

## Supplementary Material 1

**Supplementary Figure S1: Protein sequence alignment of serpins from *C. intestinalis* and *C. savignyi*.** Signal peptide and reactive center loop (RCL) regions are marked on top. P1-P2 positions of RCL and C-terminal ER-retention signals are marked in red and blue colors, respectively. Amino acid conservations are marked by black, brown and yellow colors, corresponding for 70% or more, 50-69%, and 30-49% identities, respectively.

	-----Signal Peptide-----	
Hs-A1AT	-----	-
Ci-Spn-4	-----MFLKQVLVLCVFFFTSSAFYMPMVR-----	26
Ci-Spn-3	-----MKLLICSLLLVVIATGYCQNR-----	22
Cs-Spn-5	MPILDRLGPSRYAKELQLVNTRAIISLDHLVPTIGLPEVTVLAKMKFVCLLPVPAICFYVQSSG-----	64
Ci-Spn-5	-----MRFIFLCFVLLVSAGFNEAKRTR-----	23
Ci-Spn-1	-----MYTASAYGVFLCLAIYQVGATKHLQAEFDYGEYEDDA-----	38
Cs-Spn-4	-----MGSHMLIRGVILCLVFYEVTCTKHIAEFDYGDYV-DT-----	37
Ci-Spn-2	-----MLLVIAACMLSAFNGAVGEPYAPTNA-----	26
Cs-Spn-3	-----MATIGLTLISALLVLSGQHSIEAYTS-----	26
Cs-Spn-2	-----MESYICLVLVSVLIVGGKANTLQTE-----	26
Ci-Spn-9	-----MQFLYAIVMILVLDANAKIIDTSE-----	24
Ci-Spn-10A	-----MQFLYAIVMLLVLDANAKIIDTSE-----	24
Ci-Spn-10B	-----MQFLYAIVMLLVLDANAKIIDTSE-----	24
Cs-Spn-1	-----LFALYSSLIVGITCSMEHI-----	19
Ci-Spn-7	-----MAFC-----	4
Ci-Spn-6	-----MAFC-----	4
Ci-Spn-8	-----MAFC-----	4
Hs-A1AT	-EDPOGDAAQKTDTSHHQDHP-----TFNKITPNLAEFAFSLVROLAHQ-SNST-----NIFFSVSTIA	58
Ci-Spn-4	-----THPPQMDMPAYCAEVVNAITRVVSGFILNAATHANSATDEYVAERNVFFSPFGAA	80
Ci-Spn-3	-----WINHFTDNQNTFSGSLYWAISKE-KPNK-----NVLFSPISVS	59
Cs-Spn-5	-----QFWMKFTNRQNFSGRMVQSVIROQRGK-----NVVFSPIRKS	104
Ci-Spn-5	-----VISKWRLTAIANKLFAHRLFMEVARTTPEQE-----NFFISPYAVS	64
Ci-Spn-1	NSWDPRQASITKIGKMDGLTIDQ-VELPPFEKPAARLVNNEAFKLLNEIASD-NE-D-----NVVFSPLSIF	102
Cs-Spn-4	YAWDPWQASIAKVGKMDGAAPERPTMPPLEKPAAKILNNEAFKLFNAIATE-NSTE-----NEVFSPLSIF	103
Ci-Spn-2	-----FREPVAHALYDFGMDMYNQLPSWRPTE-----NIVISPMSMY	64
Cs-Spn-3	-----SAAFRDTTAIALHNGVDLFCFLAPNWRNE-----NVAISPMSMY	67
Cs-Spn-2	-----HVAKLSEANIEFSLNLYKQLIVE-SNMK-----NVMFSPVSIS	63
Ci-Spn-9	-----HVEKLSEANIEFSLNLYKQLIEG-DPMK-----NVMFSPVSIT	61
Ci-Spn-10A	-----HVEKLSEANIEFSLNLYKQLIEG-DPMK-----NVMFSPVSIS	61
Ci-Spn-10B	-----HVEKLSEANIEFSLNLYKQLIEG-DPMK-----NVMFSPVSIS	61
Cs-Spn-1	-----KLSSGLTEFAVALYKEISKD-PG-----NVFLSPFSIS	51
Ci-Spn-7	-----KVAAAKTDFALGLYKELSQKGDG-----NLFFSPYSIS	37
Ci-Spn-6	-----KVAAAKTDFALGLYKELSQKEDG-----NLFFSPYSIS	37
Ci-Spn-8	-----KVAAAKTDFALGLYKELSQKEDG-----NLFFSPYSIS	37
Hs-A1AT	TAFAMLSLCTKADTHDEILEGTFNFLTETI-----PEAQIHEGFQELLRTLNQ-----PDS-QLOLTGNG	117
Ci-Spn-4	NVVGILRLASAGRTRERFDGLPLF--SSILQ----HNDRFMRGFQTLRSLILSVTSFPGTNPQSDKLLNSG	147
Ci-Spn-3	QTLGMVLAAGMGNLYDEITRALQM--TDL-----TPSRIHTLMRKRTRNVVM-----RPN-GQTVKLANS	116
Cs-Spn-5	-----F--TNV-----ALRHT-----GQTI RLANA	122
Ci-Spn-5	AGLSMTLYCAHSTTAREIMDTLGY--TQLSTSGNFNOAKVPRLYQKMLHQVHQ-----KDH-GFELTSVNR	127
Ci-Spn-1	TSLATLRPALNGTSLQLNDVTGL--DTI-----RESDMN-----DMYDGIFK-----KSS-SYKIKQASR	155
Cs-Spn-4	TTLATLRPGLNGNSLLQLDDVTGL--DTI-----EERDMN-----DMYDVVFE-----RST-SHKIKQANR	156
Ci-Spn-2	AILSILLPGLNGASHDOVYNALRM--TNL-----PRNGVDAE-SAMCSKIFQ-----INP-SHYDLTRANR	120
Cs-Spn-3	AVLSILLPGLQGSSYDOVYHALGM--SHL-----DGDGIDRE-SDMCGLVFQ-----ENA-NYELHRANR	123
Cs-Spn-2	AALAMTNLGAKGKTAEQISDAFFF--NKI-----EDGRFHSAFGEHLGLMFD-----KASGNVTVKSSNR	121
Ci-Spn-9	TALAIHLGAKGNTAKOIDDAFMF--SKI-----EDGRFHSAFGEHLGLLFD-----KASEKVTAKSSNR	119
Ci-Spn-10A	AALAMTNLGAKGKTAEQIDDAFMF--SKI-----EDGRFHSAFGEHLGLLFD-----KASDNVTVKSSNR	119
Ci-Spn-10B	AALAMTNLGAKGKTAEQIDDAFMF--SKI-----EDGRFHSAFGEHLGLLFD-----KASDNVTVKSSNR	119
Cs-Spn-1	TALSMTLLGTQGETREQLFKTLNL--DGV-----SENEINSGFSSLOACL-----KSS-KVILETANQ	106
Ci-Spn-7	TALMMTLGSKKTRREEMLDVGL--KDL-----NESDINSGFLQILHHLRS-----SKG-DVVLEMANK	94
Ci-Spn-6	TALMMTLGSKKTRREEMLDVGL--KDL-----NESDINSGFLQILHHLRS-----SRG-DVVLEMANK	94
Ci-Spn-8	TALMMTLGSKKTRREEMLDVGL--KDL-----NESDINSGFLQILHHLRS-----SRG-DVVLEMANK	94

