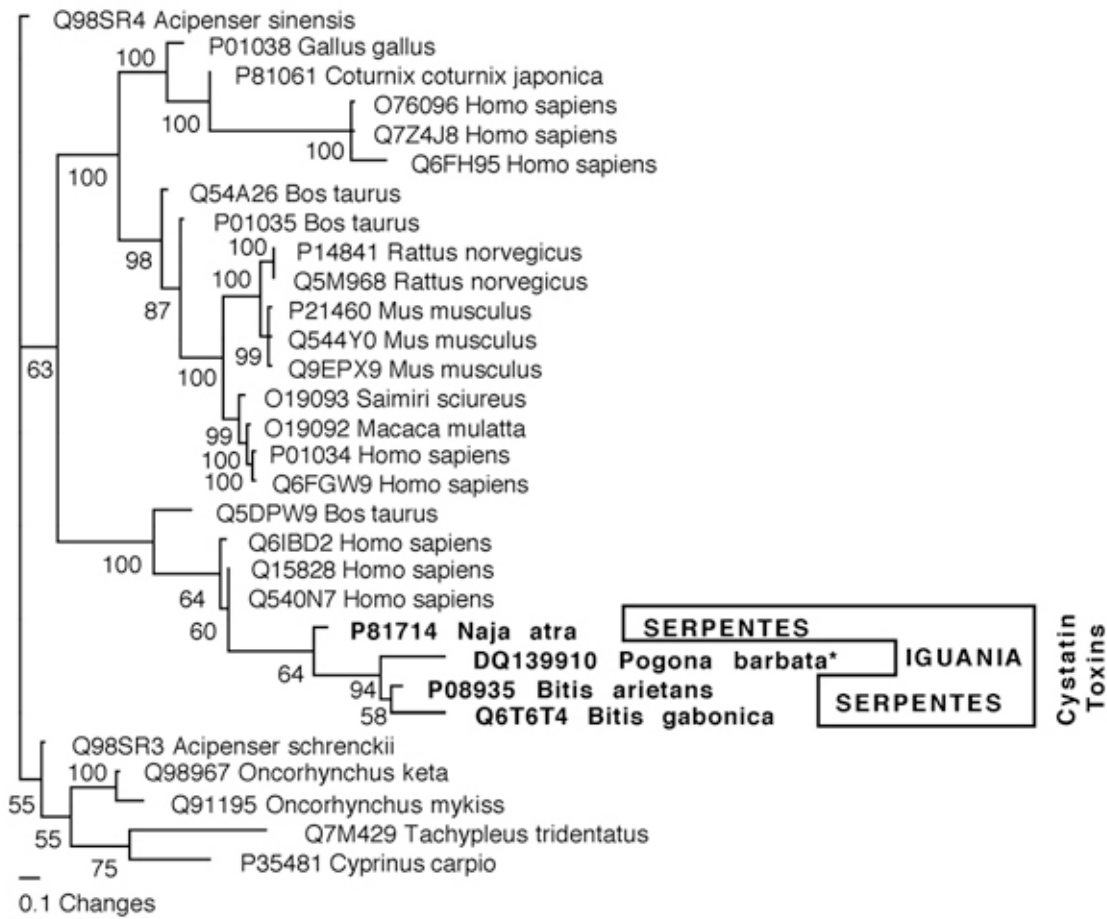
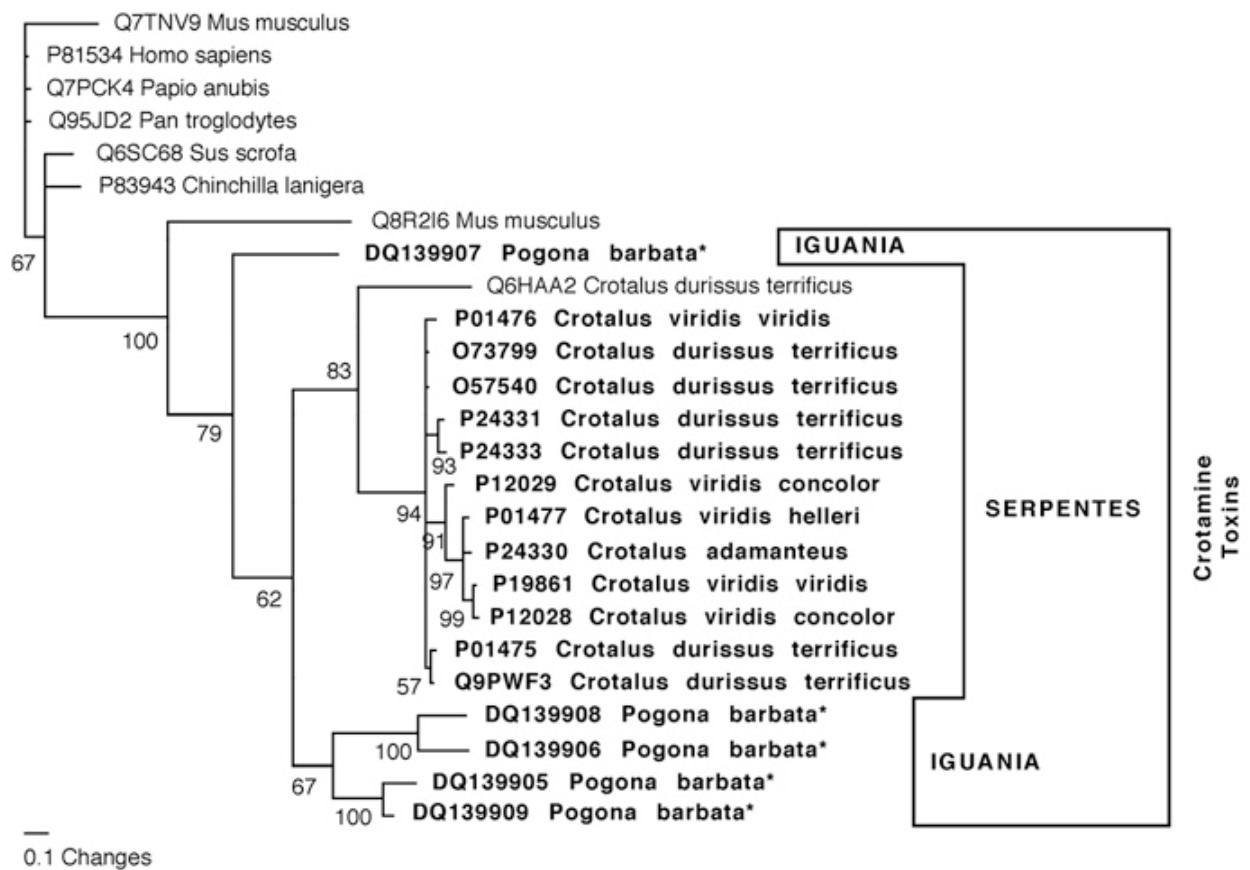


