

## Electronic Supplementary Material

### Differential gene expression in porcine SK6 cells infected with wild-type and SAP domain-mutant foot-and-mouth disease virus

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Table S1. The qPCR primers used in this study

Gene	Primers(5'→3')
CCL4	Forward: CACCTCCTGCTGCTTCACATA
	Reverse: CAGACCTGCCTGCCCTTTT
CCL2	Forward: GTCACCAGCAGCAAGTGCCT
	Reverse: ATGTGCCCAAGTCTCCGTTTA
IL6	Forward: GACAAAGCCACCACCCTAA
	Reverse: CTCGTTCTGTGACTGCAGCTTATC
IL7	Forward: GGGATGGATGAAACAGAAGG
	Reverse: GCTACTGGCAACAGAACAAGG'
IL18	Forward: GCACCTCAGACCGTATTTATT
	Reverse: CATCATGTCCAGGAACACTTC
EGR1	Forward: TCAACACCACCTACCAGTCCCA
	Reverse: GATCTTGGTATGCCTCTTGCGTT
SRPX2	Forward: AACGTGGTATGCAGGTTCAAG
	Reverse: GTAGTCACAGCGGAGTCAAGA
CREB5	Forward: TATCTTCCCTGCTACATCTTCACA
	Reverse: AACGCAGCCTTCAACCTCATT
RASAL1	Forward: GTGAAAGTGGACGACGAGGTGG
	Reverse: GGAAGCGTGTCTTCTTGATGG
RIN2	Forward: CCTTGAAGTTGCCTTATGCTGTTT
	Reverse: GCTACGTTCCCATGTGGGTGAT
GAPDH	Forward: ACATGGCCTCCAAGGAGTAAGA
	Reverse: GATCGAGTTGGGGCTGTGACT

Table S2. Differentially expressed genes involved in transcription-related functions

Gene function description	Up-regulated genes		Down-regulated genes	
	Gene number	Gene name list	Gene number	Gene name list
Transcription factor complex	9	ING2, CNOT7, TAF13, TAF9B, MNAT1, RB1, NFYB, GTF2A1, TAF2	0	-
Transcription factor binding	22	HES1, KLF4, LOC100154750, GTF2A1, LOC100739605, MDFIC, MTDH, MED13, JMJD1C, PRDM5, LOC100626982, NFYB, EGR2, NRIP1, NFKBIA, SIRT1, HMGB1, CAND1, EIF4A2, EIF4A2, EIF5B, EIF3J	0	-
Protein binding transcription factor activity	34	FGF2, JMY, SP100, IFNB1, NPAT, MTDH, CIR1, SCAI, USP16, NFE2, GABPA, SIRT1, C1D, LOC102161761, LOC102160069, TRIP11, LOC100154750, MYSM1, RB1, SS18, LOC100739605, LOC100622863, TAF9B, TMF1, MED13, NMI, COPS2, LOC102166221, TBL1XR1, CASP8AP2, NRIP1, AEBP2, KMT2E, SKIL	3	DYRK1B, PIR, TFCEP2L1
Transcription factor binding transcription factor activity	34	FGF2, JMY, SP100, IFNB1, NPAT, MTDH, CIR1, SCAI, USP16, NFE2, GABPA, SIRT1, C1D, LOC102161761, LOC102160069, TRIP11, LOC100154750, MYSM1, RB1, SS18, LOC100739605, LOC100622863, TAF9B, TMF1, MED13, NMI, COPS2, LOC102166221, TBL1XR1, CASP8AP2, NRIP1, AEBP2, KMT2E, SKIL	3	DYRK1B, PIR, TFCEP2L1
Nucleic acid binding transcription factor activity	60	KLF4, ZHX1, EGR4, ZNF24, LOC102159255, TFAM, NFIA, EGR2, GABPA, GATA3, NFE2L2, HDAC1, HDAC2, HES1, PAXBP1, ZC3H8, TAF13, CREBRF, GATA2, TOPOII, TOP2B, RBPJ, MYNN, EHF, DMTF1, ZNF84, ZBTB38, AHR, HMGB1, ZNF197, CNOT7, GCFC2, BTAF1, LOC102163244, SLC30A9, NPAT, LOC100737142, CIR1, ZNF189, ETV1, FOXN2, TBX21, SIX4, ZEB2, NFYB, EGR1, ZNF287, ARID4A, RB1, BTG2, FOS, LOC100622863, BLZF1, LOC100520627, LOC100515279, NR1D2, SCML2, HIF1A, LOC100626982, POU3F2	5	ARNT2, NR4A2, RCAN1, ZNF71, TFCEP2L1
Ligand-activated sequence-specific DNA binding RNA polymerase II transcription factor activity	1	NR1D2	1	NR4A2
Sequence-specific DNA binding transcription factor activity	5	HES1, BTG2, HIF1A, NR1D2, FOXN2	1	NR4A2
Sequence-specific DNA binding RNA polymerase II transcription factor activity	4	BTG2, HIF1A, NR1D2, FOXN2	1	NR4A2

