## Supplementary Materials: Hitchhiking with Nature: Snake Venom Peptides to Fight Cancer and Superbugs

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**Table S1.** SV-CATH precursors. SV-CATH protein precursors were collected, together with their sequences and domain information. Domains were highlighted in the protein sequence as: green, signal peptide; cathelicidin domain, blue; Glu-rich domain, yellow; mature peptide, red. Domain information (L, length; P, position) was extracted from NCBI (*https://www.ncbi.nlm.nih.gov/protein*). If no information was available (green background), domains were annotated based on bibliographic information and/or sequence similarities.

Source	Nama	NCPI	Destain program sources	Len	Len Signal		Prop	eptide	Catl	Cathelicidin		Glu-rich domain		ature
organism	Iname	NCDI	Protein precursor sequence	gth	pep 	Plide	т	р	T	Dmain P	T	nam P	pe 	pilde P
Ophiophagus hannah	Oh-CATH	<u>B6S2X2.1</u>	MEGFFWKTLLVVGALAIGGTSSLPHKPLTYEEAVDLAVSIYNSKS GEDSLYRLLEAVPPEWDPLSESNQELNFTIKETVCLVAEERSLEEC DFQEDGAIMGCTGYYFFGESPPVLVLTCKPVGEEEEQKQEEGNEE EKEVEKEEKEEDEKDQPRRVKRFKKFFKKLKNSVKKRAKKFFKKP RVIGVSIPF	191	22	1– 22	139	23– 161	66	28–93	26	125 - 150	30	162– 191
Bungarus fasciatus	Bf-CATH	<u>B6D434.1</u>	MEGFFWKTLLVVGALAIAGTSSLPHKPLIYEEAVDLAVSIYNSKSGED SLYRLLEAVSPPKWDPLSESNQELNFTMKETVCLVAEERSLEECDFQ EDGVVMGCTGYYFFGESPPVVVLTCKPVGEEGEQKQEEGNEEEKEV EEEEQEEDEKDQPRRVKRFKKFFRKLKKSVKKRAKEFFKKPRVIGVSI PF	191	22	1– 22	139	23– 161	66	28–93	26	125 - 150	30	162– 191
Naja atra	Na-CATH	<u>B6S2X0.1</u>	MEGFFWKTLLVVGALTISGTSSFPHKPLTYEEAVDLAVSVYNSKSGE DSLYRLLEAVPALKWDALSESNQELNFSVKETVCQMAEERSLEECDF QEAGAVMGCTGYYFFGESPPVLVLTCKSVGNEEEQKQEEGNEEEKE VEKEEKEEDQKDQPKRVKRFKKFFKKLKNSVKKRAKKFFKKPKVIG VTFPF	191	22	1– 22	139	23– 161	66	28–93	24	125 - 148	30	162– 191
Hydrophis cyanocinctus	Hc-CATH	<u>AKJ54480.1</u>	MQGFFWKTLLVVAALTIGGTSSLPHKPLTYEEAVDLAVSIYNSKSREE FLYRVLDAVPPPKWDPLSESNQELNFTIKETVCPVAEERSLEECGFQE DGAVMGCTGYFFFGESPPVLVLTCEPLVEEEQQKQEEGNEEEKEEKE EDEKDQPRRVKRFRKFFKRLLKSVRRAVKKFRKKPRLIGLSTLL	187	22	1– 22	135	23– 157	65	28–92	22	126 _ 147	30	158– 187

