Supplemental table 1a

	6 hours			24 hours		
	rQnestin34.5	VPA+ rQnestin34.5	p-value	rQnestin34.5	VPA+ rQnestin34.5	p-value
CD69	34 (7.8)	7 (4.7)	0.007	42 (3.6)	30 (5.8)	0.046
CD62L	63 (4.5)	41 (5.5)	0.006	71.7 (2.7)	62 (6.4)	0.032
NKp46	84 (3.0)	64 (4.0)	0.002	85 (4.9)	78 (.8)	0.027
Ly49d	40 (12.5)	18 (7.5)	0.043	51 (10.6)	23 (9.1)	0.025
Ly49c	49 (5)	23 (8.1)	0.010	73 (6.4)	47 (2.6)	0.002

Supplemental table 1a: VPA co-administration with oHSV reduces the activation phenotype of recruited NK cells and macrophages. Human U87dEGFR cells (10^5) were implanted intracranially into athymic mice brains and allowed to grow for 9 days. rQnestin34.5 (10^4 pfu/3ml vehicle) was then stereotactically inoculated, using the same coordinates. For VPA treated mice, two VPA treatments were performed at 12 hour intervals the day before oHSV inoculation. Six or twenty-four later mice were sacrificed and the surface expression of activation antigens were assessed on NK cells (CD69, CD62L, NKp46, Ly49d) and macrophages (Ly49c) from tumor bearing hemispheres using FACS (n=4-3 mice/group). The values in parentheses indicate the standard deviation.

Supplemental table 1b

	U87dEGFR+ Veh.	U87dEGFR+ VPA+Veh.	p-value
CD69	25	22	0.5
CD62L	48	51	0.46
NKp46	74	75	0.71
Ly49d	28	24	0.58
Ly6c	27	20	0.45

Supplemental table 1b: VPA administration in vehicle treated mice does not alter the activation phenotype of recruited NK cells and macrophages. Human U87dEGFR cells (10^5) were implanted intracranially into athymic mice brains and allowed to grow for 9 days. For VPA treated mice, two VPA treatments were performed at 12 hour intervals the day before HBSS inoculation. Twenty-four later mice were sacrificed and the surface expression of activation antigens were assessed on NK cells (CD69, CD62L, NKp46, Ly49d) and macrophages (Ly49c) from tumor bearing hemispheres using FACS (n=3 mice/group).

Supplemental table 2a

Symbol	**Description**	Fold Up- or Down-Regulation	T-TEST
		VPA+rQnestin34.5/rQnestin34.5	p value
Abcf1	ATP-binding cassette, sub-family F (GCN20), member 1	1.17	0.13
Bcl6	B-cell leukemia/lymphoma 6	-1.12	0.13
Cxcr5	Chemochine (C-X-C motif) receptor 5	1.30	0.07

C3	Complement component 3	-1.09	0.41
Casp1	Caspase 1	1.03	0.50
Ccl1	Chemokine (C-C motif) ligand 1	-1.05	0.69
Ccl11	Chemokine (C-C motif) ligand 11	-1.27	0.39
Ccl12	Chemokine (C-C motif) ligand 12	-1.40	0.11
Ccl17	Chemokine (C-C motif) ligand 17	-1.16	0.41
Ccl19	Chemokine (C-C motif) ligand 19	-1.25	0.37
Ccl2	Chemokine (C-C motif) ligand 2	1.34	0.15
Ccl20	Chemokine (C-C motif) ligand 20	1.19	1.00
Ccl22	Chemokine (C-C motif) ligand 22	1.07	0.96
Ccl24	Chemokine (C-C motif) ligand 24	-1.37	0.29
Ccl25	Chemokine (C-C motif) ligand 25	1.27	0.03
Ccl3	Chemokine (C-C motif) ligand 3	1.18	0.51
Ccl4	Chemokine (C-C motif) ligand 4	1.13	0.74
Ccl5	Chemokine (C-C motif) ligand 5	-1.02	0.64
Ccl6	Chemokine (C-C motif) ligand 6	-1.05	0.47
Ccl7	Chemokine (C-C motif) ligand 7	1.00	0.86
Ccl8	Chemokine (C-C motif)	-1.29	0.13

