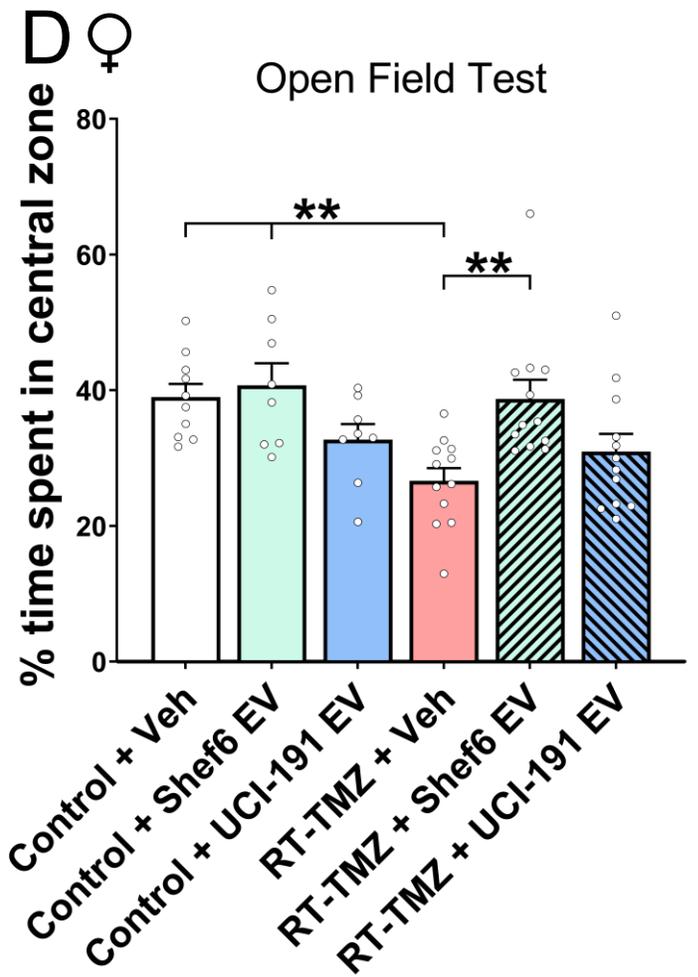
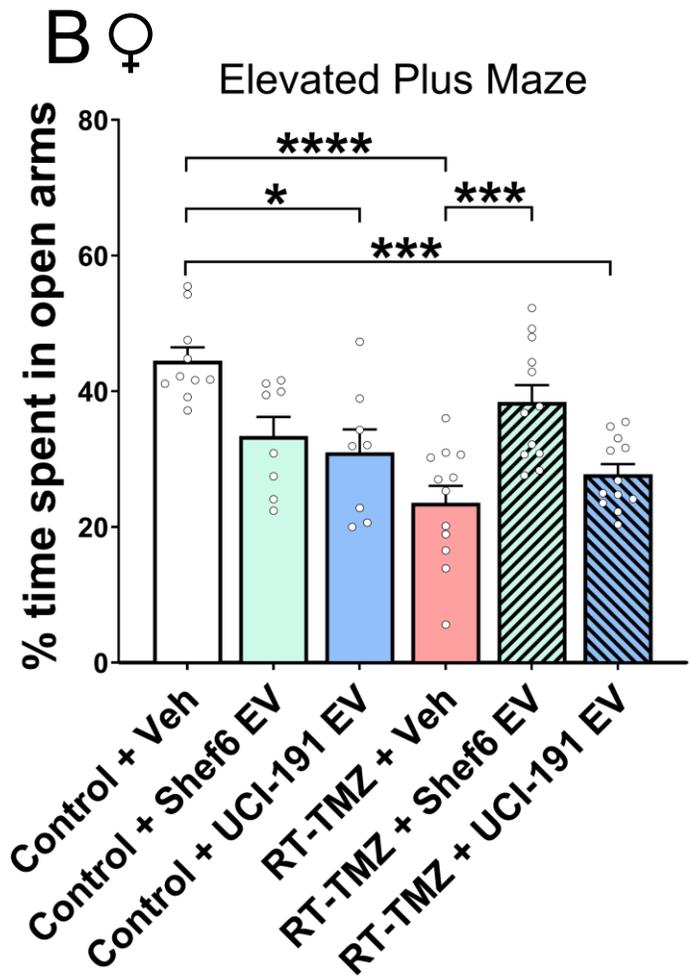