Crotalus durissus terrificus	Cdt-CATH	<u>U5KJM4.1</u>	MQGFFWKTWLVLAVCGTPASLAHRPLSYGEALELAVSVYNGKAGE ASLYRLLEAVPQPEWDPSSEGSQQLNFTLKETACQVEEERSLEECGF QEDGVVLECTGYYFFGETPPVVVLSCVPVGGVEEEEEEEEEQKAEA ENDEEVEKEKGDEEKDQPKRVKRFKKFFKKVKKSVKKRLKKIFKKP MVIGVTIPF	194	22	1– 22	142	23– 164	65	26-90	29	125 - 153	34	161– 194
Bothrops atrox	Ba-CATH	<u>U5KJC9.1</u>	MQGFFWKTWLVVALCGTSSSLAHRPLSYGEALELALSIYNSKAGEES LFRLLEAVPQPEWDPLSEGSQQLNFTIKETVCQVEEERPLEECGFQED GVVLECTGYYFFGETPPVVVLTCVPVGGVEEEEEDEEEQKAEVEKDE EKEDEEKDRPKRVKRFKKFFKKLKNSVKKRVKKFFRKPRVIGVTFPF	189	22	1– 22	133	23– 155	65	26–90	24	125 - 148	34	156– 189
Pt-CATH Pseudonaja textilis Pt-CATH	Pt-CATH1	<u>U5KJJ1.1</u>	MEGFFWKTWLVVAAFAIGGTSSLPHKPLTYEEAVDLAVSTYNGKSG EESLYRLLEAVPPPKWDPLSESNQELNLTIKETVCLVAEERSLEECDF QDDGAVMGCTGYFFFGESPPVLVLTCEPLGEDEEQNQEEEEEEEKEE DEKDQPRRVKRFKKFFMKLKKSVKKRVMKFFKKPMVIGVTFPF	184	22	1– 22	128	23– 150	66	28–93	12	132 - 143	34	151– 184
	Pt-CATH2	<u>U5KJM6.1</u>	MDGFFWKTWLVVAALAIGGTSSLPHKPLTYEEAVDLAVSTYNGKSG EESLYRLLEAVPPPKWDPLSESNQELNLTIKETVCLVAEERSLEECDF QDDGAVMGCTGYFFFGESPPVLVLTCEPLGEDEEQNQEEEEEEEKEE DEKDQPRRVKRFKKFFRKLKKSVKKRVKKFFKKPRVIGVTIPF	184	22	1– 22	128	23– 150	66	28–93	12	132 - 143	34	151– 184
Lachesis muta rhombeata	Lmr- CATH	<u>U5KJZ2.1</u>	MQGFFWKTWLVLAVCGTPASLAHRPLSYGEALELAVSVYNGKAGE ASLYRLLEAVPQPEWDPSSEGSQQLNFTLKETACQVEEERSLEECGF QEDGVVLECTGYYFFGETPPVVVLSCVPVGGVEEEEEEEEEQKAEA ENDEEVEKEKEDEEKDQPKRVKRFKKFFKKVKKSVKKRLKKIFKKP MVIGVTFPF	194	22	1– 22	138	23– 160	65	26–90	29	125 - 153	34	161– 194
Bothrops lutzi	Bl-CATH	<u>U5KJT7.1</u>	MQGFFWKTLLVVALCGTSSSLAHRPLSYGEALELALSVYNSKAGEES LFRLLEAVPQPEWDPLSEGSQQLNFTIKETVCQVEEERPLEECGFQED GVVLECTGYYFFGETPPVVVLTCVPVGGVEEEEEDEEEQKAEVEKDE EKEDEEKDRPKRVKRFKKFFKKLKNNVKKRVKKFFRKPRVIGVTIPF	189	22	1– 22	133	23– 155	65	26–90	24	125 - 148	34	156– 189
	Pb1-CATH	<u>AVI24168.1</u>	MMEGCFWRILLVAGALSASGAAALPHRPLTYEEAVAFGVELYNKK AGEDSRYRLLEAVPQPDWDPTSESIQELNFTIKETVCLVQEERAEDEC DFKDDGLVKECSGYYFFDETPPVAVLTCETVGGNEEETEEEKEEEKQ PKRVKRFKKFFRKIKKGFRKIFKKTKIFIGGTIPI	175	23	1– 23	121	24– 144	80	27–106	11	129 - 139	31	145– 175
Python bivittatus I	Pb2-CATH	<u>AVR43560.</u> <u>1</u>	MEIHPGRILLVLSLVVRGSVWAVEGEILSYDAALSLAVNLYNQESGW DVVFQLLEAKPQPEWDPSSKARQKLDFTLKETTCPTSQNLNLEVCDF KEQGVVVECSGSSLAQPGAPIIQFSCETATQGNHRVKRNGFRKFMR RLKKFFAGGGSSIAHIKLH	159	22	1– 22	108	23– 130	93	28–120	-	-	29	131– 159
	Pb3-CATH	<u>AVI24169.1</u>	MMEGCFWRILLVAGALSASGAAPPPHKPLIYEKAVALGMELYNEK AGEDSQYRLLEAVPQPDWDPTSESTQELNFTIKETVCLVQEERAKDE	175	21	1– 21	123	22– 144	78	29–106	11	129 - 139	31	145– 175

