

**Supplementary Table 1. The mean  $\pm$  SD of PWMT (g) in the sham and tumor mice.**

Day after operation	0	4	7	10	14	21	28
Sham	1.55 $\pm$ 0.28	0.58 $\pm$ 0.20	1.20 $\pm$ 0.21	1.63 $\pm$ 0.31	1.45 $\pm$ 0.38	1.58 $\pm$ 0.38	1.53 $\pm$ 0.43
Tumor	1.63 $\pm$ 0.31	0.52 $\pm$ 0.25	0.95 $\pm$ 0.26	0.58 $\pm$ 0.20	0.42 $\pm$ 0.14	0.34 $\pm$ 0.11	0.31 $\pm$ 0.12

**Supplementary Table 2. The mean  $\pm$  SD of NSF (times/2 min) in the sham and tumor mice.**

Day after operation	0	4	7	10	14	21	28
Sham	0.25 $\pm$ 0.09	3.58 $\pm$ 0.27	1.63 $\pm$ 0.29	0.63 $\pm$ 0.20	0.28 $\pm$ 0.18	0.25 $\pm$ 0.14	0.25 $\pm$ 0.26
Tumor	0.33 $\pm$ 0.15	3.10 $\pm$ 0.26	3.78 $\pm$ 0.36	5.90 $\pm$ 0.59	9.20 $\pm$ 0.57	0.73 $\pm$ 0.72	13.08 $\pm$ 0.48

**Supplementary Table 3. The mean  $\pm$  SD of PWMT (g) in mice after 4-PBA-treatment.**

Time after injection (hour)	baseline(0)	1	2	3	4	5	7	10
Tumor + vehicle	0.31 $\pm$ 0.12	0.34 $\pm$ 0.11	0.33 $\pm$ 0.16	0.31 $\pm$ 0.12	0.40 $\pm$ 0.12	0.34 $\pm$ 0.16	0.39 $\pm$ 0.17	0.37 $\pm$ 0.14
Sham + vehicle	1.80 $\pm$ 0.39	1.78 $\pm$ 0.31	1.70 $\pm$ 0.32	1.85 $\pm$ 0.28	1.70 $\pm$ 0.32	1.78 $\pm$ 0.31	1.65 $\pm$ 0.40	1.85 $\pm$ 0.28
Tumor + 4-PBA (i.p. 1mg)	0.34 $\pm$ 0.11	0.47 $\pm$ 0.16	0.75 $\pm$ 0.21	0.90 $\pm$ 0.28	0.75 $\pm$ 0.21	0.53 $\pm$ 0.10	0.48 $\pm$ 0.10	0.31 $\pm$ 0.12
Tumor + 4-PBA (i.t. 40 $\mu$ g)	0.31 $\pm$ 0.12	1.00 $\pm$ 0.30	1.20 $\pm$ 0.21	1.28 $\pm$ 0.35	1.25 $\pm$ 0.21	1.10 $\pm$ 0.28	0.80 $\pm$ 0.21	0.45 $\pm$ 0.15
Tumor + 4-PBA (i.t. 80 $\mu$ g)	0.34 $\pm$ 0.16	1.15 $\pm$ 0.21	1.63 $\pm$ 0.31	1.65 $\pm$ 0.40	1.60 $\pm$ 0.45	1.45 $\pm$ 0.38	1.05 $\pm$ 0.26	0.63 $\pm$ 0.25
Tumor + 4-PBA (i.t. 120 $\mu$ g)	0.31 $\pm$ 0.12	0.42 $\pm$ 0.18	0.42 $\pm$ 0.14	0.45 $\pm$ 0.15	0.48 $\pm$ 0.10	0.37 $\pm$ 0.14	0.34 $\pm$ 0.16	0.31 $\pm$ 0.17