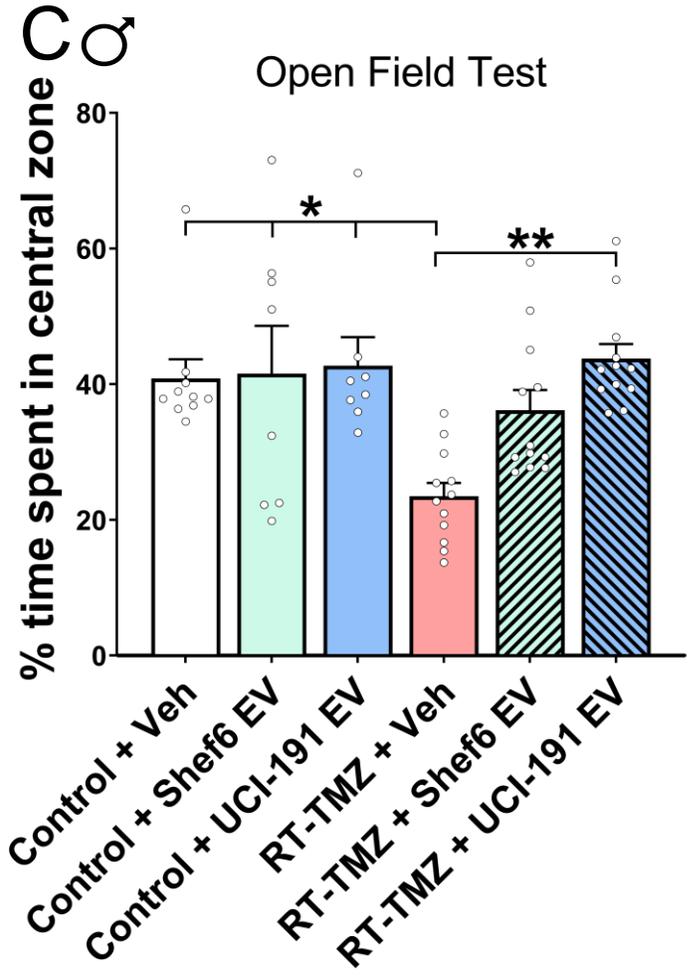
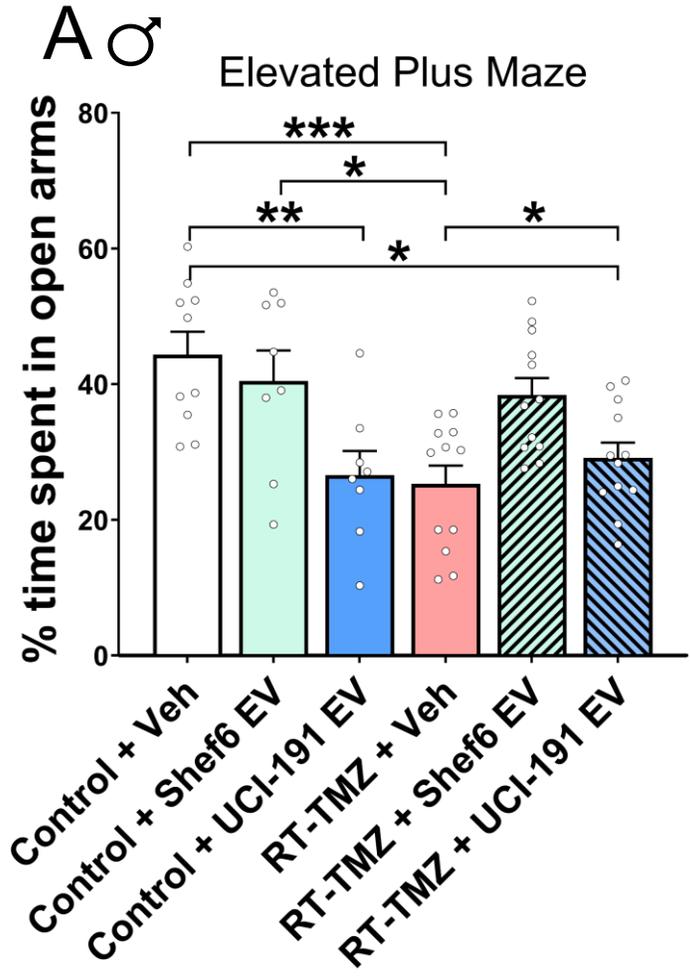