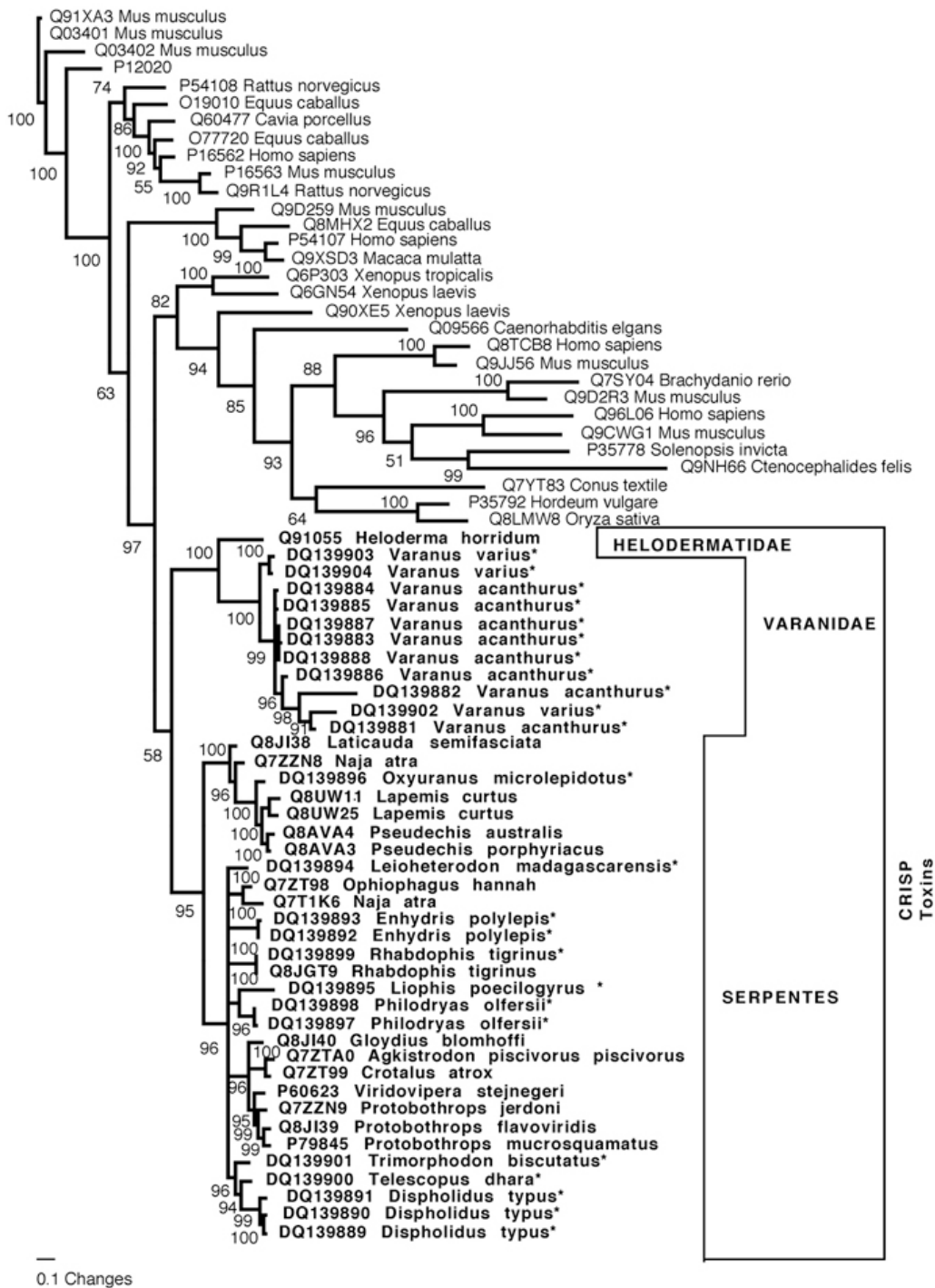
Supplementary Figure 1: Squamate molecular phylogeny. Values above branches: Bayesian posterior probabilities. Values below branches: Maximum Likelihood bootstrap values.