Hs-A1AT	LFLSEGLKLVDFKLEVDKLVHSEAFVNFQ-DTEEAKKQINDYVEKGTQGKIVDLVKE--LDRDITVFALVNY	187
Ci-Spn-4	VFTSRWLYLQTRFISDARNFYKAVVASVDFQ-DPELASSHINMWINARLQKIKTKIVSPSDLSPITLVTVFNT	219
Ci-Spn-3	VFIGSNYPVVOQYIDLLRQNYKSSVFPVNFH-NSNAAANMINEWVSNMTEDEKIRELVDPSSITAFTRMILVNA	188
Cs-Spn-5	IFVVRDEYVPKQPYIDTLRTYKSAVKTFDVR-NSTAASNLVNRWVASNTEENRITDLVDPSAFTELTRLVLVNA	194
Ci-Spn-5	MFGESRNIFVPSYVKGVEHFGAKLKKVDFRRNPERARQENITWVEEVNQTIREALPPNSVTAETLLVLMST	200
Ci-Spn-1	IYVDRGIRLSRSYRTDLYRMKISRARRLDFRRAPESRNQINKYVKKRTRKLIKELVPVGAISSATMMYLVNA	228
Cs-Spn-4	IYVDRSVKLAKKFKKELKNLKLGOARRLDFRRAEQSRKINKYVKKRTRKLIKELVPEGAVSPSTVMYLVNA	229
Ci-Spn-2	IFGDRTLTFKKSFKNETSWHHKAAHKKVDFQHYPNRARRKMNRYVSKMLDCEIQOOLIPREAVTDTTRIFLVNA	193
Cs-Spn-3	IYSDLRVQIKKSYKQAAMTHHKSPVKKVDFVLAQRKSRKKMNRYVAKHTNDEITELIPOEAITQDTKIFLVNA	196
Cs-Spn-2	VFANKQRKILEDYKNAL-TVYGAKVESMDFT-SASDAVSHINKWASDATEGKISSMLADDAINGNTALIVANA	192
Ci-Spn-9	VFADKHIIVFEDYQDSL-SVVSATVESVDFK-MPKSAVKKINDWSSDATNGVLSKSMLEEDGVNNDTALLIINA	190
Ci-Spn-10A	VFADKKRKLVEDYKNAL-TVYGAKLENVDFK-TPSNAVQINDWASDATNGKISSNMLQDDAVDSNTALIVANA	190
Ci-Spn-10B	VFADKKRKLVEDYKNAL-TVYGAKLENVDFK-TPSNAVQINDWASDATNGKISSNMLQDDAVDSNTALIVANA	190
Cs-Spn-1	LFPEISFPLEEEFVSKCKQYHGADIKGLDFVGNPENSRNAINQWVENVTKGKITDLL-SGSINSLVRLVIANA	178
Ci-Spn-7	LFPEATYKLEEDFLSKCKQFYETEIQALDFKGNPDASREAINVWAEKETS GKINDLLPNSINSLVRLVLANA	167
Ci-Spn-6	LFPEATYKLEKDFLSKCKEFYETEIQALDFKGNPDASREAINAWAEKETS GKIKDLLPSGSIDSLVRLVLANA	167
Ci-Spn-8	LFPEATYKLEKDFLSKCKEFYETEIQALDFKGNPDASREAINAWAEKETS GKIKDLLPSGSIDSLVRLVLANA	167