To be continued

Gene function description	Up-regulated genes		Down-regulated genes	
	Gene number	Gene name list	Gene number	Gene name list
Positive regulation of sequence-specific DNA binding transcription factor activity	8	MALT1, TNF, KRAS, TAB3, CHUK, LOC100620995, NFKBIA, MTDH	0	-
Regulation of sequence-specific DNA binding transcription factor activity	10	MALT1, ITCH, TNF, KRAS, TAB3, CHUK, LOC100620995, NFKBIA, LOC100153617, MTDH	1	LOC100515993
Negative regulation of sequence-specific DNA binding transcription factor activity	3	NFKBIA, LOC100153617, ITCH	1	LOC100515993
Regulation of transcription factor import into nucleus	2	NFKBIA, TNF	0	-

Table S3. Differentially expressed genes involved in immune regulation

Gene function description	Up-regulated genes		Down-regulated genes	
	Gene number	Gene name list	Gene number	Gene name list
Negative regulation of immune effector process	4	SOCSS5, IFIT1, ITCH, IL7R	1	TGFB3
Production of molecular mediator of immune response	8	MALT1, LOC100621191, TNF, XRCC4, LOC100620995, LOC100739713, IL7R, MSH2	0	-
Immune system process	94	BMPRI1A, IL18, CASP3, CXCL10, SEMA3C, TGFB1, MASP2, IFN1, IFIT1, CCL5, ROCK1, S100A12, LOC100739781, LOC100625180, LOC100518921, LOC100739781, LOC100625180, LOC100518921, CD79A, XRCC4, CD84, GATA3, IL7R, DPP8, HES1, LOC102161761, ZC3H8, CSF2, TNF, TBK1, TAB3, PIK3CA, IRG6, LOC100736872, RBPJ, BRCA2, ATM, CCL3L1, LOC100620995, AHR, HMGB1, APC, MSH2, SLAMF7, CCL20, S100A9, ADAM10, KRAS, JAK2, LTB, TNFSF10, IL7, BLM, LOC100622217, IL1RAP, SIX4, LOC100622970, LOC100738058, RTKN2, NCK1, MAP3K8, EGR1, CHUK, IL1A, LOC100739713, ANGPT1, KITLG, LOC102163753, LOC100621191, LOC100627112, RB1, MSH3, CXCL2, UBD, BMI1, FOS, LOC100628215, STXB3, MALT1, CCL2, MTAP, TNFSF15, CFH, CSF1, CD38, APOBEC1, NFKBIA, RICTOR, CCL4, KMT2E, CXCL11, ITGA6, LOC100739007, IL6ST, SKIL, IL6, LOC100620730	6	SUSD2, GRB7, MAP2K6, GPX2, LOC102166152, LOC100522330
Cytokine production involved in immune response	4	MALT1, LOC100620995, LOC100621191, TNF	0	-

To be continued

Gene function description	Up-regulated genes		Down-regulated genes	
	Gene number	Gene name list	Gene number	Gene name list
Somatic recombination of immunoglobulin genes involved in immune response	3	LOC100739713, MSH2, XRCCA4	0	-
Somatic diversification of immunoglobulins involved in immune response	3	LOC100739713, MSH2, XRCCA4	0	-
Immunoglobulin production involved in immunoglobulin mediated immune response	3	LOC100739713, MSH2, XRCCA4	0	-
Regulation of immune system process	48	LOC100737466, IL18, CASP3, ITCH, ADAM10, MASP2, IFNB1, IFIT1, CCL5, EDN1, IL7, BLM, LOC100622217, CD79A, TBX21, LOC100622970, LOC100738058, NCK1, MAP3K8, CHUK, IL7R, SOCS5, LOC100627112, LOC100737558, TNF, TBK1, RB1, TAB3, PIK3CA, FOS, ELMOD2, LOC100628215, MALT1, CCL2, HIF1A, ATM, ACVR2A, CFH, CSF1, CD38, RICTOR, LOC100620995, NFKBIA, KMT2E, DDX58, LOC100739007, IL6, APC	5	TNFSF4, MAP2K6, SEMA7A, TGFB3, LOC102161418
Somatic diversification of immune receptors via germline recombination within a single locus	5	LOC100739713, HMGB1, MSH3, MSH2, XRCCA4	0	-
Immune response	19	IL18, LOC100621191, TNF, MASP2, IFNB1, IFIT1, BMI1, IL7, STXBP3, S100A12, MALT1, CCL2, CFH, XRCCA4, LOC100620995, LOC100739713, GATA3, IL6ST, MSH2	1	GPX2
Adaptive immune response	10	MALT1, IL18, TNF, MASP2, XRCCA4, LOC100620995, LOC100739713, GATA3, IL6ST, MSH2	0	-
Somatic diversification of immune receptors	5	LOC100739713, HMGB1, MSH3, MSH2, XRCCA4	0	-
Immune system development	29	KITLG, ZC3H8, RB1, MSH3, TGFB1, BMI1, JAK2, LTB, RBPJ, BLM, LOC100628215, LOC100739781, MALT1, BRCA2, ATM, LOC100518921, CD79A, SIX4, MTAP, RTKN2, XRCCA4, EGR1, CHUK, LOC100739713, HMGB1, IL7R, APC, ANGPT1, MSH2	1	LOC102166152