# Supplemental Information

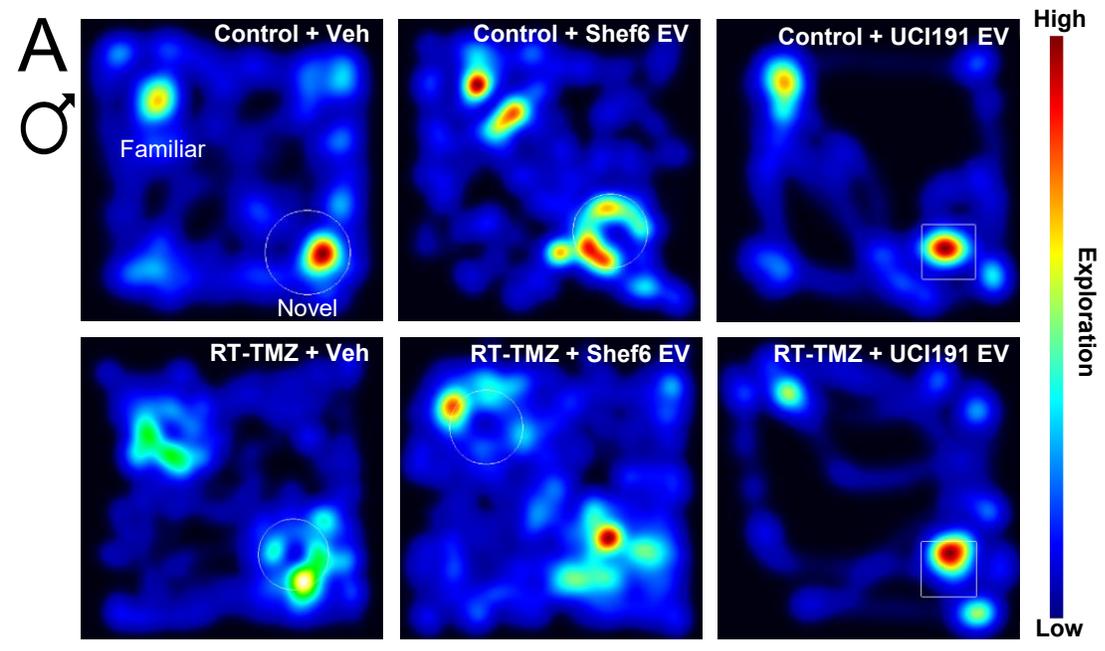


## Supplemental Figure S1

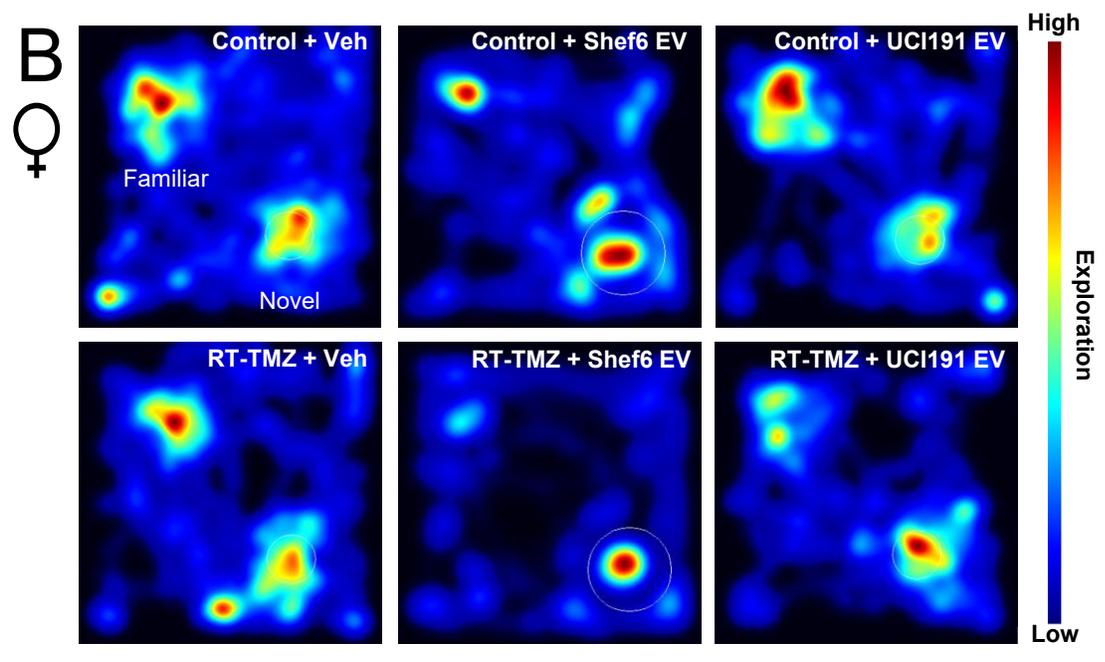
Effects of combined cranial radiotherapy and chemotherapy, or hNSC-derived EVs, on anxiety-like behavior.

Analysis of percent time spent in the open arms of elevated plus maze (EPM) and the percentage time spent in the central zone of an open field arena in the open field test (OFT) is shown for the male (**A** and **B**) and female (**C** and **D**) mice after treatment with cranial radiation therapy (RT) and temozolomide (TMZ) followed by bilateral RO injections of either vehicle (RT-TMZ + Veh) or hNSC-EVs (RT-TMZ + Shef6 EV; RT-TMZ + UCI-191 EV). Combined RT and TMZ exposure (RT-TMZ + Veh) significantly reduced percentage times spent in either open arms (**A, C**; EPM) or the central zone (**C, D**; OFT) by male and female mice. Data are represented by mean  $\pm$  SEM (N = 5-12 animals/group). P values were derived from one-way ANOVA and Bonferroni's multiple comparisons tests. \*,  $P \leq 0.05$ ; \*\*,  $P \leq 0.01$ ; \*\*\*  $P \leq 0.001$ ; \*\*\*\*,  $P \leq 0.0001$ .