			CDFKDDGLVKECSGYYFFDETPPVAVLTCETVGGNEEETEEEKEEEK											
			QPKRVKRFQNFFRELEKKFREFFRVYRITIGATIRF											
			MTGVWALLLLLGVAAAAPPAQVVTYDQAIASAVNLYNQQKTTPFA											
	Ph4 CATH	AVI24170 1	FRLLEAEPQPNWDPRGKTTQGLKFTIKETVCPSAQSQNLTQCNFKE	154	16	1–	100	17–	98	21 118			20	126–
	104-CAIII	<u>AV124170.1</u>	DGVDQDCSGTYSTQQEPPNLTVQCENIDQELNRITRSRWRRFIRGAG	154	10	16	109	125	90	21-110	-	-	29	154
			RFARRYGWRIALGLVG											
			MGLILLGAAWVALGILGSAASPTAEAPWLVLPRDAARLAVEDYNH					21–						
		AVR43562.	RSPTPPSVFRLFKLRSTHKTRLEWGIHFSLHFTIKETHCQKTAGYRIGD	1 171	20	1–	110		07	22 110			22	139–
	PD5-CATH	<u>1</u>	CRYKPNGLIQDCSAEVSFLNLMWDSPVTSMKCGQAKWKKTKPHAS	1/1	20	20	118	138	87	33-119	-	-	33	171
			PPQAMGFPPQVNVEHYIPASYSVAALTVTEEE											
			MHSFWVLLLFISPATTNFLSLSLTYPEALEEAVRLYNEEEGVKFLYRL											
Pb6-CATH		VRAEPRPDWDPEAEGVQSLKFSMKETVCSAIEGLDFSKCDFKDDGE												
		AVR43561.	VKVCSASYKYQKKPQMNHVDVLCYCRQFCLFLFRQKAHTRLPVFR	240	1.	1–	105	17–	= (	<b>22</b> 00			<b>0-</b>	212-
	Pb6-CATH	1	KSPHRFEAQAGQRSEGETGIPRPAMFRRPREGSKRAGGGRAGGPAR	248	16	16	195	211	76	23–98	-	-	37	248
			PALRCHLEARRGRADVSGEARGLRRARAAPORRLRAMARLKKFAE											
			AGGADPDSGGLRARFPER											
			MEGCFWKILLVVGALTIGGTSTLAHKPLTYDEAVDLAVSIYNSKSGE											
		0000	DSLYRLLEAVPPSEWDPLSESNQDLNFTIKETVCQVAEERSLEECDFQ			4						10(		150
Sinonatrix	Sa-CATH	<u>QBZ68899.</u>	EDGVVMECTGYYFFGETPPVLVLTCEAVGEEEEAEQQQEEGNGEEA	191	24	1-	133	20- 157	78	28-105	17	126-	34	158-
annularıs		<u>1</u>	EKEEKDEDKKDQPRRVKRFKKFFKKLKKSVKKHVKKFFKKPKVIGVS			24		157				142		191
			IPF											
	Cdc-	AGS36136.	MEGSSGRPGWCWPSAGKEKEDEEKDQPKRVKRFKKFFKKVKKSVK	0.4									= 4	01 04
	CATH1	<u>1</u>	KRLKKIFKKPIFKKVKKSVKKRLKKIFKKPMVIGVTIPF	84	-	-	-	-	-	-	-	-	54	31–84
	Cda	A C 826127	MQGFFWKTLLVLAVCGTPASLAHRPLSYGEALELAVSVYNGKAGE			1		22						102
	CATU2	<u>AG550157.</u> 1	ASLYRLLEAVPQPEWDPSSEGSQQLNFTLKETACQVEEERSLEECGF	136	22	22	80	102	65	26-90	-	-	34	105-
Crotalus durissus	CAIHZ	<u>1</u>	QEDGDQPKRVKRFKKFFKKVKKSVKKRLKKIFKKPMVIGVSIPF			22		102						130
cascavella			MQGFFWKTWLVLAVCGTPASLAHRPLSYGEALELAVSVYNGKAGE											
	Cla	A C C 2 ( 1 2 0	ASLYRLLEAVPQPEWDPSSEGSQQLNFTLKETACQVEEERSLEECGF			1		22				125		171
		<u>AG550159.</u>	QEDGVVLECTGYYFFGETPPVVVLSCVPVGGVEEEEEEEEEQKAEA	194	22	1-	138	25-	65	26-90	29	-	34	101-
(	CATH3	<u>1</u>	ENDEEVEKEKGDEEKDQPKRVKRFKKFFKKVKKSVKKRLKKIFKKP			22		160				153		194
			MVIGVTIPF											
			MEGCFWKALLVVGALAIGGTSTLAHKPLTYDEAVNLAVSTYNNKS									125		
Thamnophis		<u>XP_013912</u>	GEGTLYRLLEAVPPPEWDPLSEGNQELNFTIKETVCKVGEELSLEECS	190	24	1– 24 131	121	25-	65	<u> </u>	24	125	24	156-
sirtalis	15-CAIII	<u>467.1</u>	FQEDGAVMECTAYFFFGEKPPLLVLTCEAVSEEEQQEEEEEGNEEEK	189	24		24	131	155	65	20-92	24	-	34
			EAGKEEDEKDQPRRVKRFKKFFKKIKKSVKKRVKKLFKKPRVIPISIPF									140		