Gene function description	Up-regulated genes		Down-regulated genes	
	Gene number	Gene name list	Gene number	Gene name list
Myeloid cell activation involved in immune response	2	S100A12, STXBP3	0	-
Somatic diversification of immune receptors via somatic mutation	2	LOC100739713, MSH2	0	-
Adaptive immune response based on somatic recombination of immune receptors built from immunoglobulin superfamily domains	9	MALT1, IL18, TNF, MASP2, XRCC4, LOC100620995, LOC100739713, GATA3, MSH2	0	-
Regulation of production of molecular mediator of immune response	2	TBX21, TNF	2	SEMA7A, TGFB3
Negative regulation of immune system process	5	CASP3, SOCS5, IFIT1, ITCH, IL7R	1	TGFB3
Regulation of immune effector process	11	LOC100737466, SOCS5, TBX21, ITCH, TNF, IFNB1, IFIT1, DDX58, ELMOD2, IL6, IL7R	2	TGFB3, SEMA7A
Immunoglobulin mediated immune response	5	LOC100739713, TNF, MASP2, MSH2, XRCC4	0	-
Positive regulation of immune system process	28	IL18, SOCS5, LOC100627112, ITCH, TBK1, ADAM10, TAB3, MASP2, IFNB1, PIK3CA, FOS, CCL5, EDN1, BLM, LOC100622217, TBX21, CD79A, CFH, LOC100622970, LOC100738058, NCK1, MAP3K8, CD38, RICTOR, CHUK, LOC100620995, NFKBIA, IL6	2	TNFSF4, MAP2K6
Regulation of cytokine production involved in immune response	0	-	2	SEMA7A, TGFB3
Innate immune response	2	CCL2, IFIT1	0	-
Activation of innate immune response	8	LOC100622970, TBK1, TAB3, LOC100738058, CHUK, LOC100620995, NFKBIA, FOS	1	MAP2K6
Innate immune response-activating signal transduction	8	LOC100622970, TBK1, TAB3, LOC100738058, CHUK, LOC100620995, NFKBIA, FOS	1	MAP2K6

Gene function description	Up-regulated genes		Down-regulated genes	
	Gene number	Gene name list	Gene number	Gene name list
Immune effector process	14	S100A12, STXBPF3, MALT1, CFH, TNF, MASP2, XRCCA, APOBEC1, LOC100620995, IRG6, KMT2E, LOC100739713, GATA3, MSH2	0	-
Positive regulation of innate immune response	8	LOC100622970, TBK1, TAB3, LOC100738058, CHUK, LOC100620995, NFKBIA, FOS	1	MAP2K6
Regulation of innate immune response	8	LOC100622970, TBK1, TAB3, LOC100738058, CHUK, LOC100620995, NFKBIA, FOS	1	MAP2K6
Regulation of immune response	17	SOCS5, TBK1, TAB3, MASP2, PIK3CA, FOS, TBX21, CD79A, LOC100622970, CFH, LOC100738058, NCK1, CD38, CHUK, LOC100620995, NFKBIA, IL6	3	TGFB3, MAP2K6, SEMA7A
Immune response-activating cell surface receptor signaling pathway	7	NCK1, CD38, PIK3CA, NFKBIA, LOC100620995, CHUK, CD79A	0	-
Immune response-regulating cell surface receptor signaling pathway	7	NCK1, CD38, PIK3CA, NFKBIA, LOC100620995, CHUK, CD79A	0	-
Activation of immune response	14	CD79A, CFH, LOC100622970, TBK1, TAB3, MASP2, LOC100738058, NCK1, CD38, PIK3CA, CHUK, LOC100620995, NFKBIA, FOS	1	MAP2K6
Immune response-activating signal transduction	12	CD79A, LOC100622970, TBK1, TAB3, LOC100738058, NCK1, CD38, PIK3CA, CHUK, LOC100620995, NFKBIA, FOS	1	MAP2K6
Immune response-regulating signaling pathway	12	CD79A, LOC100622970, TBK1, TAB3, LOC100738058, NCK1, CD38, PIK3CA, CHUK, LOC100620995, NFKBIA, FOS	1	MAP2K6
Positive regulation of immune response	14	CD79A, CFH, LOC100622970, TBK1, TAB3, MASP2, LOC100738058, NCK1, CD38, PIK3CA, CHUK, LOC100620995, NFKBIA, FOS	1	MAP2K6
Humoral immune response mediated by circulating immunoglobulin	2	TNF, MASP2	0	-
Humoral immune response	3	CFH, TNF, MASP2	0	-
Cell activation involved in immune response	2	S100A12, STXBPF3	0	-
Leukocyte activation involved in immune response	2	S100A12, STXBPF3	0	-
Positive regulation of immune effector process	3	SOCS5, TBX21, IL6	0	-