**Supplementary Table 4. The mean  $\pm$  SD of NSF (times/2 min) in mice after 4-PBA-treatment.**

Time after injection (hour)	baseline(0)	1	2	3	4	5	7	10
Tumor + vehicle	7.63 $\pm$ 1.36	8.13 $\pm$ 1.36	7.62 $\pm$ 1.01	8.63 $\pm$ 0.92	8.13 $\pm$ 0.84	7.50 $\pm$ 1.20	8.38 $\pm$ 1.41	7.75 $\pm$ 1.28
Sham + vehicle	0.50 $\pm$ 0.54	0.13 $\pm$ 0.35	0.38 $\pm$ 0.52	0.25 $\pm$ 0.46	0.38 $\pm$ 0.52	0.38 $\pm$ 0.51	0.50 $\pm$ 0.54	0.25 $\pm$ 0.46
Tumor + 4-PBA (i.p. 1mg)	8.13 $\pm$ 1.13	7.63 $\pm$ 1.41	5.75 $\pm$ 0.71	5.00 $\pm$ 0.76	5.13 $\pm$ 0.84	7.13 $\pm$ 1.13	8.00 $\pm$ 1.31	8.13 $\pm$ 0.84
Tumor + 4-PBA (i.t. 40 $\mu$ g)	8.00 $\pm$ 1.31	5.38 $\pm$ 1.06	4.38 $\pm$ 0.92	3.50 $\pm$ 0.93	4.63 $\pm$ 0.92	5.75 $\pm$ 1.04	6.88 $\pm$ 1.00	8.00 $\pm$ 1.31
Tumor + 4-PBA (i.t. 80 $\mu$ g)	8.00 $\pm$ 1.20	6.00 $\pm$ 1.07	3.25 $\pm$ 1.04	0.88 $\pm$ 0.64	2.38 $\pm$ 0.92	4.25 $\pm$ 1.04	6.50 $\pm$ 1.41	8.50 $\pm$ 0.93
Tumor + 4-PBA (i.t. 120 $\mu$ g)	7.88 $\pm$ 1.36	8.25 $\pm$ 1.04	8.13 $\pm$ 1.00	7.88 $\pm$ 1.46	7.75 $\pm$ 1.17	8.25 $\pm$ 1.17	8.13 $\pm$ 1.13	8.13 $\pm$ 1.13

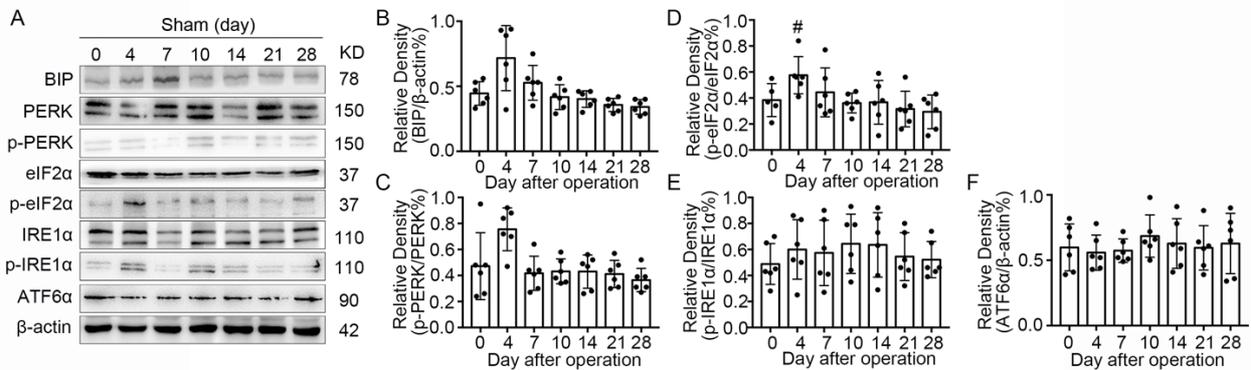
**Supplementary Table 5. The mean  $\pm$  SD of PWMT (g) in mice after GSK2606414-treatment.**