Hs-A1AT	IFFKGNWERPFEVKDIT-----EEDTEHYDQVTTVKVPM-----KR	223
Ci-Spn-4	LFFEALWKHPFTTGRIT-----SNSTFVLANGTPVLTTPMMEVTANHFLHY	263
Ci-Spn-3	VYFQADWAISEFRIPIT-----KQNFSLNNGTTVOVPPM-----VR	223
Cs-Spn-5	IYFQASWKHKFSAAGILYNSMLYAVFDNGLGYIFKELNFITSSTFQEQFQLANGESVMVPPM-----HL	259
Ci-Spn-5	LYFKGLWEKPEINL-----RSTFYTTNNEQYQTFV-----Q	233
Ci-Spn-1	IYVKAKNDIPFOKSLIT-----RMRRFRVSNNESIRVETM-----IS	264
Cs-Spn-4	IYVKAKNSIGFSKSHIT-----KMRRFKISDSESRKVPTM-----WN	265
Ci-Spn-2	IAFKAAWKSSFIKDAIT-----TLTNGEHSPTKVKQAATM-----YT	229
Cs-Spn-3	IYVKVLWQTSFIRQAIT-----TKANFQISPTRSKQVSTM-----YT	232
Cs-Spn-2	VYFRGNWHSKFIESQIT-----DRRAFVYVSHYKVVETPPM-----FQ	228
Ci-Spn-9	LYFRGNWDYEFDEGRIT-----KRRPFYVSKDKAVETSEFM-----FQ	226
Ci-Spn-10A	VYFRGDWHSKFNEMQIT-----ERRAFVYVSHYKIVETPPM-----FQ	226
Ci-Spn-10B	VYFRGDWHSKFNEMQIT-----ERRAFVYVSHYKIVETPPM-----FQ	226
Cs-Spn-1	VYFKGDWLNPFKEGAT-----VLKDFEHVQKDVTKKVHMM-----NM	214
Ci-Spn-7	VYFKGSWLHKFKDYDS-----IESNTEHVKEGTTTQVKMM-----NQ	203
Ci-Spn-6	VYFKGSWLHKFKEQOIT-----TMKDFHIRENKVEKVNM-----FM	203
Ci-Spn-8	VYFKGSWLHKFKEQOIT-----TMKDFHIRENKVEKVNM-----FM	203