	Ts-CATH2	<u>XP_013917</u> <u>356.1</u>	MDGFFWKIWLAVGALTIGGTSSLPRKPLTYDKAVELGVAIYNSKAG EDSLYRLLEAVPQPEWDPYSESYQELNFTIKQTVCPVEEEFSTDECDF KENGLVRQCTGYYFLEERPPVAVLTCDTVGGTAEEEEKEKKEEEVVE KEEEEEEEKERRDFC	156	22	1– 22	-	-	66	28–93	24	128 - 151	-	-
	Ts-CATH3	<u>XP_013928</u> <u>483.1</u>	MEGFLWKTLLLVGALSASGRSAPSPKLLTYDEAVVQAVVNYNGKA KEGSLYQLLEAAPQPDWDPNFEGTQELKFTIKETVCRAEEEGSLDKC DFKEDGVVRDCTATYFLGEKTPVAFLDCKAVGETEEEEEEVEEKEEG TEEEESVERSRKRIKKRRRIRVQITVKITFKI	171	21	1– 21	131	22– 153	66	28–93	22	126 _ 147	18	154– 171
	Ts-CATH4	<u>XP_013912</u> <u>465.1</u>	MEGSFWKTWLVVGALLVFGCSSLPHKPLTYEKAVDLAVAIYNSKAG EDCVYRLLEALAEPQWDPISDSHEELNFTIKETMCLLEDVVFFDECD FKEDGVIRQCTGYYYFDERPPVVVLTCVVVAGMEEEKGEEVGKKEE EKQEEEEEKEEENQARNKEEEEKKEEEEEKEEGKETEKQEEKEEEEKL KKGLKKLFKRKKVVAGYVTA	207	22	1– 22	165	23– 187	54	28–81	59	127 - 185	20	188– 207
Protobothrops mucrosquamatus	Pm-CATH	<u>XP 015682</u> <u>911.1</u>	MEGFFWKTLMLVGVLSVSGRPHLPHEPLTYDDALCLGVEIFNKKAG EGSLYRLLDGVPQPEWDPVSEGNQALNFTVKETVCPAEEDFSTDRC DFKEDGMVRQCTGYYFLEERPPVAVLTCHTVGGTVKEEEKEEEEEK KKKKDQPKRVKRFAGFFQFVVGVSFRF	165	19	1– 19	129	20– 148	66	28–93	9	129 _ 137	17	149– 165

**Table S2.** SV-defensins. Summary of SV-defensins identified to date, their sequences and accession numbers. A unified name was given to each SV-defensin according to the initial of the snake.