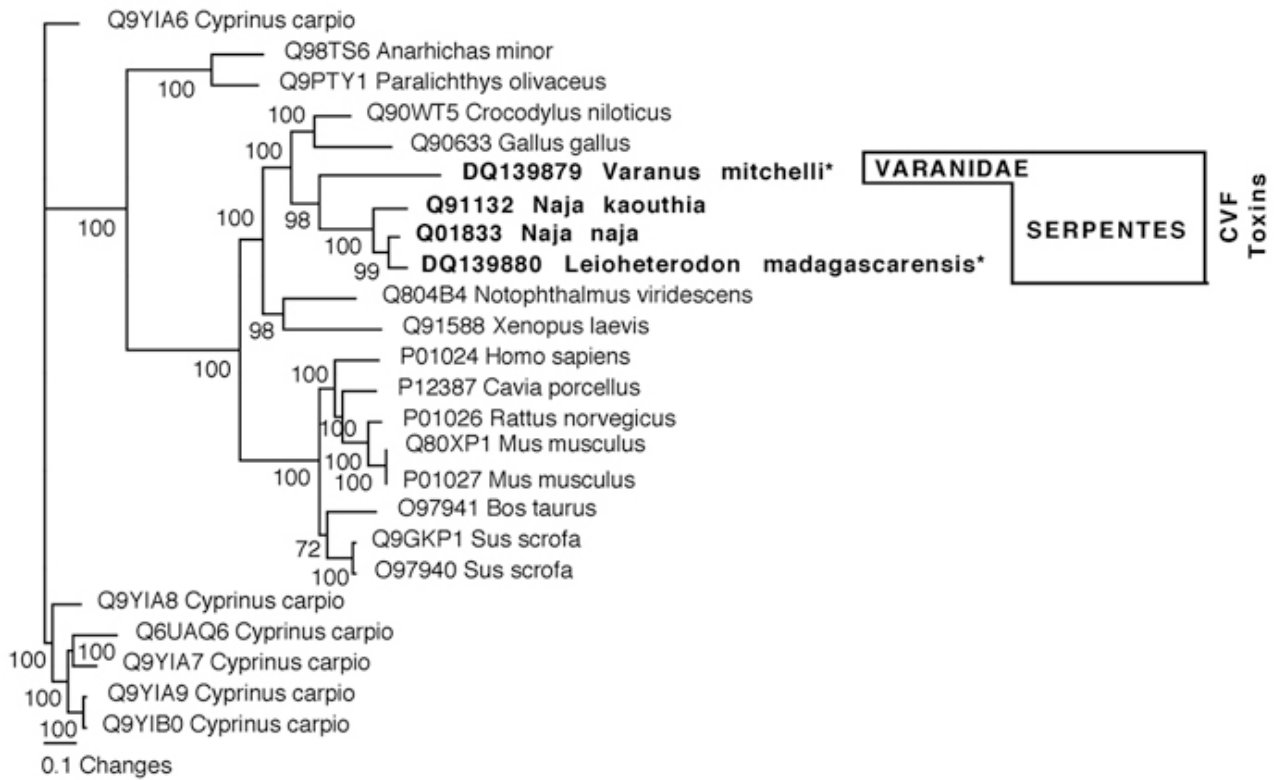
Supplementary Figure 2: Bayesian analysis of representative Cystatin-related sequences. In order to minimize confusion, all sequences are referred to by their SWISS-PROT accession numbers (<http://www.expasy.org/cgi-bin/prot-search-ful>). * Designates transcripts obtained in this study.



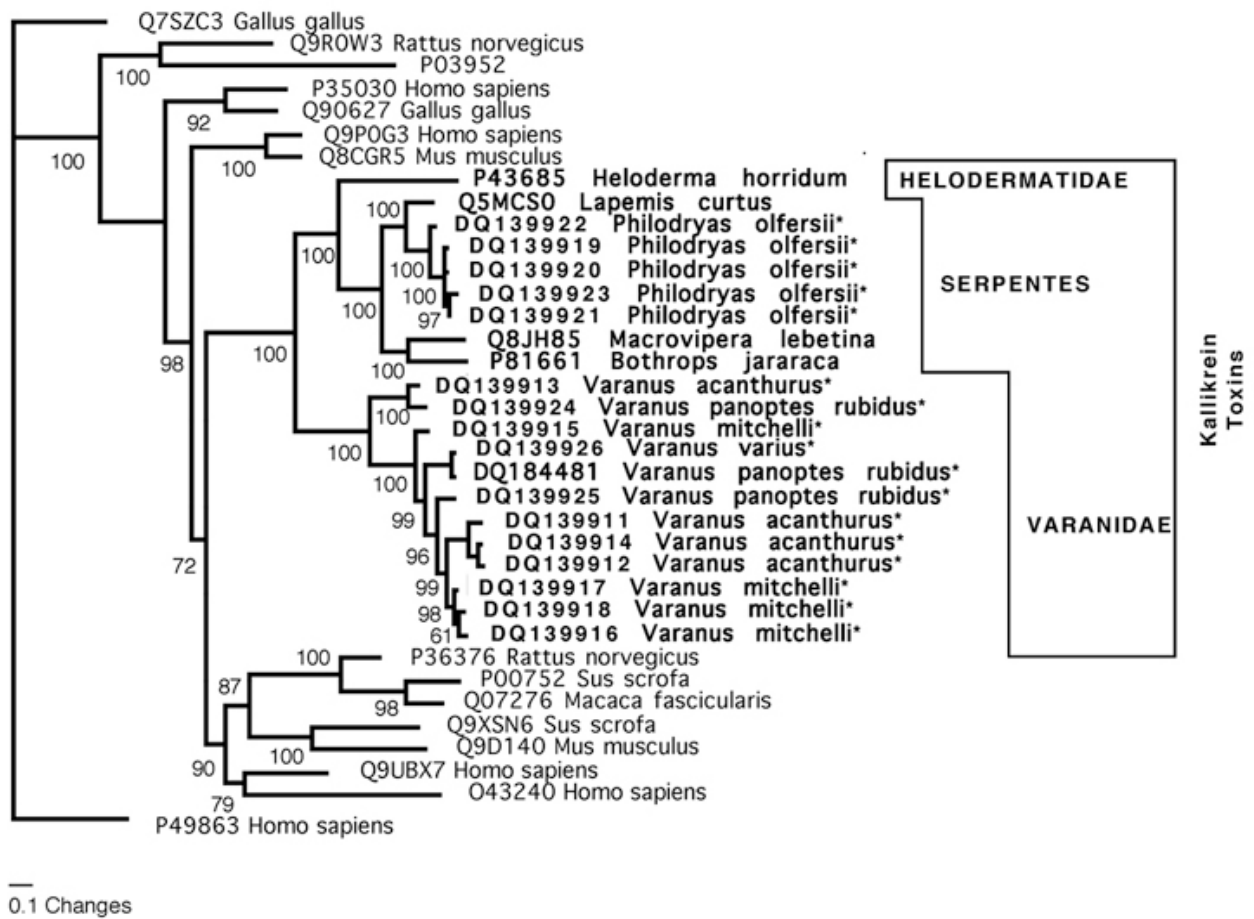
Supplementary Figure 3: Bayesian analysis of representative Crostamine-related sequences. In order to minimize confusion, all sequences are referred to by their SWISS-PROT accession numbers (<http://www.expasy.org/cgi-bin/sprot-search-ful>). * Designates transcripts obtained in this study. UPP and LOW respectively refer to transcripts from the maxillary and mandibular glands of *Pogona barbata*.