Table S4. Differentially expressed genes involved in cytokine-related functions

Gene function description	Up-regulated genes		Down-regulated genes	
	Gene number	Gene name list	Gene number	Gene name list
Cytokine receptor binding	25	KITLG, CSF2, IL20, ITCH, TNF, TGFB, IFN1, IFNB1, CCL5, JAK2, LTB, TNFSF10, IL7, LOC100739781, CCL2, IL1RAP, TNFSF15, CSF1, CASP8AP2, IL1A, LIFR, LOC100739007, IL6ST, IL6, LOC100620730, ANGPT1, CCL2, CCL20, CXCL10, CXCL2, CCL3L1, CCL4, CCL5, CXCL11, LOC100620730	3	TGFB3, TNFSF4, LOC100515993
Cytokine activity	9	IL1RAP, LIFR, IL12RB2, IL6ST, IL7R	0	-
Cytokine receptor activity	5	IL1RAP, LIFR, IL12RB2, IL6ST, IL7R	0	-
Positive regulation of cytokine production	18	CSF2, LOC100737466, IL18, TNF, TBK1, IFNB1, POLR3G, NOX1, IL12RB2, MALT1, HIF1A, LOC100622970, LOC100620995, IL1A, DDX58, GATA3, IL6, IL6ST	1	TNFSF4
Regulation of cytokine production	26	CSF2, LOC100737466, IL18, ITCH, TNF, TBK1, IFNB1, IFIH1, POLR3G, NOX1, IL12RB2, LTB, RNF125, ATG5, MALT1, HIF1A, LOC100625180, TNFSF15, LOC100622970, ZNF287, LOC100620995, IL1A, GATA3, DDX58, IL6ST, IL6	5	LOC780431, TGFB3, TNFSF4, SEMA7A, ACP5
Response to cytokine stimulus	17	CASP3, SP100, TNF, ADAM10, UBD, IFIT1, IFIT3, RPS6KB1, EDN1, ACSL4, CCL2, IFIT2, EGR1, CD38, LIFR, HMGB1, IL6	2	LOC100515993, LOC102161418
Cytokine production involved in immune response	4	MALT1, LOC100620995, LOC100621191, TNF	0	-
Regulation of cytokine secretion	3	IL1A, TNFSF15, TNF	1	TNFSF4
Negative regulation of cytokine production	9	ATG5, LOC100737466, ITCH, LOC100622970, TNF, TBK1, IFIH1, DDX58, RNF125	3	TGFB3, TNFSF4, ACP5
T cell cytokine production	2	MALT1, LOC100620995	0	-
Cytokine production	9	MALT1, IL18, HIF1A, IL1RAP, LOC100621191, TNF, LOC100620995, IL12RB2, JAK2	1	ACP5
Negative regulation of cytokine-mediated signaling pathway	2	CCL5, IL6ST	0	-
Negative regulation of response to cytokine stimulus	2	CCL5, IL6ST	0	-
Cytokine-mediated signaling pathway	9	EGR1, CCL2, IFIT1, LIFR, IFIT3, SP100, IL6, TNF, IFIT2	1	LOC102161418
Cellular response to cytokine stimulus	9	EGR1, CCL2, IFIT1, LIFR, IFIT3, SP100, IL6, TNF, IFIT2	1	LOC102161418
Positive regulation of cytokine biosynthetic process	6	LOC100625180, IL1A, LTB, LOC100622970, TNF, TBK1	0	-

To be continued

Gene function description	Up-regulated genes		Down-regulated genes	
	Gene number	Gene name list	Gene number	Gene name list
Regulation of cytokine production involved in immune response	0	-	2	SEMA7A, TGFB3
Regulation of cytokine biosynthetic process	7	LOC100625180, IL1A, LTB, IL6, LOC100622970, TNF, TBK1	0	-
Regulation of cytokine-mediated signaling pathway	4	SOCS1, CCL5, JAK2, IL6ST	0	-
Regulation of response to cytokine stimulus	4	SOCS1, CCL5, JAK2, IL6ST	0	-

Table S5. Differentially expressed genes involved in inflammation, chemokine production-, and apoptosis-related functions

Gene function description	Up-regulated genes		Down-regulated genes	
	Gene number	Gene name list	Gene number	Gene name list
Chronic inflammatory response	8	TNF, PTGER3, PLA2G4A, CCL5, IL1A, IL6, IL6ST, PTGS2	0	-
Acute inflammatory response	11	HIF1A, TNF, PTGER3, IFNB1, PLA2G4A, CCL5, IL1A, HMGB1, IL6, IL6ST, PTGS2	1	GPX2
Inflammatory response	1	TNF	1	GPX2
Inflammatory response to antigenic stimulus	8	TNF, PTGER3, PLA2G4A, CCL5, IL1A, IL6, IL6ST, PTGS2	0	-
Chemokine receptor binding	4	CCL2, CCL5, ITCH, LOC100620730	0	-
CCR chemokine receptor binding	2	CCL2, CCL5	0	-
Regulation of execution phase of apoptosis	5	BRCA2, LOC100624979, LOC100739713, PMAIP1, MSH2	0	-
Induction of apoptosis	13	CD38, LOC100738156, LOC100622580, MAP3K5, CUL5, TNFSF10, XIAP, TNF, BLM, BCLAF1, CASP3, CASP4, CASP8AP2	1	LOC102161387