Snake	Unified name	Other name	NCBI	Peptide sequence	Length	Ref
Phalotris	Pm1- defensin	-	<u>JAS0313</u> <u>6.2</u>	MKILYLLFALLFLAFLSEPGNAQPRCHSQGGRCYFLLCPWNTIDHGQLDCPGTRICCEPKCPG K	64	[1]
mertens	Pm2- defensin	-	<u>JAS0313</u> <u>5.2</u>	MKILYLLFALLFLAFLSEPGNAQRICLGGRGFCHSTPCPRSTIDYGKKDCWGSLRCCEPKRPGK	64	[1]
	Coh1- defensin	Beta_Defensi n-CohLL-1	<u>JAA9804</u> <u>1.1</u>	MKILYLLFAFLFLAFLSEPGNAYKRCHKKGGHCFPKTVICLPPSSDFGKMDCRWKWKCCKKGSV NNAISI	70	NCBI
Crotalus oreganus helleri	Coh2- defensin	Beta_Defensi n-CohPH-6	<u>JAA9801</u> <u>3.1</u>	MKILYLLFAFLFLAFLSEPGNAYKRCHKKGGHCFPKEKICIPPSSDFGKMDCRWKWKCCKREVE NNAISI	70	NCBI
	Coh3- defensin	Beta_Defensi n-CohID-3	<u>JAA9798</u> <u>3.1</u>	MKILYLLFAFLFLAFLSEPGNAYKRCLKKGGHCFPKTVICLPPSSDFGKMDCRWKWKCCKKGSV NNAISI	70	NCBI
Crotalus durissus terrificus	Cdt-defensin	Crotasin	<u>AAT474</u> <u>37.1</u>	MKILYLLSAFLFLAFLSESGNAQPQCRWLDGFCHSSPCPSGTTSIGQQDCLWYESCCIPRYEK	63	[2]
	Lm1- defensin	beta- defensin-like protein	<u>AGF253</u> <u>95.1</u>	MKILYLLFPFLFLAFLSEPGNAQGQCHQQRGRCFLHQCPLSHYFLGRLDCGPGRRCCRRRK	61	[3]
Lachesis muta	Lm2- defensin	beta- defensin-like protein	<u>AGF253</u> <u>94.1</u>	MKILYLLFPFLFLAFLSEPGNAQEWCRGLGGFCSFYQCRPGHDLGPQDCWPERRCCRWGK	60	[3]
Bothrops pauloensis	Bp-defensin	beta- defensin-like protein	<u>AGF253</u> <u>93.1</u>	MKILYLLFTFPFLAFLSEPGNAQPECLRQGGMCRPRPCPYVSLGHLDCQMGQMCCIRKPRK	61	[3]
Bothrops neuwiedi	Bn-defensin	beta- defensin-like protein	<u>AGF253</u> <u>92.1</u>	MKILYLLFTFLFLAFLSEPGNAQPECCQEGGICHSKQCPLGYSSLGRLDCQLGQRCCIRIFGK	63	[3]
Bothrops	Bm1- defensin	beta- defensin-like protein	<u>AGF253</u> <u>91.1</u>	MKILYLLFTFLFLAFLSEPGNAQRRCRQRRGICRPRPCPPENFSLGRLDCQMGQMCCRRRFGK	63	[3]
matogrossensis	Bm2- defensin	beta- defensin-like protein	<u>AGF253</u> <u>90.1</u>	MKILYLLFTFLFLAFLSEPGNAQRRCRQRRGICRPRPCPPENFSLGRLDCQMGRMCCRRRFGK	63	[3]