Time after injection (hour)	baseline(0)	1	2	3	4	5	7	10
Tumor + vehicle	0.42 $\pm$ 0.14	0.40 $\pm$ 0.12	0.31 $\pm$ 0.12	0.37 $\pm$ 0.14	0.34 $\pm$ 0.11	0.34 $\pm$ 0.16	0.34 $\pm$ 0.11	0.31 $\pm$ 0.12
Sham + vehicle	1.70 $\pm$ 0.32	1.78 $\pm$ 0.31	1.80 $\pm$ 0.39	1.70 $\pm$ 0.32	1.73 $\pm$ 0.40	1.85 $\pm$ 0.28	1.70 $\pm$ 0.32	1.73 $\pm$ 0.40
Tumor + GSK (i.t. 50 $\mu$ g)	0.34 $\pm$ 0.11	0.42 $\pm$ 0.14	0.45 $\pm$ 0.09	0.58 $\pm$ 0.20	0.48 $\pm$ 0.10	0.40 $\pm$ 0.12	0.34 $\pm$ 0.11	0.31 $\pm$ 0.12
Tumor + GSK (i.t. 100 $\mu$ g)	0.34 $\pm$ 0.11	0.80 $\pm$ 0.21	0.90 $\pm$ 0.19	0.95 $\pm$ 0.26	0.75 $\pm$ 0.28	0.70 $\pm$ 0.26	0.55 $\pm$ 0.21	0.34 $\pm$ 0.11
Tumor + GSK (i.t. 200 $\mu$ g)	0.37 $\pm$ 0.08	0.90 $\pm$ 0.19	1.25 $\pm$ 0.21	1.38 $\pm$ 0.31	1.10 $\pm$ 0.19	0.95 $\pm$ 0.26	0.70 $\pm$ 0.26	0.42 $\pm$ 0.12

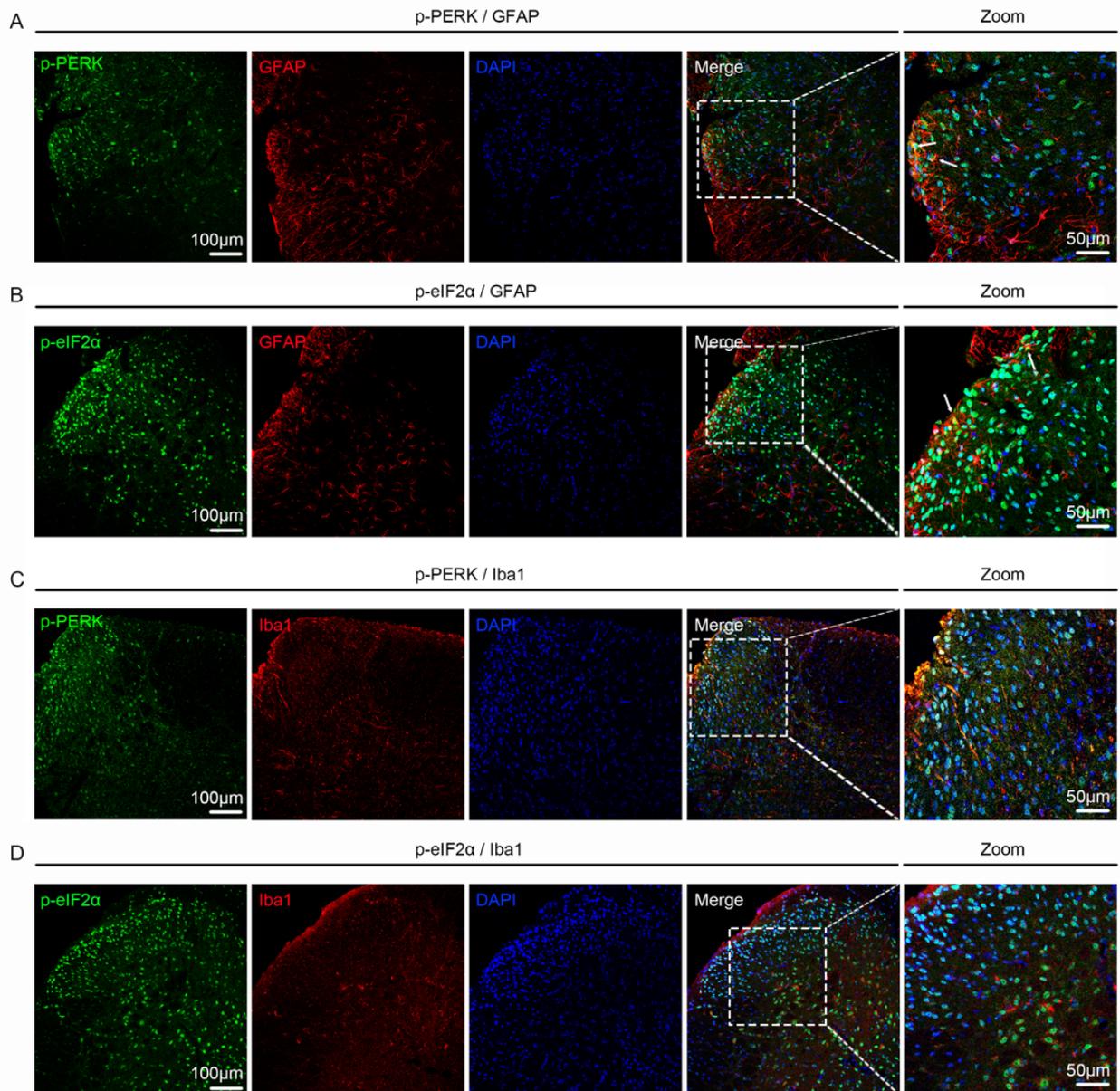
**Supplementary Table 6. The mean  $\pm$  SD of NSF (times/2 min) in mice after GSK2606414-treatment.**