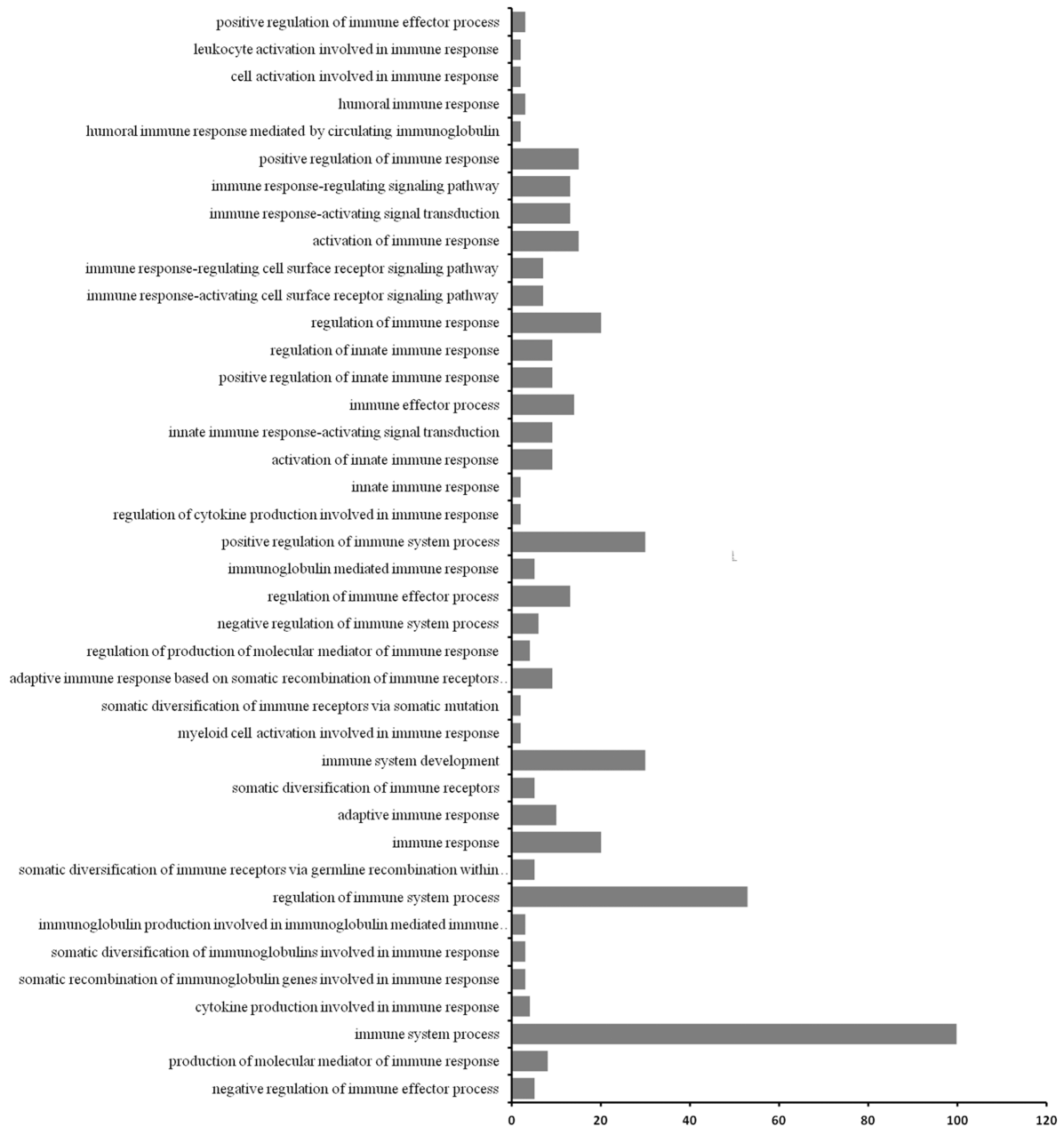


Figure S1. GO analysis of the immune-related genes indicating altered expression in rA-SAP-FMDV-infected SK6 cells as compared with rA-FMDV-infected SK6 cells. The X-axis indicates the correspondent number of genes.

