

## ORF-GIF Family Alignment

GIF_ORFVgORF117	MA[C]...LRVFLAVFAL[C]GS...VHSAQWIGERDF[C]MAHAQDVFARLQVWMRIDR	48
GIF_SB87_gp117	MAADGLRLLLALAAVLGGGPARARAHKGFHGGEDFCRAHERDIYPSLQIWVRVDR	55
GIF_PCPV_gp121	MA[C]...LRVFLAVLAL[C]GS...VHSTPWIGERDF[C]AAHAQDVFSRLOQVIRIDR	48
GIF_ORFVgORF117	NVTAAADNNSA[C]ALAIETPPSNFDADVVAAGI[NVS]VSAINC[G]FFFSMRQVETTYDT	104
GIF_SB87_gp117	DPGVARNAST[C]TLNVEAHPSGFDAHAYVAAAGV[NVSLATKHF]GKFSRLLRRTTFSP	111
GIF_PCPV_gp121	NVTIADNNSA[C]ALAIETPPSNFDADVVAAGI[NVS]VSAINC[G]FFFNMRQVEATYDT	104
GIF_ORFVgORF117	ARRQMYYVMDTWDWPVWLDPPQLPFS...QEYE[NET]LP.YLLEVLLELARLYIRVGC[TV	157
GIF_SB87_gp117	EKDKIYVYLDWSWPWTR.SVDPLFR[NGS]GAD[NGT]DPNLLLEVLLETARLSVEVGC[SA	166
GIF_PCPV_gp121	ARRQMYYVTDWDWPVWLDNPPQIF...QEYE[NDT]LP.YLLEVLLEFSRMYIRVGC[TV	157
GIF_ORFVgORF117	PGEQPFVEVITGIDYPHTSMEFLLQHVLRPNRRFAPAKLHMDLEVDYR[C]VSAVYVKAF	213
GIF_SB87_gp117	PGFRPDLADP...LETHADPDLTLTDTHDRKRDPGAVEVDLREVDYR[C]VRSAYVKV	220
GIF_PCPV_gp121	PGEQPFVEVIGIDYPHHSMEFLQHVLRPNRRFSPAKLHIDLREVDYR[C]VSAHVKAF	213
GIF_ORFVgORF117	LQDA[C]S...ARKAR.TPLYFAGHGSNHPDRRPKNPVPRPQHVSSPMSRKC[LMQ]TAR	265
GIF_SB87_gp117	LRDA[C]FQQAMHHRQRPRRRLPRQSRRLQQLKQKQPQHVSS[C]RNERR[K]IQ...	272
GIF_PCPV_gp121	LQDA[C]S...ARKAR.TPLYFAGHGSNHPDNRPKNPVPRPQQVWSSSSRKC[RMQ]TVR	265

**Figure S13.** Sequence alignment of the ORF-GIF family members. Cysteine residues are boxed in yellow. Predicted N-linked glycosylation sites are boxed in blue.