Bothrops leucurus	Bl-defensin	beta- defensin-like protein	<u>AGF253</u> <u>89.1</u>	MKILYLLFTFLFLAFLSEPGNAQRRCRQKGGMCLPGPCPPGYVSLGQQDCRRGQMCCIRFGK	62	[3]
Bothrops jararacussu	Bja-defensin	beta- defensin-like protein	<u>AGF253</u> <u>88.1</u>	MKILYLLFTFLFLAFLSEPGNAQRRCHQKGGMCLPGPCPPGYDSLGQQDCRRGQKCCIKRFGK	63	[3]
	Bj1-defensin	beta- defensin-like protein Defb_Bj-03	<u>AVN978</u> <u>91.1</u>	MKILYLLFTFLFLAFLSEPGNAQPECCQQGGICHSKQCPLGYSSLGRLDCQLGQRCCIRIFGK	63	[4]
Bothrops jararaca	Bj2-defensin	beta- defensin-like protein	<u>AGF253</u> <u>87.1</u>	MKILYLLFTFLFLAFLSEPGNAQVRCRRLGGICILSRCPLRYDSLGQQDCLKGQKCCRRRFGK	63	[3]
	Bj3-defensin	beta- defensin-like protein	<u>AGF253</u> <u>86.1</u>	MKILYLLFTFLFLAFLSEPGNAQEECLQQGGFCRLIRCPFGYDSPEQQDCRKGQRCCIRKPRK	63	[3]
Bothrops erythromelas	Be-defensin	beta- defensin-like protein	<u>AGF253</u> <u>85.1</u>	MKILYLLFTFLFLAFLSEPGNAQEGCLQQGGFCRLIRCPFGYDSLEQQDCRKGQRCCIRKPRK	63	[3]
Bothrops diporus	Bd-defensin	beta- defensin-like protein	<u>AGF253</u> <u>84.1</u>	MKILYLLFTFLFLAFLSEPGNAQPECLRQGGMCRPRLCPYVSLGQLDCQNGHVCCRKKPRK	61	[3]
Bothrops atrox	Ba-defensin	beta- defensin-like protein	<u>AGF253</u> <u>83.1</u>	MKILYLLFTFLFLAFLSEPGNAQRECYWQRGFCRSKGCPFGYDSLGRLDCPLGYVCCRI	59	[3]
Thamnophis siralis	Ts-defensin	-	<u>XR 0013</u> <u>13470.1</u>	MKIFYLLFAFLFLAFLSEPGSAQSLCHRKRGRCLEICPKGTKDIHRWDCRHGLTCCVPARGK	62	NCBI
Protobothrops mucrosqumatus	Pmu- defensin	crotasin-like	<u>XM_015</u> 824769.1	MKILYLLFTFLFLAFLSEPGNAQPPECRNIGGQCYQSRCPDGKNNNGWKDCEWGQLCCNRKW KIMPSPSTTMDTIKIWPMT	81	NCBI
Crotalus adamanteus	Ca-defensin	myotoxin	<u>HQ4141</u> <u>00.1</u>	MKILYLLFAFLFLAFLSEPGNAYKRCHKKGGHCFPKTVICLPPSSDFGKMDCRWRWKCCKKGV	63	[5]
Ovophis okinavensis	Oo-defensin	crotasin- like_protein	<u>AB85200</u> <u>5.1</u>	MKILYLLFAFLFLAFLSEPGNAQGQCYRPGGLCLSDPCPSGHLDLGQVDCQPGQKCCRRGSGK	63	[6]

Pb-CATH5	100																								
Cdc-CATH1	12.9	100		_																					
Ts-CATH3	20.27	31.03	100																						
Pb-CATH1	21.38	66.67	52.83	100		_																			
Pb-CATH3	21.38	47.62	53.46	84.57	100																				
Ts-CATH4	20	27.42	44.91	52.63	51.46	100																			
Pm-CATH	19.87	56.67	55.62	58.12	57.5	47.24	100																		
Ts-CATH2	20.42	35.29	57.24	64.34	64.34	61.29	67.57	100																	
Ba-CATH	19.38	75	48.8	59.65	56.73	48.66	58.28	63.4	100																
Bl-CATH	19.38	75	50	60.82	57.89	47.59	57.67	62.09	97.88	100															
Cdc-CATH2	23.33	97.5	50.85	61.36	53.03	45.52	61.34	58.82	83.09	84.56	100														
Cdc-CATH3	20	83.93	49.1	62.57	56.14	49.48	58.9	57.79	85.19	85.19	98.53	100													
Cdt-CATH	20	83.93	49.1	62.57	56.14	49.48	58.9	57.79	85.19	85.19	98.53	100	100												
Lmr-CATH	20	83.93	49.1	62.57	56.14	50	59.51	58.44	86.24	85.19	97.79	98.97	98.97	100											
Ts-CATH1	21.6	69.23	52.41	60.12	54.34	49.2	53.94	58.28	66.12	66.67	72.06	65.78	65.78	65.78	100										
Hc-CATH	20.37	54	46.39	55.49	53.18	47.03	52.12	61.59	64.48	63.93	65.44	60	60	60.54	71.51	100		i							
Sa-CATH	21.6	69.23	52.38	63.58	59.54	50.26	58.18	63.4	71.35	71.35	73.53	67.72	67.72	67.2	78.84	74.33	100								
Pt-CATH1	20.99	77.55	50.61	62.43	58.38	50.55	53.94	61.74	71.98	70.33	72.06	70.33	70.33	71.43	76.63	79.89	79.35	100							
Pt-CATH2	20.99	79.59	51.22	63.58	59.54	51.1	53.33	63.09	72.53	71.98	72.79	70.88	70.88	70.88	78.26	81.52	80.43	96.74	100						
Na-CATH	22.22	73.08	51.19	60.69	57.23	51.85	55.76	62.09	67.57	67.57	69.85	64.55	64.55	65.61	69.31	76.47	78.01	80.43	80.43	100	100				
BI-CAIH	23.46	69.23	52.38	63.01	61.27	54.5	56.36	64.71	68.65	68.65	72.06	66.67	66.67	66.67	73.54	79.14	79.06	8.,7	85.87	84.82	100				
Un-CATH	23.46	73.08	23.27	64.16	60.12	56.08	37.38	67.32	/1.89	71.89	75	6/./2	6/./2	6/./2	77.78	83.42	83.25	86.41	88.04	89.01	92.67	100	100	1	
Pb-CATH6	19.87	14.29	34.84	30.95	30.95	22.62	33.12	30.66	29.76	29.76	34.62	29.76	29.76	29.76	29.41	27.65	28.82	29.41	28.82	28.82	28.82	28.82	25.52	100	
Pb-CATH4	22.3	6.9	39.29	35.33	34.67	30.26	29.66	34.33	30.26	30.26	31.62	29.61	29.61	29.61	29.87	31.82	32.47	31.17	32.47	27.92	30.52	31.82	35.53	100	100
Pb-CATH2	21.57	24.14	30.99	35.55	31.37	27.27	32.65	33.82	35.71	35.06	42.02	37.66	37.66	37.66	33.33	29.49	34.62	30.77	30.77	30.13	31.41	32.05	28.76	39.61	100
	b-CATH5	dc-CATH	s-CATH3	b-CATH1	b-CATH3	s-CATH4	m-CATH	s-CATH2	3a-CATH	81-CATH	dc-CATH	dc-CATH.	dt-cath	00-CATH	s-CATH1	Jc-CATH	sa-CATH	t-CATH1	t-CATH2	Va-CATH	8f-CATH	oh-CATH	b-CATH6	b-CATH4	b-CATH2
	4	Ŭ	F	Ъ	Р	H	- <b>L</b>	F	اطر 		Ŭ	Ŭ	UŞ	3	H	L +•	<b>U</b>	<b>-</b>	<u> </u>	4	-	0	4	Ъ	4