	ligand 8		
Ccl9	Chemokine (C-C motif) ligand 9	-1.72	0.09
Ccr1	Chemokine (C-C motif) receptor 1	-1.14	0.20
Ccr2	Chemokine (C-C motif) receptor 2	-1.38	0.14
Ccr3	Chemokine (C-C motif) receptor 3	-1.24	0.13
Ccr4	Chemokine (C-C motif) receptor 4	-2.32	0.22
Ccr5	Chemokine (C-C motif) receptor 5	-1.19	0.16
Ccr6	Chemokine (C-C motif) receptor 6	-1.41	0.47
Ccr7	Chemokine (C-C motif) receptor 7	1.01	0.93
Ccr8	Chemokine (C-C motif) receptor 8	-2.46	0.12
Ccr9	Chemokine (C-C motif) receptor 9	-1.08	0.55
Crp	C-reactive protein, pentraxin-related	1.17	0.47
Cx3cl1	Chemokine (C-X3-C motif) ligand 1	-1.05	0.28
Cxcl1	Chemokine (C-X-C motif) ligand 1	1.37	0.30
Cxcl10	Chemokine (C-X-C motif) ligand 10	1.35	0.22
Cxcl11	Chemokine (C-X-C motif) ligand 11	-1.10	0.69
Cxcl12	Chemokine (C-X-C motif) ligand 12	-1.06	0.48

Cxcl13	Chemokine (C-X-C motif) ligand 13	1.06	0.57
Cxcl15	Chemokine (C-X-C motif) ligand 15	N/A	N/A
Pf4	Platelet factor 4	-1.02	0.94
Cxcl5	Chemokine (C-X-C motif) ligand 5	-1.74	0.07
Cxcl9	Chemokine (C-X-C motif) ligand 9	-1.00	0.94
Cxcr3	Chemokine (C-X-C motif) receptor 3	-2.02	0.04
Ccr10	Chemokine (C-C motif) receptor 10	-1.00	0.97
Ifng	Interferon gamma	-1.84	0.02
Il10	Interleukin 10	-1.27	0.22
Il10ra	Interleukin 10 receptor, alpha	1.10	0.43
Il10rb	Interleukin 10 receptor, beta	-1.01	0.96
Il11	Interleukin 11	-1.27	0.05
Il13	Interleukin 13	-1.09	0.61
Il13ra1	Interleukin 13 receptor, alpha 1	1.07	0.40
Il15	Interleukin 15	1.10	0.32
Il16	Interleukin 16	-1.34	0.35
Il17b	Interleukin 17B	-1.55	0.02
Il18	Interleukin 18	-1.14	0.19
Il1a	Interleukin 1 alpha	1.39	0.10
Il1b	Interleukin 1 beta	1.58	0.12
Il1f6	Interleukin 1 family,	-1.20	0.59

	member 6		
Il1f8	Interleukin 1 family, member 8	1.01	0.97
Il1r1	Interleukin 1 receptor, type I	-1.10	0.16
Il1r2	Interleukin 1 receptor, type II	1.41	0.15
Il20	Interleukin 20	1.11	0.67
Il2rb	Interleukin 2 receptor, beta chain	1.02	0.86
Il2rg	Interleukin 2 receptor, gamma chain	1.08	0.15
Il3	Interleukin 3	1.35	0.49
Il4	Interleukin 4	-1.09	0.61
Il5ra	Interleukin 5 receptor, alpha	1.00	0.97
Il6ra	Interleukin 6 receptor, alpha	-1.15	0.01
Il6st	Interleukin 6 signal transducer	-1.12	0.74
Il8rb	Interleukin 8 receptor, beta	1.33	0.22
Itgam	Integrin alpha M	-1.11	0.28
Itgb2	Integrin beta 2	1.07	0.65
Lta	Lymphotoxin A	-1.55	0.05
Ltb	Lymphotoxin B	-1.20	0.30
Mif	Macrophage migration inhibitory factor	1.03	0.46
Scye1	Small inducible cytokine subfamily E, member 1	1.06	0.30
Spp1	Secreted phosphoprotein 1	-1.26	0.02

Tgfb1	Transforming growth factor, beta 1	1.05	0.59
Tnf	Tumor necrosis factor	1.29	0.07
Tnfrsf1a	Tumor necrosis factor receptor superfamily, member 1a	1.06	0.51
Tnfrsf1b	Tumor necrosis factor receptor superfamily, member 1b	-1.20	0.15
Cd40lg	CD40 ligand	-1.62	N/A
Tollip	Toll interacting protein	1.05	0.39
Xcr1	Chemokine (C motif) receptor 1	-1.36	0.60
Gusb	Glucuronidase, beta	1.03	0.65
Hprt1	Hypoxanthine guanine phosphoribosyl transferase 1	1.04	0.44
Hsp90ab1	Heat shock protein 90 alpha (cytosolic), class B member 1	1.03	0.47
Gapdh	Glyceraldehyde-3-phosphate dehydrogenase	-1.01	0.58
Actb	Actin, beta	-1.09	0.11