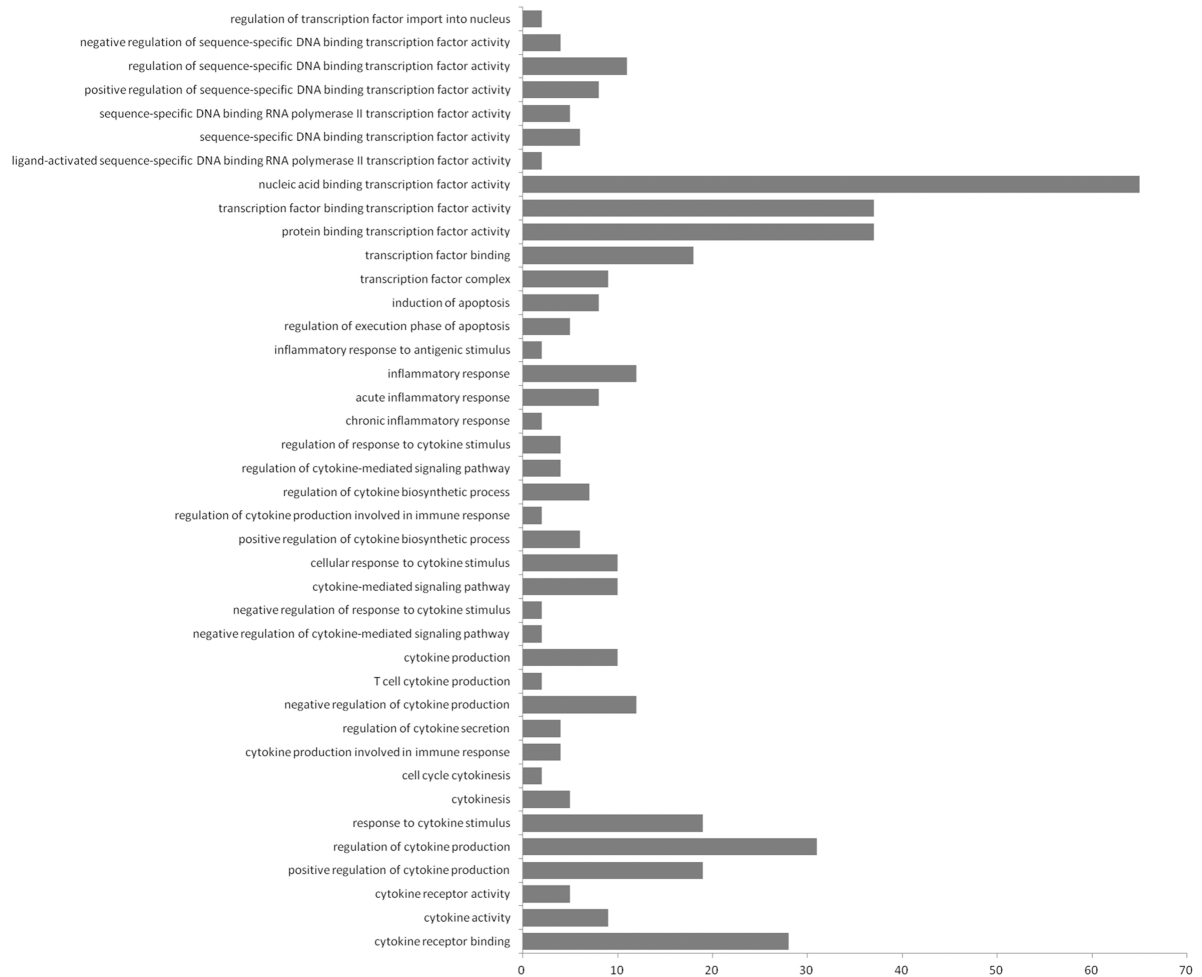


Figure S2. GO analysis of the transcription factor-, inflammatory response-, apoptosis- and cytokine-related genes showing altered expression in rA-SAP-FMDV-infected SK6 cells as compared with rA-FMDV-infected SK6 cells. The X-axis indicates the correspondent number of genes.