Motif I

Hs-A1AT	LGMFN--IQ--HCKKLSWVLLMKVYLG---ATAI--FFLEDEG---KLOHLENE---LTHDIITKFLNED	280
Ci-Spn-4	SGEFCQLFSMRRCHPNTDPDIVLPPYKGE---RROMI--VLIENQNI--TIREIE-R---QFGTNEKWRSSLV	325
Ci-Spn-3	WEAVV--KS--YNYRDKIEFFFIRYKTTSNQNTYFV--VGLPGDNY--NLQOFS-R---EAQQILSRFRNTINK	284
Cs-Spn-5	RKML---YT--YFNRIVEFVKLPPYKSLNFTSYFV--VGLPLAGR--SLNQVK-S---NMHRILPRFNSGVW	319
Ci-Spn-5	QTMFA--LHS-FSEQFAHIVELPFKTSSS-RYKVMVMQLILPESRGADNINLIEDQ---FDEENFDFAEDQE	299
Ci-Spn-1	KNTFC--TRV-NNRDLQASVTVLSLGG---FSFV--IMSEHSAG--NFSRFYDDGVTMTQEKMTRAFINKI	326
Cs-Spn-4	PNAFC--THI-NNRRLQASLTVLSLGGK-----GKG-----VRE-----	296
Ci-Spn-2	SSAVC--FHQSHDAQLES DLIVLPPKGA---KTTMV--FIVEIVAG--NFGPLKGA---VGASKISOALDRYW	290
Cs-Spn-3	SSARC--FFQPNYPSLQSDIVLPPKGN---AMSMI--FIVETSPG--NFAPLESA---TASGDLROMMEVW	293
Cs-Spn-2	RGQFK--YA--YIHDLTQIVEMDYAGK---DYSMV--LLMP-ENF--DLAKVEEQ---LNHANITKWLAKLK	286
Ci-Spn-9	NEHFK--YA--YINELTLQVLEMDYAGT---DYSMV--LLMP-ENF--DLAKVEAN---LNHANITKWLAKLK	284
Ci-Spn-10A	RGHFK--YA--YISELTLQVLEMDYAGK---DYSMV--LLMP-ENF--DLAKVEAN---LNHANITNWLAKLK	284
Ci-Spn-10B	RGHFK--YA--YISELTLQVLEMDYAGK---DYSMV--LLMP-ENF--DLAKVEAN---LNHANITNWLAKLK	284
Cs-Spn-1	ERKFP--FN--YDSNLDLHAVELPYVGE---KYSMV--VFVPAKRY--GLEEIAKN---LTATKISELISGLF	273
Ci-Spn-7	KEWFN--FK--TDPDLGLKIAELFYKGG---DYSMV--VLLPDEKY--GLNKCLEK---LTSEKLOHISSGMM	262
Ci-Spn-6	KRFR--FN--FDQSLGLQVVEIPYIGN---KLSMV--VFLPETERF--ALNKIENA---LTHEKHGLLAGLW	262
Ci-Spn-8	ERKFP--FN--FDESGLQVVEIPYIGN---KLSMV--VFLPETERF--ALNKIENA---LTHEKHGLLAGLW	262

Hs-A1AT	-----RRSASLHLPKLSITGTY-DLKSVLGQLGITKVFNSG-ADLSCVTE--EAPLKLKSKAVHKAVLTI	340
Ci-Spn-4	-----DGNVELHLPKFEELKSNL-DLKSVLRSEGLTEPFNRRTTADYSTMTS---ROLAISKLFQOTASISM	385
Ci-Spn-3	M-----FRITHFKMLIELSHKT-DVKEVLQTLGVVDLFDSGASNLTGIST--VEQLVYSEFTQKAYINV	346
Cs-Spn-5	T-----KQLVEMSPVFRLSKKI-DVKDVIIRSMGVRDLFTSARANLSAISD--EYLYVSDFTODSFLOV	380
Ci-Spn-5	-----NISVTIRLPKFRLEYET-DLKEETLYNMGIQSLFSRGEADLSGIST--NGDLISLGSAAHKKTFIQV	360
Ci-Spn-1	TRRGNRQ--QQLCSVKLPKFKVDYAE-NLKEVLLKGLGIDIFISIN-ADFSRLSVRNNRELYVSEARHSAVLSA	395
Cs-Spn-4	-----QQLCSLKLPKFKVDVAK-SLNSVLRGVGLLDVFDPNLADMSRMTSGGIRELYVSEARHSAVLRA	359
Ci-Spn-2	TGYRNMPIPMRVCEVRMPKFKITHSVDDLMGAMRAMNVTDLFESTE-ADFSPTMP---ELVVYVDMRHKAVIKV	359
Cs-Spn-3	N--THYP-EMETCEVHLPKFKVHHTVDLIGALQLMNVSDFSPDDADLSLMTT---EQLVYVSDMRHQAVIKV	360
Cs-Spn-2	-----YKSVDLTVPKFSLEETI-HLKEVLPKMGVTDVFDKRLCDLSGISK--SSDLSVDQIIHKTVLEV	347
Ci-Spn-9	-----HESVDLTIKFKLEETL-QLQEVLPKMGVTDLFDROACDLTGIAN--RNNLFVDQIVHKTVLDV	345
Ci-Spn-10A	-----YKSVDLSVPKFKLEETL-QLQEVLPKMGVTDLFDROACDLTGISK--SKDLNVDQIVHKTVLEV	345
Ci-Spn-10B	-----YKSVDLSVPKFKLEETL-QLQEVLPKMGVTDLFDROACDLTGISK--SKDLNVDQIVHKTVLEV	345
Cs-Spn-1	-----EEKVNFSPKMKFEKSL-DLVEILKKNLGLVDLFEAENKALEGISK--TGELEFVSOVQHKAFIEV	334
Ci-Spn-7	-----RTELALSLPHMKFEKQL-DLVGSLKKLGLVDLFEKGNKSLRGISD--DGDLEFVSOVAHKAFIEV	323
Ci-Spn-6	-----EETLMLSLPRMKFEQDF-DLGGVLKMKGMDFDERAANFEATSG--SRDLVISKVVHKAFFIEV	323
Ci-Spn-8	-----EETLMLCLPRMKFEQDF-QLQEVLLKMGMDAFSKGAANFEATSG--SRDLVISKVVHKAFFIEV	323