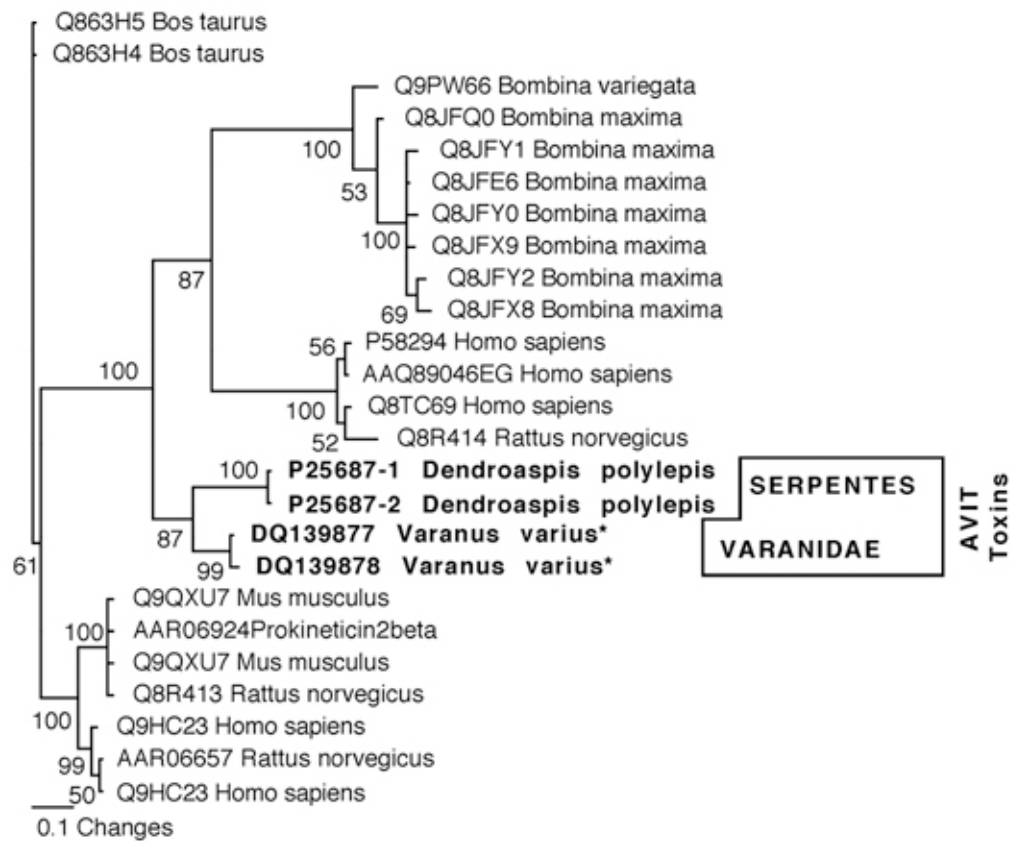
Supplementary Figure 4: Bayesian analysis of representative CRISP-related sequences. In order to minimize confusion, all sequences are referred to by their SWISS-PROT accession numbers (<http://www.expasy.org/cgi-bin/sprot-search-fun>). * Designates transcripts obtained in this study.



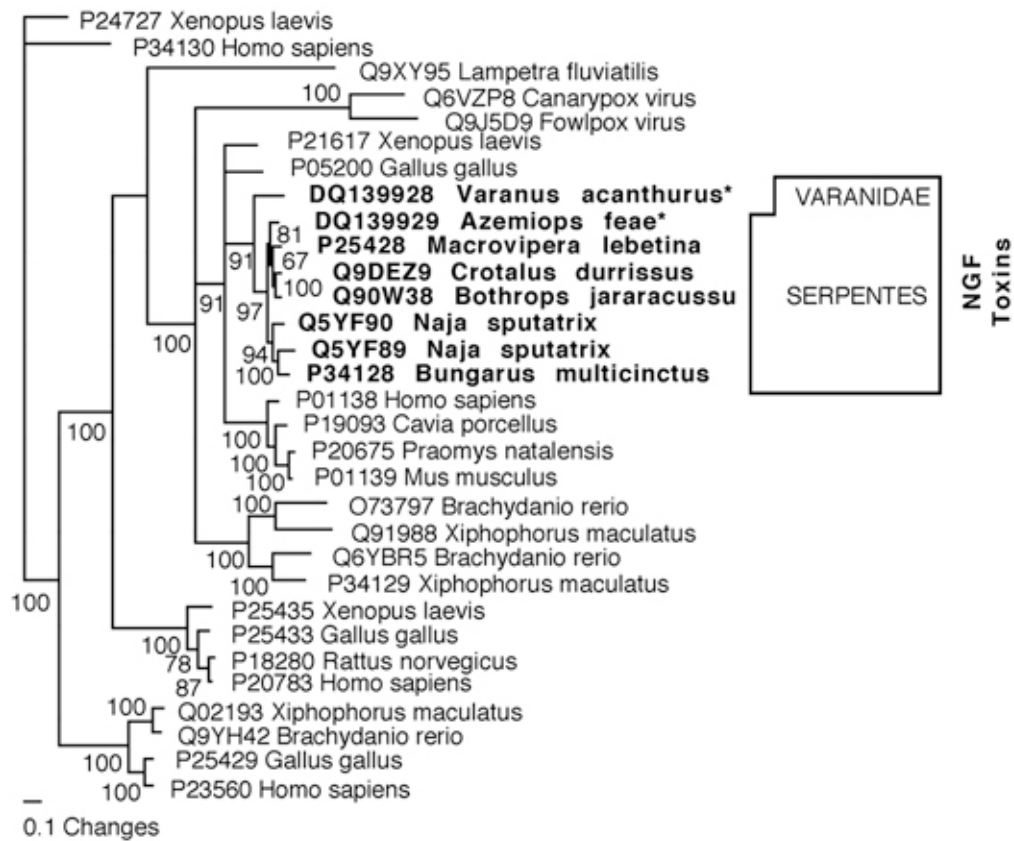
Supplementary Figure 5: Bayesian analysis of representative Cobra Venom Factor-related sequences. In order to minimize confusion, all sequences are referred to by their SWISS-PROT accession numbers (<http://www.expasy.org/cgi-bin/prot-search-ful>). * Designates transcripts obtained in this study.