### Object Location Memory

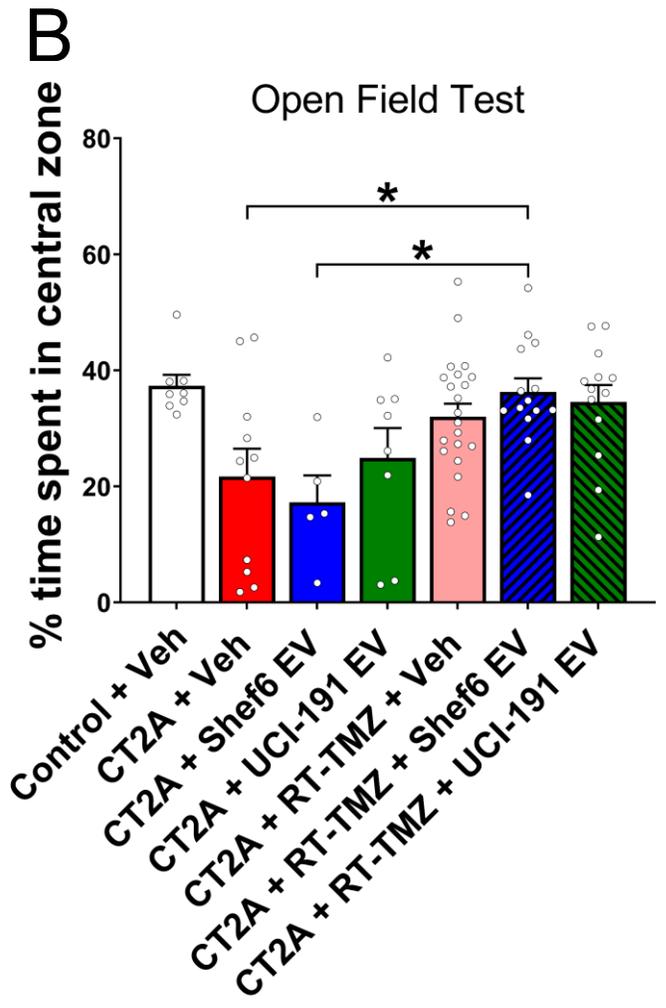
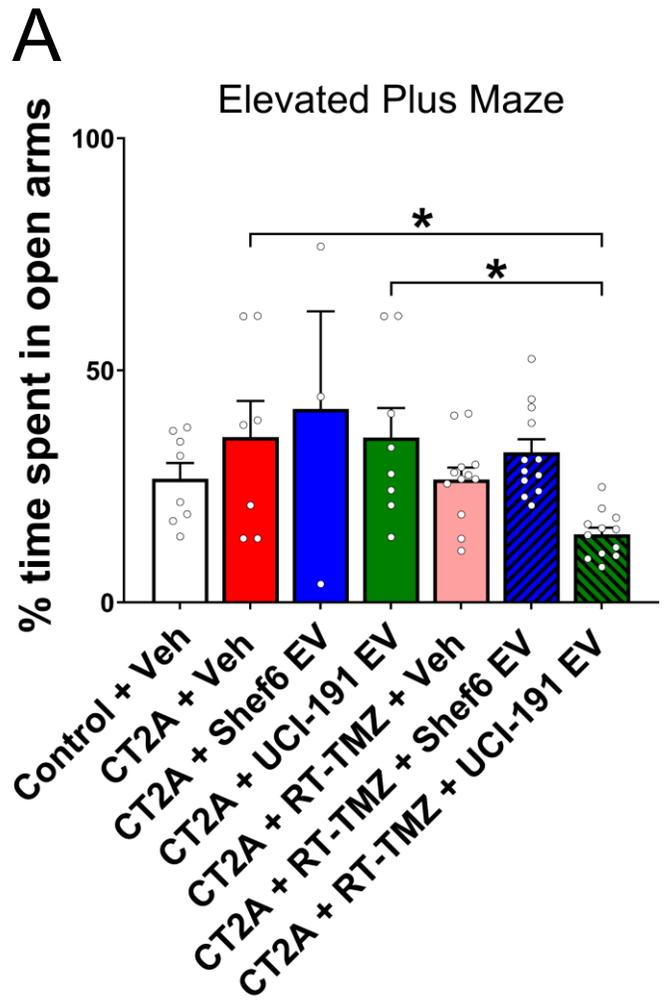


### Object Location Memory



## Supplemental Figure S2

Representative heatmaps depicting exploration throughout object location memory (OLM) test arena for male (**A**) and female (**B**) mice for the data presented in **Figures 2C** and **2E**.