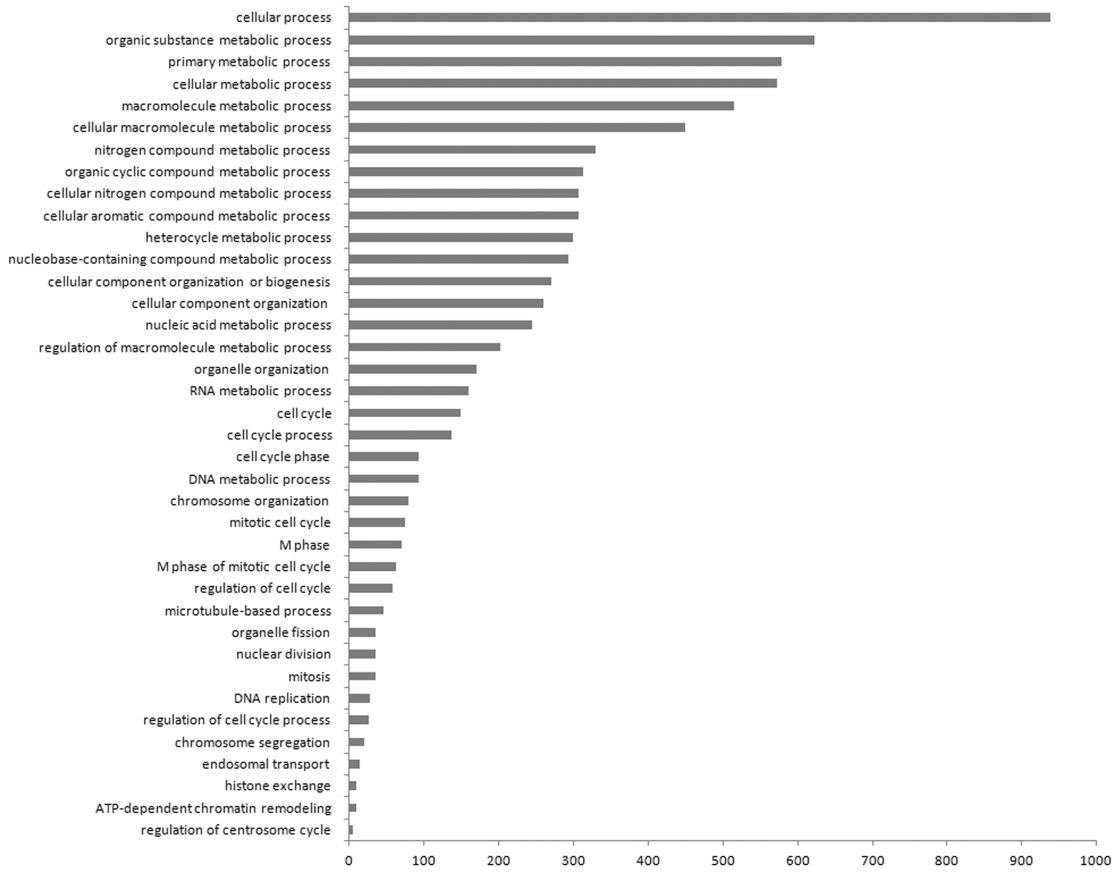


Figure S3. Biological processes derived from GO annotations for the differentially expressed genes. The X-axis indicates the correspondent number of genes.

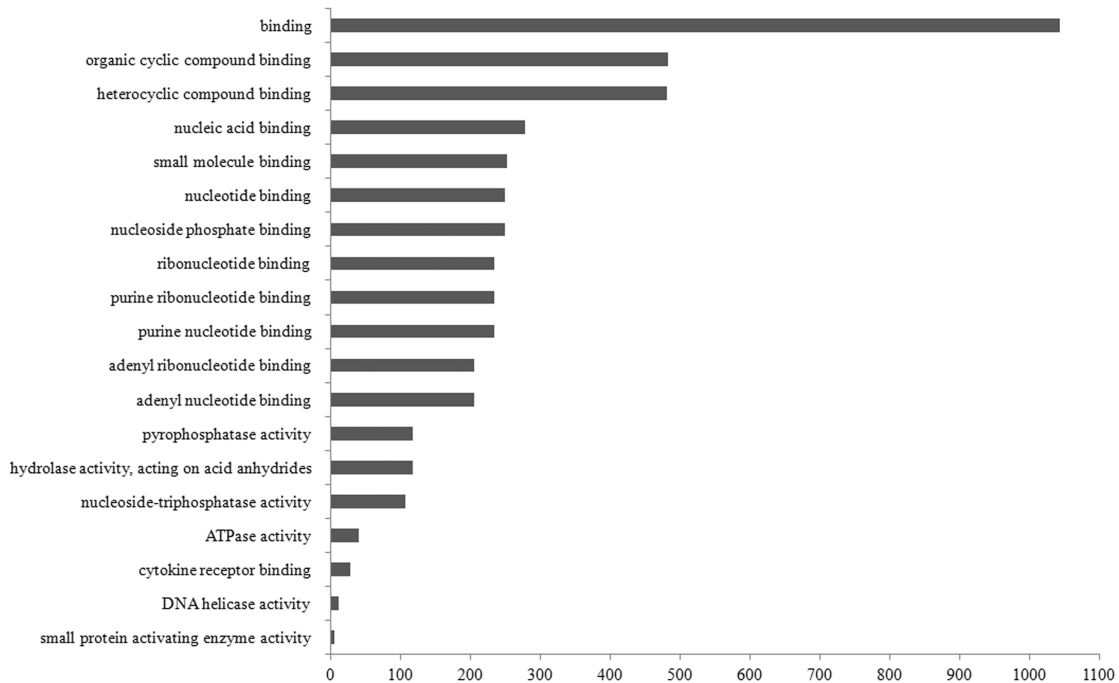


Figure S4. Molecular functions derived from the GO annotation for differentially expressed genes. The X-axis indicates the correspondent number of genes.