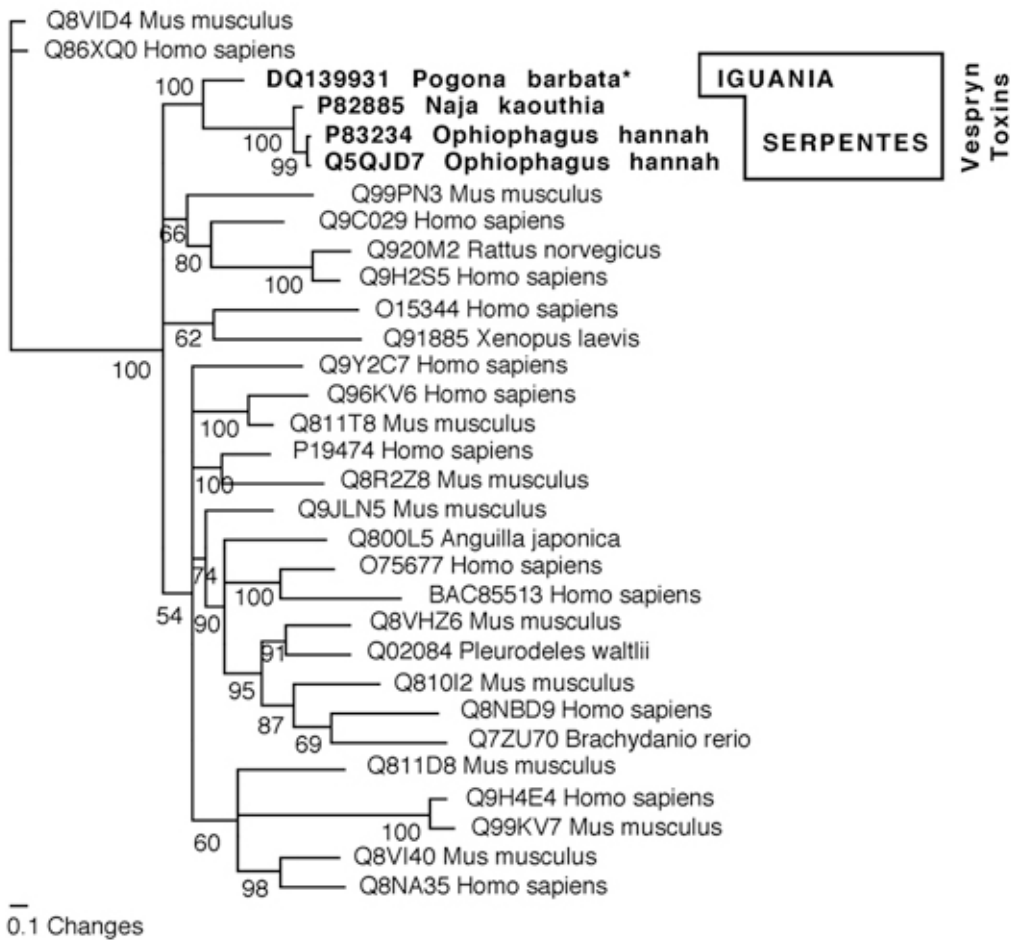
Supplementary Figure 6: Bayesian analysis of representative Kallikrein-related sequences. In order to minimize confusion, all sequences are referred to by their SWISS-PROT accession numbers (<http://www.expasy.org/cgi-bin/sprot-search-ful>). * Designates transcripts obtained in this study.



Supplementary Figure 7: Bayesian analysis of representative AVIT-related sequences. In order to minimize confusion, all sequences are referred to by their SWISS-PROT accession numbers (<http://www.expasy.org/cgi-bin/sprot-search-ful>). * Designates transcripts obtained in this study.