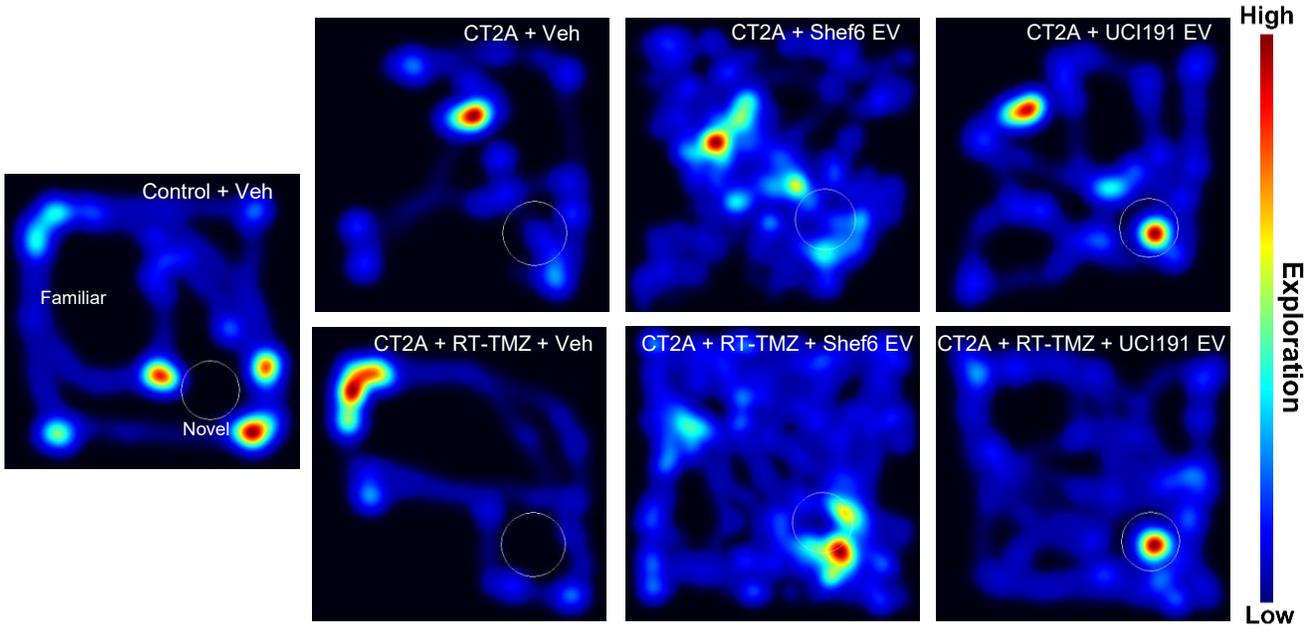


### Supplemental Figure S3

Effects of combined cranial radiotherapy and chemotherapy, or hNSC-derived EVs, on anxiety-like behavior in glioma-bearing mice.