Supplemental table 2b

Symbol	**Description**	Fold Up- or Down-Regulation	T-TEST
		VPA+rQnestin34.5/rQnestin34.5	p value
Abcf1	ATP-binding cassette, sub-family F (GCN20), member 1	1.02	0.80
Bcl6	B-cell leukemia/lymphoma 6	1.07	0.34
Cxcr5	Chemochine (C-X-C motif)	1.12	0.50

	receptor 5		
C3	Complement component 3	-1.07	0.54
Casp1	Caspase 1	1.06	0.93
Ccl1	Chemokine (C-C motif) ligand 1	1.20	0.54
Ccl11	Chemokine (C-C motif) ligand 11	-1.13	0.88
Ccl12	Chemokine (C-C motif) ligand 12	1.32	0.20
Ccl17	Chemokine (C-C motif) ligand 17	1.37	0.06
Ccl19	Chemokine (C-C motif) ligand 19	-1.61	0.79
Ccl2	Chemokine (C-C motif) ligand 2	1.27	0.42
Ccl20	Chemokine (C-C motif) ligand 20	1.83	0.06
Ccl22	Chemokine (C-C motif) ligand 22	-1.21	0.52
Ccl24	Chemokine (C-C motif) ligand 24	1.25	0.51
Ccl25	Chemokine (C-C motif) ligand 25	-1.00	0.89
Ccl3	Chemokine (C-C motif) ligand 3	1.18	0.83
Ccl4	Chemokine (C-C motif) ligand 4	1.33	0.34
Ccl5	Chemokine (C-C motif) ligand 5	1.32	0.31
Ccl6	Chemokine (C-C motif) ligand 6	1.10	0.94
Ccl7	Chemokine (C-C motif) ligand 7	1.36	0.34

Ccl8	Chemokine (C-C motif) ligand 8	-1.30	0.46
Ccl9	Chemokine (C-C motif) ligand 9	-1.45	0.08
Ccr1	Chemokine (C-C motif) receptor 1	1.02	0.73
Ccr2	Chemokine (C-C motif) receptor 2	-1.15	0.38
Ccr3	Chemokine (C-C motif) receptor 3	-1.09	0.53
Ccr4	Chemokine (C-C motif) receptor 4	1.35	0.68
Ccr5	Chemokine (C-C motif) receptor 5	-1.05	0.67
Ccr6	Chemokine (C-C motif) receptor 6	-2.38	0.31
Ccr7	Chemokine (C-C motif) receptor 7	1.49	0.15
Ccr8	Chemokine (C-C motif) receptor 8	-1.12	N/A
Ccr9	Chemokine (C-C motif) receptor 9	-1.15	0.39
Crp	C-reactive protein, pentraxin-related	1.29	N/A
Cx3cl1	Chemokine (C-X3-C motif) ligand 1	1.00	0.93
Cxcl1	Chemokine (C-X-C motif) ligand 1	1.05	0.59
Cxcl10	Chemokine (C-X-C motif) ligand 10	1.56	0.14
Cxcl11	Chemokine (C-X-C motif) ligand 11	1.70	0.15
Cxcl12	Chemokine (C-X-C motif)	1.00	0.98

	ligand 12		
Cxcl13	Chemokine (C-X-C motif) ligand 13	-1.10	0.54
Cxcl15	Chemokine (C-X-C motif) ligand 15	N/A	N/A
Pf4	Platelet factor 4	-1.01	0.74
Cxcl5	Chemokine (C-X-C motif) ligand 5	-1.19	0.76
Cxcl9	Chemokine (C-X-C motif) ligand 9	1.18	0.78
Cxcr3	Chemokine (C-X-C motif) receptor 3	-1.28	0.45
Ccr10	Chemokine (C-C motif) receptor 10	-1.08	0.42
Ifng	Interferon gamma	2.26	0.17
Il10	Interleukin 10	-1.08	0.74
Il10ra	Interleukin 10 receptor, alpha	1.01	0.95
Il10rb	Interleukin 10 receptor, beta	1.09	0.74
Il11	Interleukin 11	-1.15	0.22
Il13	Interleukin 13	1.27	0.58
Il13ra1	Interleukin 13 receptor, alpha 1	-1.01	0.84
Il15	Interleukin 15	1.02	0.93
Il16	Interleukin 16	1.02	0.99
Il17b	Interleukin 17B	-1.24	0.23
Il18	Interleukin 18	-1.12	0.30
Il1a	Interleukin 1 alpha	1.05	0.86
Il1b	Interleukin 1 beta	-1.12	0.59
Il1f6	Interleukin 1 family,	1.67	0.25