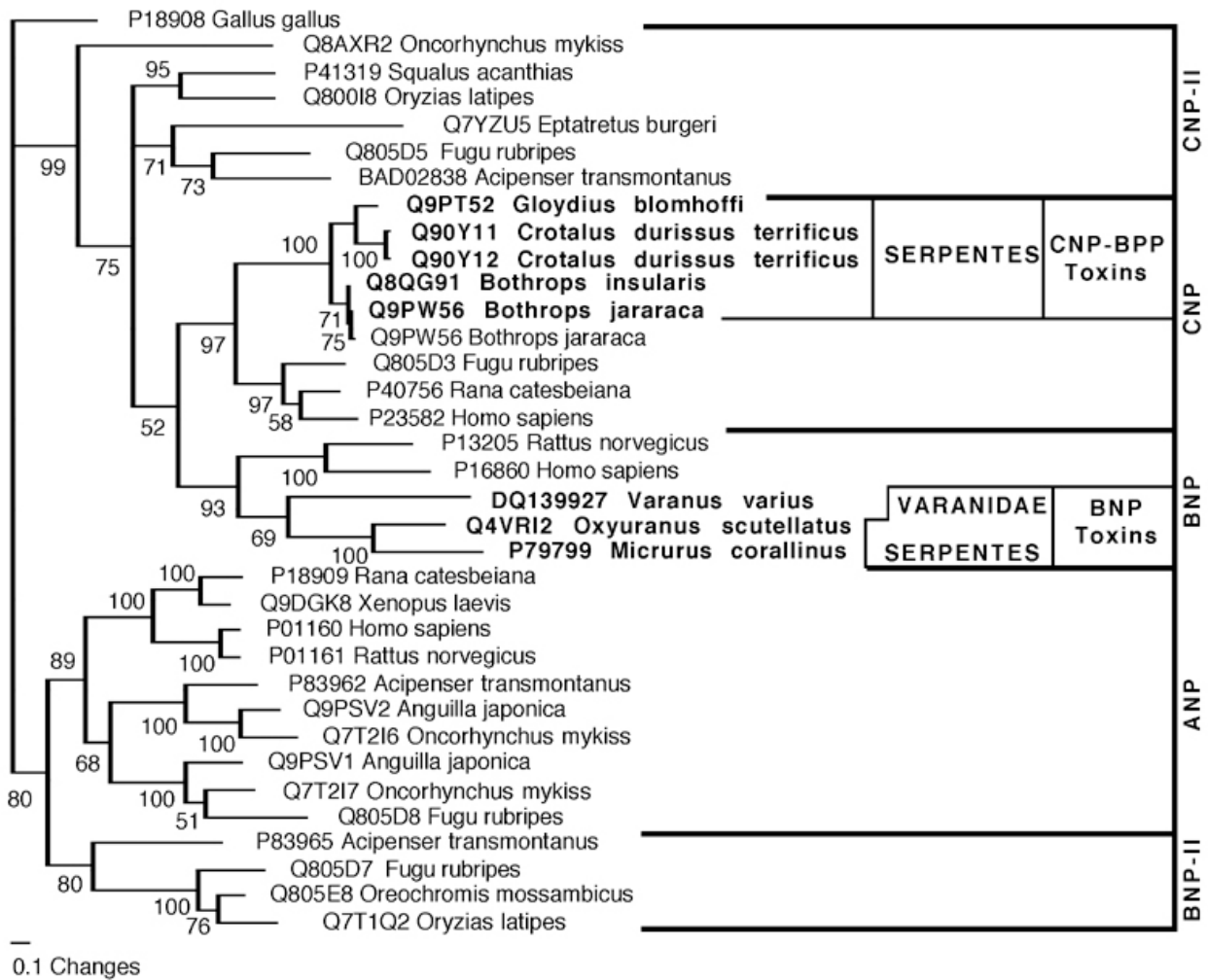


Supplementary Figure 8: Bayesian analysis of representative NGF-related sequences. In order to minimize confusion, all sequences are referred to by their SWISS-PROT accession numbers (<http://www.expasy.org/cgi-bin/sprot-search-ful>). * Designates transcripts obtained in this study.



Supplementary Figure 9: Bayesian analysis of representative Vespryn-related sequences. In order to minimize confusion, all sequences are referred to by their SWISS-PROT accession numbers (<http://www.expasy.org/cgi-bin/sprot-search-ful>). * Designates transcripts obtained in this study.

A)