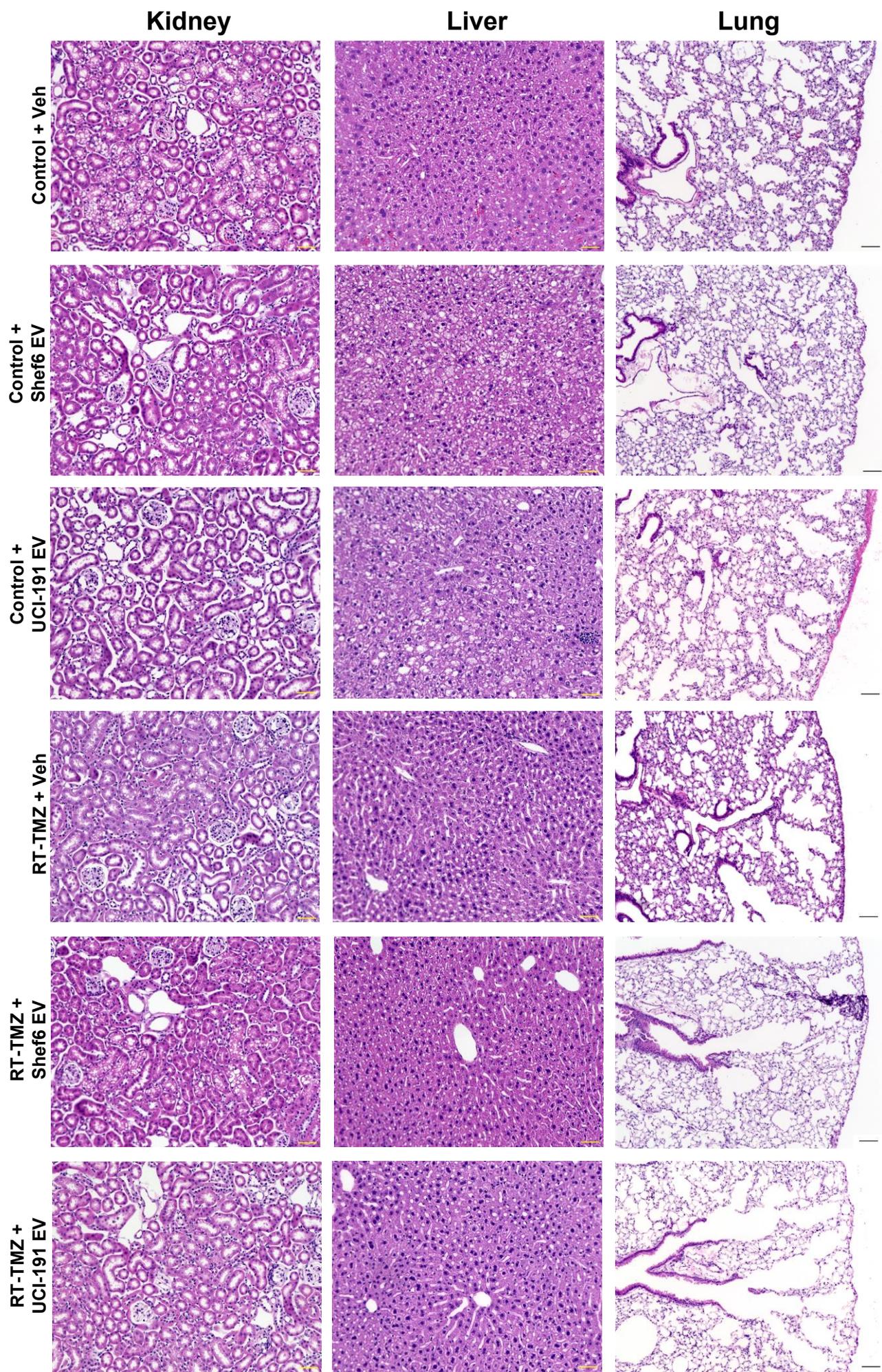
Analysis of percent time spent in the open arms of the elevated plus maze (EPM, **A**) and the percentage time spent in the central zone of an open field arena in the open field test (OFT, **B**) in the control (Control + Veh) and glioma-bearing mice. After confirmation of CT2A-Luc<sup>+</sup> cancer burden, mice were treated with cranial radiation therapy (RT) and chemotherapy followed by bilateral RO injections of hNSC-EVs (CT2A + RT-TMZ + Shef6 EV, CT2A + RT-TMZ + UCI-191 EV) or vehicle (CT2A + RT-TMZ + Veh; sterile PBS). Data are represented by mean  $\pm$  SEM (N = 5-12 animals/group). P values were derived from one-way ANOVA and Bonferroni's multiple comparisons tests. \*,  $P \leq 0.05$ ; \*\*,  $P \leq 0.01$ ; \*\*\*  $P \leq 0.001$ ; \*\*\*\*,  $P \leq 0.0001$ .