Time after injection (hour)	baseline(0)	1	2	3	4	5	7	10
Tumor + vehicle	7.87 $\pm$ 1.13	8.13 $\pm$ 1.25	7.62 $\pm$ 1.30	8.00 $\pm$ 1.07	7.63 $\pm$ 1.19	7.75 $\pm$ 1.23	8.13 $\pm$ 1.13	7.88 $\pm$ 1.13
Sham + vehicle	0.38 $\pm$ 0.52	0.25 $\pm$ 0.46	0.38 $\pm$ 0.52	0.50 $\pm$ 0.54	0.63 $\pm$ 0.52	0.50 $\pm$ 0.54	0.38 $\pm$ 0.52	0.63 $\pm$ 0.52
Tumor + GSK (i.t. 50 $\mu$ g)	8.13 $\pm$ 1.13	7.88 $\pm$ 0.64	6.50 $\pm$ 0.76	6.25 $\pm$ 0.71	6.63 $\pm$ 0.74	7.37 $\pm$ 0.92	8.00 $\pm$ 0.76	8.38 $\pm$ 1.06
Tumor + GSK (i.t. 100 $\mu$ g)	8.37 $\pm$ 1.06	7.25 $\pm$ 1.04	6.13 $\pm$ 0.84	4.75 $\pm$ 0.71	5.00 $\pm$ 0.54	5.62 $\pm$ 0.92	7.25 $\pm$ 1.04	8.25 $\pm$ 1.04
Tumor + GSK (i.t. 200 $\mu$ g)	8.00 $\pm$ 0.93	6.75 $\pm$ 1.04	4.87 $\pm$ 1.13	3.25 $\pm$ 1.04	4.38 $\pm$ 1.06	5.88 $\pm$ 0.99	7.13 $\pm$ 0.84	8.38 $\pm$ 1.06