	-----RCL-----	
Hs-A1AT	DEKGTAAAGAMFLEAIPMSIPPE----VKFNKPFVFLMIEQNTKSPLEFMCKVNVNPTQK-----	394
Ci-Spn-4	DETGVRATSTAAFFELRSFFFR---TRINANKPFLFIIEDIHTRTPLFLGRVTDPRPL-----	441
Ci-Spn-3	NENGTVAASAAATVQGRSLSIP---RQVTVDRPFFIGVYQEKSNLFLFLCKVENPLEN-----	402
Cs-Spn-5	NEEGTVGAAATAAAILSGRSGGVA---RNFVVNRPFVFGVYNERSDSCVFLCK-----	429
Ci-Spn-5	DESGTTAGASYAQQGFRRVSDLD----LVFNHPFIVIIREKYTQMPMFMGRVVARPMY-----	413
Ci-Spn-1	DEAGVEAAGATAFGISLRSLSLQ----VTVNKPFIFALRHDPSGALIFVCKIVRPSVG-----	449
Cs-Spn-4	DEVGIEAAGASGMGMVFRSISKR---VTINKPFIFALRHDPTGAILFLCKVVRPGAD-----	413
Ci-Spn-2	NEQGVKATAATSIGLTGRSLPIR----VEINRPFMYMIRHEPTGALLFLGRVVDPTK-----	412
Cs-Spn-3	DELGVKATGATSIGISGRSYPTL----VQINRPFMYMIRHEATGALLFMGRIVNPK-----	412
Cs-Spn-2	FENGGDVLAEAEANRTPCNDRT---LFYADHPFLVIVRGRAKNAFHLFCAYKRPEGRIRSHDEL	409
Ci-Spn-9	NEQGSEAAATTSVRTQCDVAFN--PISFVADHPFLWAIRHROSELLIFMGRFSRPEGPLLHDEF	409
Ci-Spn-10A	DEQGSEAAATTVRIQARSLNSR---PSFVADHPFLWAIRHROSELLIFMGRFSRPEGPLLHDEF	408
Ci-Spn-10B	EENGGAVPQERADANQTPALDRP---VVYVDHPFIIIVRGRANNAFHLFCAYKRPAKIRSHDEL	407
Cs-Spn-1	DEKGTVAASAAATAVVMMLRSLVVP--PVRVTCDHFFLVIRKPKSKNILEMGRYSGP-----	388
Ci-Spn-7	NETGTEAAAATAMIAMQSMAMPVPPVQFNCDHPFLFLIRENPTNSVLFGRCSDP-----	380
Ci-Spn-6	NEEGSEAAAATAVVMMLRSMPA--PPVMVNCDHFFLVIRHNOKTKTILELGRFSGP-----	377
Ci-Spn-8	NEEGSEAAAATAVVVKARSMPCCL--PEMVNCDHPFLFLIRENPTKTKTILELGRFSGPSI-----	379

Motif II

Motif III