## Orphan Alignment

COTV030	MNSLKLIIIFILYVSTIYSFNYSNV[NITI]EINDVNNSDYNIK[NYI]NLNIY	50
CPXV_GER91_007_	MGRSIIIFLALIG[C]AISNYVTPQKPTDNQFNVEITFFMTPNIEGKYTTY	50
SCPIlike_COTV007	MIIMKHIIILFINFVSFVYSEKFNKVDINLYIFSL[NNT]DYDIYTLSDNQYK	50
SCPIlike_COTV179	MIIMKHIIILFINFVSFVYSEKFNKVDINLYIFSL[NNT]DYDIYTLSDNQYK	50
A41-like_COTV011	MNTHLLLLLVGVISS[C]YAG.NKNWVKPELVSIFSDTENPLTKVFKV[C]DTE	49
A41-like_COTV175	MNTHLLLLLVGVISS[C]YAG.NKNWVKPELVSIFSDTENPLTKVFKV[C]DTE	49
SB87_gp113	MKTLLLAAVVIISLANSLP[LLS]NKDAF[C]SSTKEEIHQIMIAMR[NRT]V	50
DPXV_-016	MIKYTLLTSFIFFIT[C]YHVSXVSNNEEIQNKFTMFVDLTVYDKNLINDV[S]C	50
BPSVgORF117	MWLPRALLALSVI[C]GTASSYRGMHDGGEF[C]RAHSREIFTSFQMWMRIQRN	50
COTV030	KIITQDFTIELTKRSKQRFIYTDYVNIINNTGIATFYTDIGNRFSYRGSYS	100
CPXV_GER91_007_	SHRRFHAVNSDKWIVGITAINLDDLPNK[NIT]LTQLVPS[NAT]IVKFTFGSND	100
SCPIlike_COTV007	VNTTEVSIYITAYDIPLEFAKNVYIEQIQDLSVINLSTDTGIFQTG[NKS]II	100
SCPIlike_COTV179	VNTTEVSIYITAYDIPLEFAKNVYIEQIQDLSVINLSTDTGIFQTG[NKS]II	100
A41-like_COTV011	NVFMGMYLNIFAKVNKYTPR[C]TSLDIKKDNAYVVGGGVIINTTLQD[C]PFP	99
A41-like_COTV175	NVFMGMYLNIFAKVNKYTPR[C]TSLDIKKDNAYVVGGGVIINTTLQD[C]PFP	99
SB87_gp113	SEPPTY[C]ELDMQDDLLLEGTMDSTAYFEANGV[NAT]VSIMGEGIDMTLSSL	100
DPXV_-016	KRYDHDNFYSMYIINDF[NVS]ITLSD[C]GDAGTEGYVTVNRNNTMELGYFT	100
BPSVgORF117	VQTAR[NAT]Q[C]ALDVEAPPDMFVDVAYANTAGIAVYATANVGRVDVRTLQ	100
COTV030	IELT[C]ESIFNIYGDYLY[C]DNTNT[NYI]NNKIKNFFTIFYGS[C]VKKAKIKFV	150
CPXV_GER91_007_	IFQTKKVKFIIGIT[C]KETAKTLRSLNLRMSSLDKHFTEYINTNHVSYYG	150
SCPIlike_COTV007	YLDID[C]NNKNIISDNKKMLKGIWNIIFKRYMDFVYIHGS[C]IDRVNARIYR	150
SCPIlike_COTV179	YLDID[C]NNKNIISDNKKMLKGIWNIIFKRYMDFVYIHGS[C]IDRVNARIYR	150
A41-like_COTV011	VSTVAEEVYDSDILNVIFFSTVNPITDKDKTNFITKDESKNIPKK[C]KVFS	149
A41-like_COTV175	VSTVAEEVYDSDILNVIFFSTVNPITDKDKTNFITKDESKNIPKK[C]KVFS	149
SB87_gp113	RVEYPTTDAEIMYAFISSWAPWVKNKDLALNNREELA[NFT]RNLIALK	150
DPXV_-016	PIIMYKGLNFDSSR[C]IVRIIT[C]DGDNNLVMTPQRKPKKQKHADHIEK	150
BPSVgORF117	VLYST[NKS]SMFYLLDWTSPWTKYTRLYS[NAS]ADAH[NET]IDCLEVLDDL	150
COTV030	YLNTLTKKILLIIYILETALLFNQKVKIKYHKFVYKMDADYIF...	195
CPXV_GER91_007_	N[C]FNLYLSDVINYNKNTETGVYDFYYSTNSAQYVDKGSIVKI...	191
SCPIlike_COTV007	SNTKSRLFESSYFTNNF...	167
SCPIlike_COTV179	SNTKSRLFESSYFTNNF...	167
A41-like_COTV011	MK[C]KQDEHFSEESFDEHEYDDDYEEAVPINVDNEILATFNRNKAPIKVND	199
A41-like_COTV175	MK[C]KQDEHFSEESFDEHEYDDDYEEAVPINVDNEILATFNRNKAPIKVND	199
SB87_gp113	V[D]CDHKQKFPVPTTEAPTPTPTTESPTTTISVTETR[NET]TPSVEEDDE	200
DPXV_-016	LILYGK[C]IDGKADVTYDYGSRVDTSSIIYGTISDISGLLPNT[C]PK...	196
BPSVgORF117	KVHVVDVGC[AVED]IPVDVVDPIDYPRVYDPPDLLRYVIPKNRKQNPGYVFD	200
COTV030	...	195
CPXV_GER91_007_	...	191
SCPIlike_COTV007	...	167
SCPIlike_COTV179	...	167
A41-like_COTV011	ILTLIDIKS[C]VQEVVSRLRINDL[C]ESVKRYPESSYVQEVSYPESSKFEDF	249
A41-like_COTV175	ILTLIDIKS[C]VQEVVSRLRINDL[C]ESVKRYPESSYVQEVSYPESSKFEDF	249
SB87_gp113	EPPVDVHTNRKHEPMDISFSTMINQQ[C]IQDLAVRVVIRDA[C]EYRKTETPL	250
DPXV_-016	...	196
BPSVgORF117	LSVDSY[C]VHVSVNKVTVLRDA[C]IHKKNETPLNFYGRENFPLHKSPNSVIP	250
COTV030	...	195
CPXV_GER91_007_	...	191
SCPIlike_COTV007	...	167
SCPIlike_COTV179	...	167
A41-like_COTV011	EKNTPGYPTL[C]...	260
A41-like_COTV175	EKNTPGYPTL[C]...	260
SB87_gp113	GMLGTHGNDFRQELKKMKTKRT[C]SMHLKNEETVDEEVSEELSE	292
DPXV_-016	...	196
BPSVgORF117	HKRGFST[C]EMITGQ...	264

**Figure S14.** Sequences of orphan PIE domains. Cysteine residues are boxed in yellow. Predicted N-linked glycosylation sites are boxed in blue.