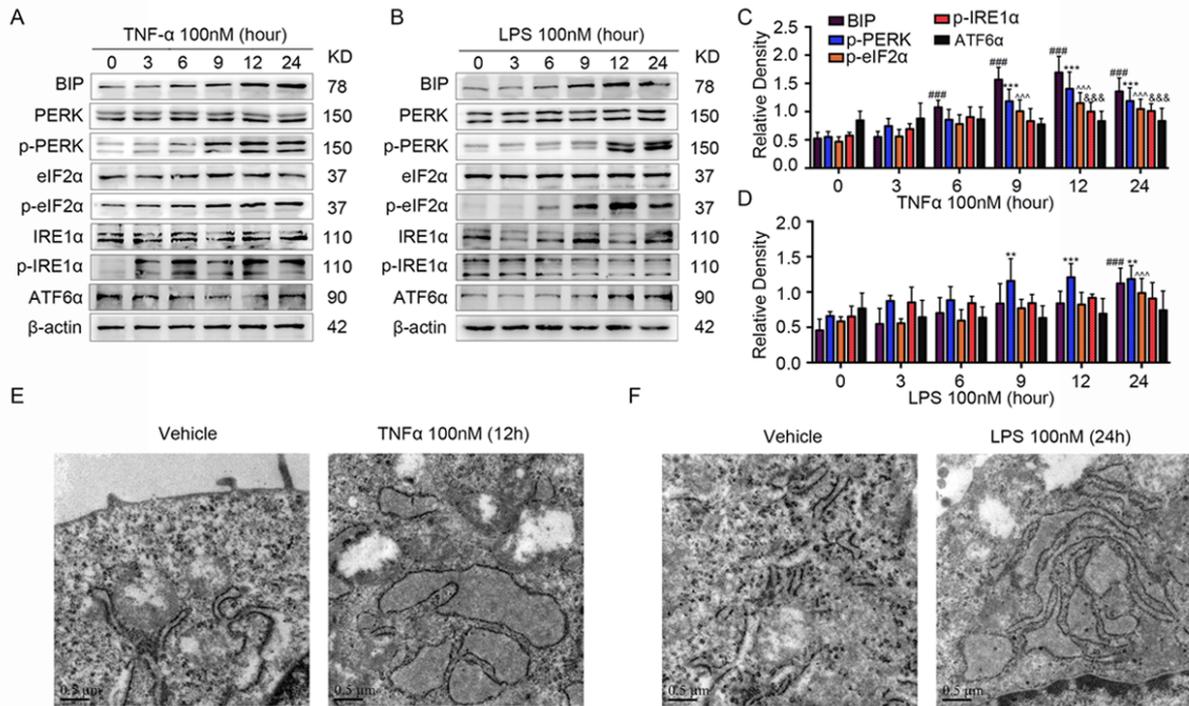
**Supplementary Fig 1. Expression of ER-stress-related proteins in sham mice on postoperative days.** (A) The level of ER-stress related proteins in sham mice. (B) (C) (D) (E) (F) Quantification of ER-stress-related proteins in the spinal cord in sham group mice. One-way ANOVA with Bonferroni post-hoc test, # $P < 0.05$ , ## $P < 0.01$ , ### $P < 0.001$  compared with day 0;  $n = 6$  per group. Data are expressed as mean  $\pm$  SD.



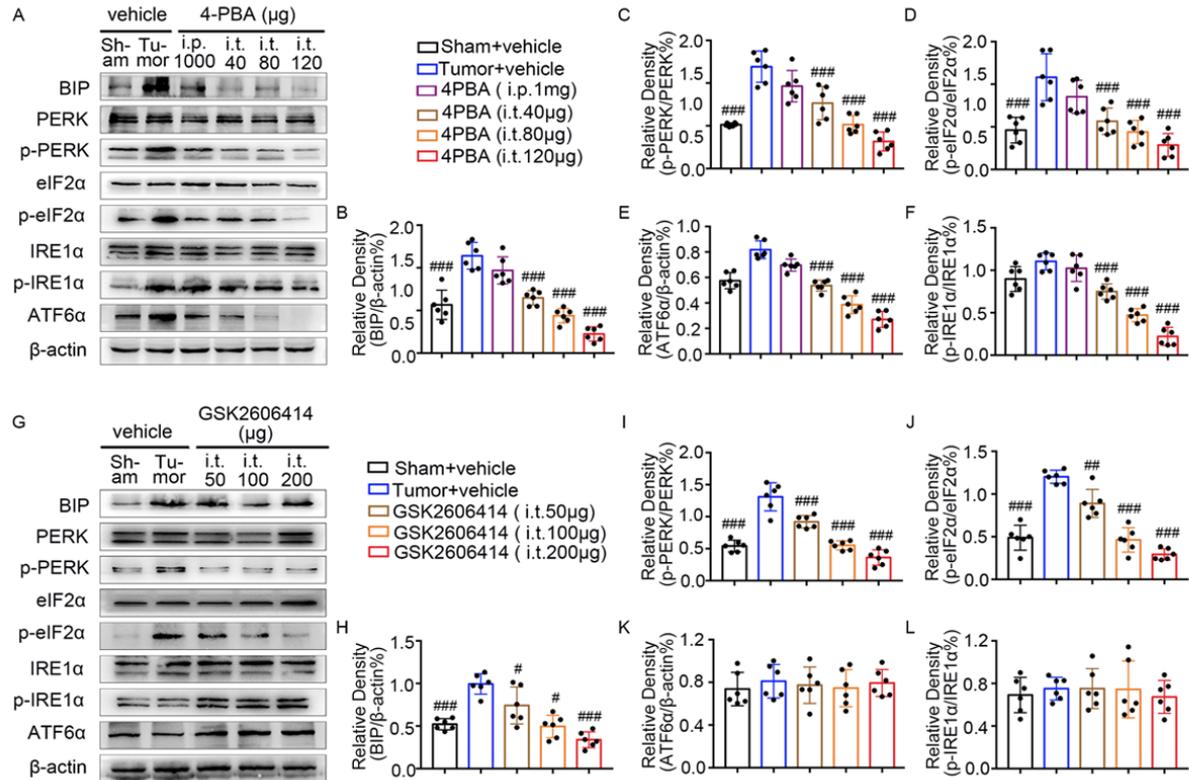
**Supplementary Fig 2. Colocalization of p-PERK/p-elf2 $\alpha$  with GFAP and Iba1 in the dorsal horn of BCP mice.** (A) Double immunostaining with p-PERK (green) and the astrocyte marker GFAP (red); (B) Double immunostaining with p-elf2 $\alpha$  (green) and the astrocyte marker GFAP (red); (C) Double immunostaining with p-PERK (green) and the microglia marker Iba1 (red); (D) Double immunostaining with p-elf2 $\alpha$  (green) and the microglia marker Iba1 (red); Scale bar: 100  $\mu$ m.