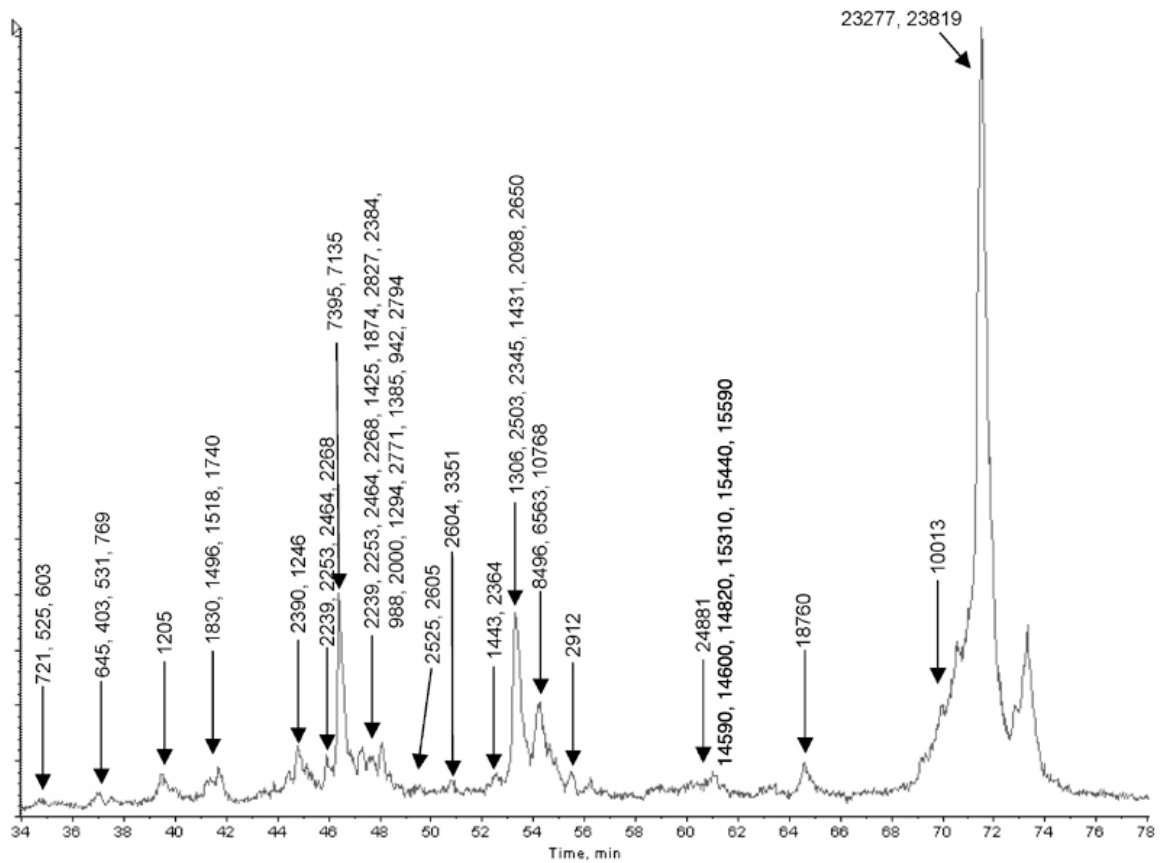


B)

1. GNP-1	-----EKRLQPEGSC + FGQKMDRIGHVSGMGC + KNKFDPNKGSSTGKK
2. TNP-c	-----SDSKIGNC + CFGFPLDRIGSVSGLGC + NRIMQNPPKKFSGE-
3. DNP	-----EVKYDPC + FGHKIDRINHVSNLGC + PSLRDPRPNAPSTSA
4. Lebetin	-GDNKPPKGGPP-NG + CFGHKIDRIGSHSGLGC + KNKVDNKG-----
5. BNP Rat	IQERLRNSKMAHSS + CFGQKIDRIGAVSRLGC + DGLRLF-----

Supplementary Figure 10: A) Bayesian analysis of representative full-length natriuretic toxins and related sequences. In order to minimize confusion, all sequences are referred to by their SWISS-PROT accession numbers (<http://www.expasy.org/cgi-bin/sprot-search-ful>). * Designates transcripts obtained in this study. B)) Sequence comparison of GNP-1 (DQ139927) from *V. varius* (Lace Monitor), 2) TNP-c (P83230) from *Oxyuranus microlepidotus* (Inland taipan), 3) DNP (P28374) from *Dendroaspis angusticeps* (Eastern Green Mamba), 4) Lebetin (Q7LZ09) from *Macrovipera lebetina* (Elephant snake) and 5) BNP from the rat (P13205) brain and atria. + designates conserved functional residues.

Varanus varius



Supplementary Figure 11: Liquid Chromatography/Mass Spectrometry analysis of crude mandibular secretions from *Varanus varius* (Lace Monitor). Reconstructed masses in Daltons are shown above each peak.

A) **W G G** **HD**

1* ^ GAFIMPGLTWGAGADSASDRSDLGAFQGGPDSCCQOHHDCSSVQITTAALQRKHGIFNLRPYTISHCQCDPTRFRRTCLMIDLNDFTIAD-SW
2 ^ GAFIMPGLTWGAGNNAASDYSQDLGTEKEDFDWCCRDDHDCSDTMAALEYKHGMRNRYRPHTVSHCQCDNQFRSCLMNVKDRITADFSQ
3 ^ GAFIMPGLTWGAGNNAASDYSQDLGTEKEDFDWCCRDDHDCSDTMAALEYKHGMRNRYRPHTVSHCQCDNQFRSCLMNVKDRITADFSQ

B) **H** **D**

1* ITGGQECNEDSHHPWLVLLYAASFMCCGATLLINQDWVLPAAHCCYDSRPTHL YFGIHNTRKQPRGHEDQARDAVSTFCYPPDSPGTNNSCPSFRL-----DRGDDI-MLIKLNASVTYNHEIAPMAL
2* ITGGECNEDSHHPWLVIYTEANTMCCGATLLINQDWVLPAAHCCYKRGKIMLNFGVHNREOARGDEEYREA VGTFCYPPDSPGTNNSCPSFYTL-----DHGDDI-MLIKLNASVTYNHEIAPMAL
3 ITGGQECDETHHPWLALLHRSEGSTWSGVLLNRDWILPAAHCEELGPMKICFGMKRNRYLRGDEQVKA AVKKCYPATAG-TIYNQNYVNTVIMNNDLLKRELFPMLIKLDSVDYNERVAPLSL
4 VIGGHECDINEHPFLAFMYSPQYFCGMTLINQEWVLPAAHCD-KTYMRIYLGIHTPSVANDDEVIRYPKEKFTGPNKKKNVITD-----KDI-MLIRLNRPVKNSPHIAPISL
5* ^ IIGGECNONHEHSIVLLYNSGGFFCSGTLINHEWVLPAAHQN-RENTQIKLGVHNHPNEDDEQIRVPKEKYCGLGTMNCPQWN-----QDI-MLIRLNSSVNYSPHIAPISL
6 IIGGHECNPSEHRSIVLYLYNSAGFFCSGTLINHEWVLPAAHQN-REDIQIRLGVHNHVHVYEDEQIRVPKEKLCGLSTNNCPQFS-----QDI-MLIRLNSSVNYSEHIAPISL
7 IIGGHECNKPHSQPWQAAALFEKTRLLCGATLIPRWLLPAAHCLKPRYIV-HLGGHNLQKEEGCEQTRTATETSEFPHPGFNNSL-----P-----NKDHRNDI-MLYKMASPVSITWAVRPLITL