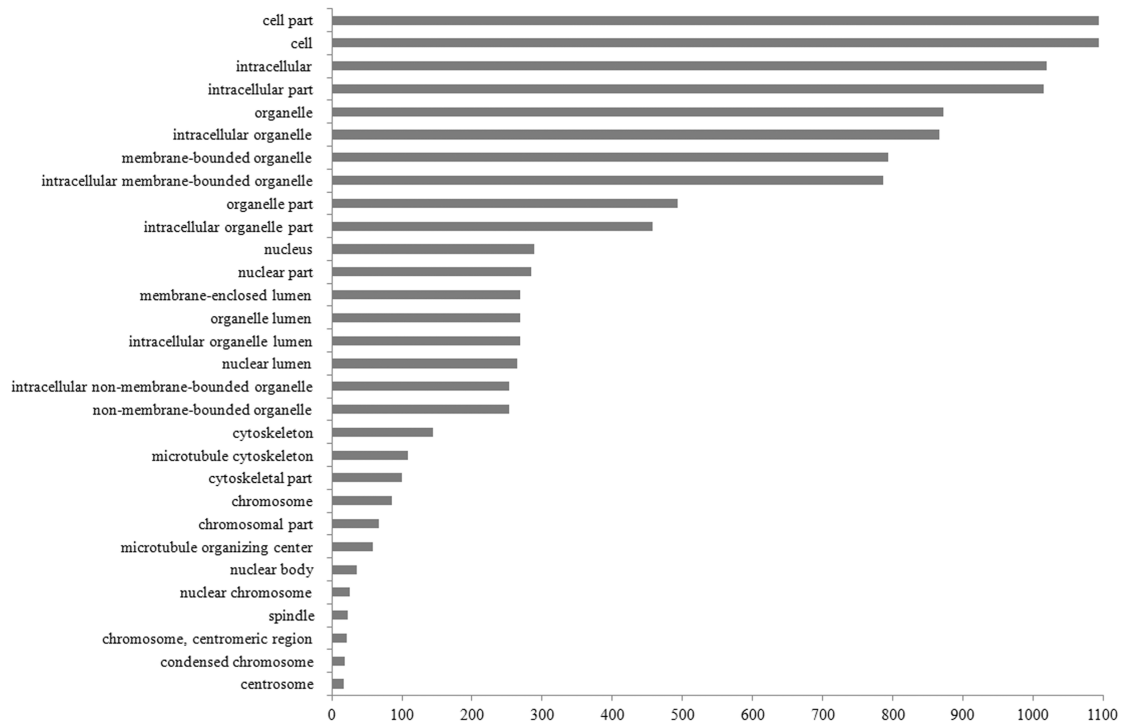


Figure S5. Annotations of cellular components associated with the differentially expressed genes. The X-axis indicates the correspondent number of genes.

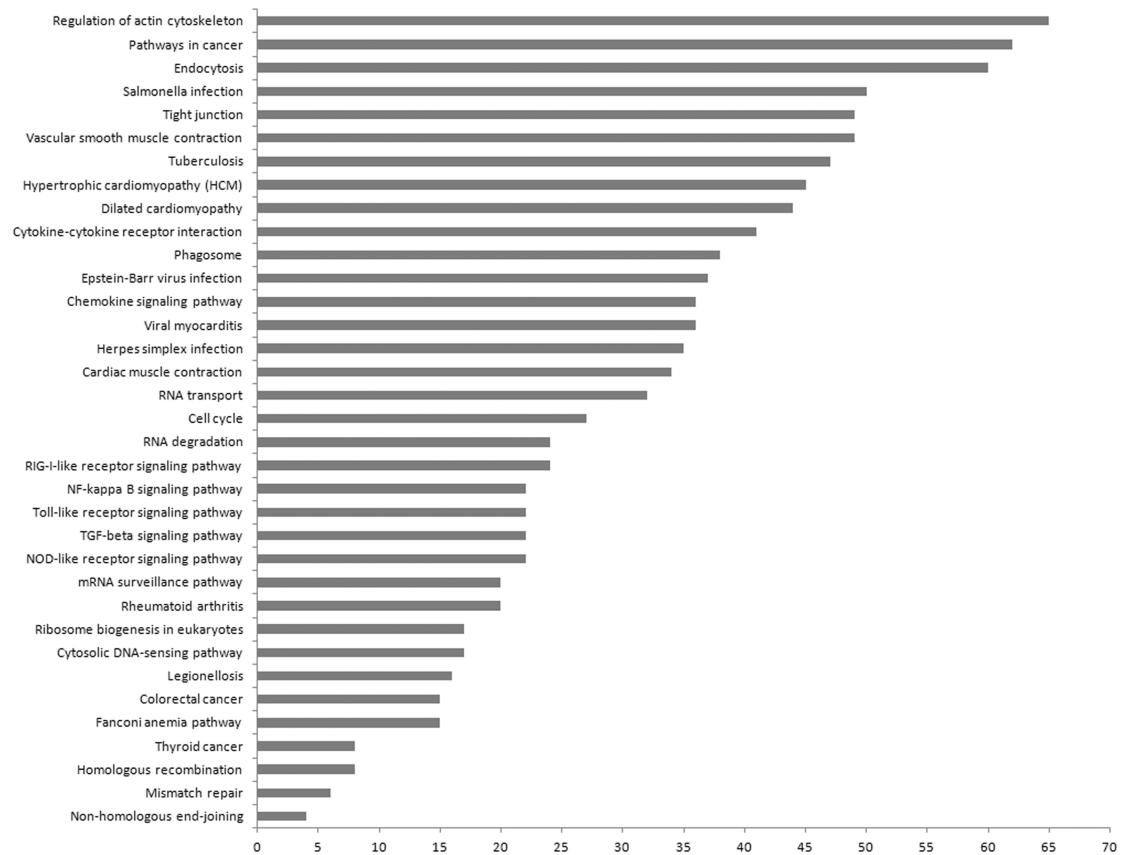


Figure S6. Pathway annotations for the differentially expressed genes. The X-axis indicates the correspondent number of genes.