**Supplementary Fig 3. Elevated ER stress in the primary cortical neuron stimulated with TNF- $\alpha$  and LPS.** (A) (B) The level of ER-stress-related proteins in the spinal cord in primary cortical neurons stimulated with TNF- $\alpha$  (100nM) and LPS (100nM). (C) (D) Quantification of ER-stress-related proteins in different groups. One-way ANOVA with Bonferroni post-hoc test, #P < 0.05, ##P < 0.01, ###P < 0.001 compared with the expression of BIP at 0 h; \*P < 0.05, \*\*P < 0.01, \*\*\*P < 0.001 compared with the expression of p-PERK at 0 h; ^P < 0.05, ^^P < 0.01, ^^P < 0.001 compared with the expression of p-elf2 $\alpha$  at 0 h; &P < 0.05, &&P < 0.01, &&&P < 0.001 compared with the expression of p-IRE1 $\alpha$  at 0 h; n = 6 per group. Data are expressed as mean  $\pm$  SD. (E) (F) Electron microscopic analysis of primary neurons treated with TNF- $\alpha$  (100nM) and LPS (100nM) respectively. After treatment, both ER cisternae were swollen compared with normally narrow ER cisternae in vehicle treated primary neurons.



**Supplementary Fig 4. Inhibition of ER stress by 4-PBA and inhibition of PERK-elf2 $\alpha$  by GSK2606414 in BCP mice.** (A) The level of ER-stress-related proteins in the spinal cord in BCP mice treated with 4-PBA. (B) (C) (D) (E) (F) Quantification of ER-stress-related proteins in different groups. One-way ANOVA with Bonferroni post-hoc test, # $P < 0.05$ , ## $P < 0.01$ , ### $P < 0.001$  compared with tumor + vehicle group mice;  $n = 6$  per group. (G) The level of ER-stress-related proteins in the spinal cord in BCP mice treated with GSK2606414. (H) (I) (J) (K) (L) Quantification of ER-stress related proteins in different groups. One-way ANOVA with Bonferroni post-hoc test, # $P < 0.05$ , ## $P < 0.01$ , ### $P < 0.001$  compared with tumor + vehicle group mice;  $n = 6$  per group. Data are expressed as mean  $\pm$  SD.



**Supplementary Fig 5. Activation of microglia in the spinal cord after treatment with 4-PBA and GSK2606414 in tumor group mice.** (A) (C) Fluorescent photomicrographs of the microglia marker Iba1 in the spinal cord 3 h after 4-PBA and GSK2606414 injection respectively in tumor group mice. Scale bar: 100  $\mu$ m. (B) (D) Quantification of the Iba1-positive area. One-way ANOVA with Bonferroni post-hoc test, # $P < 0.05$ , ### $P < 0.01$ , #### $P < 0.001$  compared with tumor + vehicle mice;  $n = 6$  per group. Data are expressed as mean  $\pm$  SD.