% Identity: <50 50-70 70-90 >90

**Figure S1.** Percentage identity matrix of SV-CATH precursors. Estimation of the homology/divergence between SV-CATH precursor proteins (sequences and NCBI accession numbers available in Table S1) illustrated by percentage identity matrix.

## **References:**

- Campos, P.F.; Andrade-Silva, D.; Zelanis, A.; Paes Leme, A.F.; Rocha, M.M.; Menezes, M.C.; Serrano, S.M.; Junqueira-de-Azevedo Ide, L. Trends in the Evolution of Snake Toxins Underscored by an Integrative Omics Approach to Profile the Venom of the Colubrid Phalotris mertensi. *Genome Biol. Evol.* 2016, *8*, 2266–2287.
- 2. Radis-Baptista, G.; Kubo, T.; Oguiura, N.; Prieto da Silva, A.R.; Hayashi, M.A.; Oliveira, E.B.; Yamane, T. Identification of crotasin, a crotamine-related gene of Crotalus durissus terrificus. *Toxicon* **2004**, *43*, 751–759.
- 3. Correa, P. G.; Oguiura, N., Phylogenetic analysis of beta-defensin-like genes of Bothrops, Crotalus and Lachesis snakes. *Toxicon* 2013, 69, 65-74.
- 4. de Oliveira, Y. S.; Correa, P. G.; Oguiura, N., Beta-defensin genes of the Colubridae snakes Phalotris mertensi, Thamnodynastes hypoconia, and T. strigatus. *Toxicon* **2018**, *146*, 124-128.
- 5. Rokyta, D.R.; Wray, K.P.; Lemmon, A.R.; Lemmon, E.M.; Caudle, S.B. A high-throughput venom-gland transcriptome for the Eastern Diamondback Rattlesnake (Crotalus adamanteus) and evidence for pervasive positive selection across toxin classes. *Toxicon* **2011**, *57*, 657–671.
- 6. Aird, S.D.; Watanabe, Y.; Villar-Briones, A.; Roy, M.C.; Terada, K.; Mikheyev, A.S. Quantitative high-throughput profiling of snake venom gland transcriptomes and proteomes (Ovophis okinavensis and Protobothrops flavoviridis). *BMC Genom.* **2013**, *14*, 790.