1* PDRAAPLIGTECDIIGWGETELITIGS----VSHIPFCASINTMDNHFCDVSSVTITTD-DMIAGVLEGGPDAKGDSSGGPILLGGQLQGLVSRFGGYPGQPMMPGVYTKLIFS YREWLYSHIR-----
2* PDHAVPLIGTECDIIGWGETELIYVD---TASDVPILCASISTRENHFCEDAYSANMTPD-DMICAGDLKGGPDACR-DSSGPIILCGQLQGLVSRFGGIPCGQPKKPGVYTKLIFNYRKWIIRSS-----
3 PITSPASLGAECSYIAGWGTTPDDVT---LPDVPVCVNIEIFNNAVCQVAR-DLWKEFTNKLCAGVDFGGKDSCK-DSSGPIILCGNQLTGNVSWGFN-CEGEEKYYGIKLIKFN-WIDNIIOGGTG
4 PSNPPSVGSVCRIMGWGAITTSBDT---YPDVPHCANINLFNNTVCRKAYNGLPAR--TLCAGVYOGGIDTGC-DSSGPIILCGNQLFOGILSWGSDPCAEPKRPAPYTKVFDYLPWISIIAAGNKG
5 PSNPPSVGSVCRIMGWGTITTSBEVT---YPKVPHCVNIQILHKEICBAAYPIILGNSNII CAGKILGDKDSCK-DSSGPIILCGNQLFOGIVSWGSDPCAQFLSLASTPSSLIIITGSRILW-----G
6 PSNPPSMGSVCCVMGWGTITTSBEVT---YPEVPHCVDINILHIPVCAAYPTMSGK-NILCAGIIEGGKDSCK-DSSGPIILCGNQLFOGIVSWGSDPCAQFLPEGIYTKVFDYKDWIEGIIAAGNSG
7 SSRQVTAAGTSLISGWGSTSS---POLRLPHTLRGANLTIIEHOKENAYPGNITD-TMVGCA SVQEGGKDSCK-DSSGPIILCGNQLFOGIVSWGSDPCAQFLTRKPGVYTKVCKYVDWITQETMKNN-G

1* -----
2* -----
3 --TQP-
4 TATQPP
5* ^ -----
6 NVLQBP-
7 -----

Supplementary Figure 12: A) Alignment of Type III PLA₂: 1. *Varanus varius* (Lace Monitor) DQ139930 and *Heloderma suspectum* (Gila Monster)

2. P80003 and 3. P16354. B) Alignment of representative kallikrein (minus signal peptides): toxin forms 1. *Varanus mitchelli* (Mitchell's Water Monitor) DQ139915, 2. *Varanus acanthurus* (Spiny-tailed Monitor) DQ139914, 3. *Heloderma horridum* (Beaded Lizard) P43685, 4. *Bothrops jararaca* (Jararaca) P81661, 5. *Philodryas olfersii* (Argentine Racer) DQ139923, 6. *Lapemis curtus* (Spine-bellied Sea Snake) Q5MCS0 and tissue kallikrein 7. *Homo sapiens* (Human) Q9UBX7. * Designates transcripts obtained in this study. ^ Designates partial sequence.

1* MIVFILL-SLAAVLQÖFVA-D--VNFSESEPRRTEKÖTEIVDMHNSFRRSVNPTARNMLKMEWYPEAADNAEERWA^{KR}YÖCI-YDHSANSERVIGGIÖ^ECGENIYKSSNPRAWTEIIQSWYDEIQNFEY
2 MIAFILL-CFAAVLQÖSFG-N--VDFNSESEPRRKKÖKETEVDLHNSLRRRVSPPTASNMLKMEWYPEAASNAEERWANTCS-LNHSPPDNLRVLEGIÖ^FCGESIYMSSNARWTTEIIHLWDEYKNFVY
3* MEFVILL-SLAAVLQÖSFG-N--VDFNSESEPR IKAKÖREIVDKHNAFRRSV RPTASNMLRMEWYSEASNAEERVA RCI-LDHSPKTSR ILNGIK^ECGENIYMSSI PMWIDI IKLWDEYKNFVY
4* MIVFILL-SLAAVLEQÖSFG-N--VDFNSESEPRRPEKÖKETEVDRHNSFRRSVRPTASNMLKMEWYSEASNAEERVA RCN-LGHS PDSSR ILDGIK^ECGENIYMSSNPRAWTEIIQSWYDEYKNFVY
5 MIAFVILLSLAAVLQÖSSG-T--VDFASESSNKKYÖKETEVDKHNLRRSVKPTARNMLÖMKWNSRAAÖN^{KR}AKR WANRC-T-FASHPNKRITVGLR^ECGENIFMSSÖPFPMSSG VVQAWYDEYKFFVY
6* MIAFVILLSLAAVLQÖSSG-T--VDFASESSNKKDYRKEIVDKHNDLRRSV KPTARNMLÖMKWNSRAAÖN^{KR}AKR WANRC-T-FASHPYTRITVGLR^ECGENIFMSSÖPFPMSSG VVQAWYDEYKFFVY
7* MILLKLYLTLAATLQÖSRGWTSLDDLDMTNPETIQNETINKHNDLRRTVDP PAKNMLKMSWDNTIAESAK^{KR}RALRCN^EYKHEHTSIAERTIGV^ECGENHFMSNPRTWSSSIQSWFDERNSFMF
8 MILLSLYLCLAAMLHÖSEGEASPK-LPGLMTPNPDQÖTETITDKHNLRRIVEPTASNMLKMTWSNKIAÖNAÖRSANQCT-LEHTSKEERTIDGVE^ECGENLFPSSAPYTWMSYAIQNWFERKYYFRF

Supplementary Figure 13: Sequence comparison of CRISP toxins: 1) DQ139892 *Enhydryis polylepsis* (Macleay's water snake), 2) Q7TIK6 *Naja*

atra (Taiwanese cobra), 3) DQ139890 *Dispholidus typus* (Boomslang), 4) DQ139901 *Trimorphodon biscutatus* (Lyre snake), 5) Q8AV A4 *Pseudochis australis* (Mulga snake) , 6) DQ139896 *Oxyuramus microlepidotus* (Inland taipan), 7) DQ139904 *Varanus varius* (Lace monitor) and 8) Q91055

Heloderma horridum (Beaded lizard).