	member 6		
Il1f8	Interleukin 1 family, member 8	-1.09	0.84
Il1r1	Interleukin 1 receptor, type I	1.03	0.82
Il1r2	Interleukin 1 receptor, type II	1.04	0.86
Il20	Interleukin 20	-1.30	N/A
Il2rb	Interleukin 2 receptor, beta chain	1.28	0.34
Il2rg	Interleukin 2 receptor, gamma chain	-1.03	0.79
Il3	Interleukin 3	-1.66	0.31
Il4	Interleukin 4	-1.01	0.70
Il5ra	Interleukin 5 receptor, alpha	-1.32	0.06
Il6ra	Interleukin 6 receptor, alpha	-1.06	0.63
Il6st	Interleukin 6 signal transducer	-1.03	0.67
Il8rb	Interleukin 8 receptor, beta	-1.15	0.53
Itgam	Integrin alpha M	-1.03	0.75
Itgb2	Integrin beta 2	1.05	0.93
Lta	Lymphotoxin A	1.60	0.07
Ltb	Lymphotoxin B	1.26	0.44
Mif	Macrophage migration inhibitory factor	1.17	0.11
Scye1	Small inducible cytokine subfamily E, member 1	-1.31	0.36
Spp1	Secreted phosphoprotein 1	-1.13	0.57
Tgfb1	Transforming growth factor, beta 1	1.01	0.90
Tnf	Tumor necrosis factor	1.35	0.32

Tnfrsf1a	Tumor necrosis factor receptor superfamily, member 1a	1.07	0.73
Tnfrsf1b	Tumor necrosis factor receptor superfamily, member 1b	1.00	0.92
Cd40lg	CD40 ligand	-2.41	N/A
Tollip	Toll interacting protein	1.04	0.30
Xcr1	Chemokine (C motif) receptor 1	-1.06	0.80
Gusb	Glucuronidase, beta	-1.02	0.73
Hprt1	Hypoxanthine guanine phosphoribosyl transferase 1	1.06	0.57
Hsp90ab1	Heat shock protein 90 alpha (cytosolic), class B member 1	-1.02	0.70
Gapdh	Glyceraldehyde-3-phosphate dehydrogenase	1.05	0.44
Actb	Actin, beta	1.03	0.80

Supplemental table 2: List of inflammatory cytokines in tumor tissue after either oHSV treatment or VPA treatment followed by oHSV administration. Human U87dEGFR cells (10^5) were implanted intracranially into athymic mice brains and allowed to grow for 9 days. rQnestin34.5 (10^4 pfu/3ml vehicle) was then stereotactically inoculated, using the same coordinates. For VPA treated mice, two VPA treatments were performed at 12 hour intervals the day before oHSV inoculation. Twenty-four (a) or seventy-two hours later (b), mice were sacrificed for mRNA isolation of the tumor bearing hemisphere. Following mRNA conversion to cDNA, the expression of 84 mouse inflammatory genes were analyzed by RT-qPCR array. Values > 1 indicate genes that

are up-regulated compared rQnestin34.5 treated mice and values < 1 indicate genes that are down-regulated compared to rQnestin34.5 treated mice.

Supplemental Figure 1: VPA administration in vehicle treated mice does not alter immune cell infiltration. Human U87dEGFR cells (10^5) were implanted intracranially into athymic mice brains and allowed to grow for 9 days. For VPA treated mice, two VPA treatments were performed at 12 hour intervals the day before HBSS inoculation. Twenty-four hours later, mice were sacrificed and tumor bearing hemispheres were harvested to quantify the number of recruited NK, macrophages, and lymphocytes by FACS.

Supplemental Figure 2: Comparison of IFN-γ production by NK cells upon stimulation with cytokines or Toll-like receptor stimuli in the presence or absence of VPA. Data showed that in vitro NK cells respond to cytokine stimulation to produce IFN-γ and the responsiveness is inhibited by VPA. However, the level of IFN-γ production by NK cells upon stimulation with Toll-like receptor stimuli, LPS and Pam2CSK4, was very low or undetectable.

Supplemental figure 3: VPA does not alter the rate of encephalitis onset in mice treated with wild-type HSV. Glioblastoma free athymic mice were treated with either vehicle or two VPA treatments at 12 hour intervals the day before wild-type HSV inoculation. The following day, wild-type HSV (10^4 pfu) was inoculated intracranially and mice were monitored for the onset of neurological symptoms.