### Object Recognition Memory



**Supplemental Figure S4**

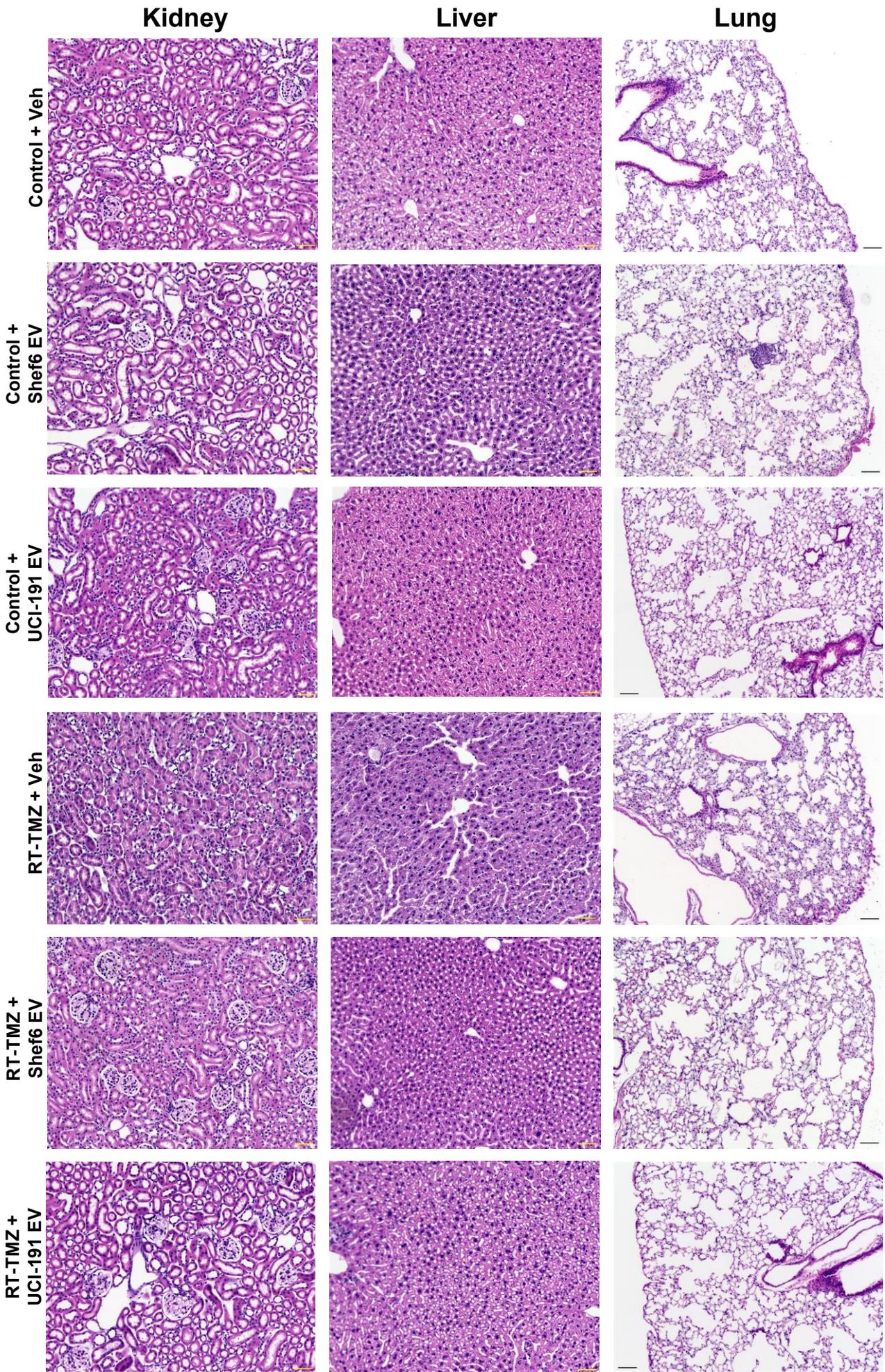
Representative heatmaps depicting exploration throughout the object recognition memory (ORM) test for the data presented in **Figure 5E**.



## **Supplemental Figure S5**

Histopathology of peripheral organs across treatment groups in males.

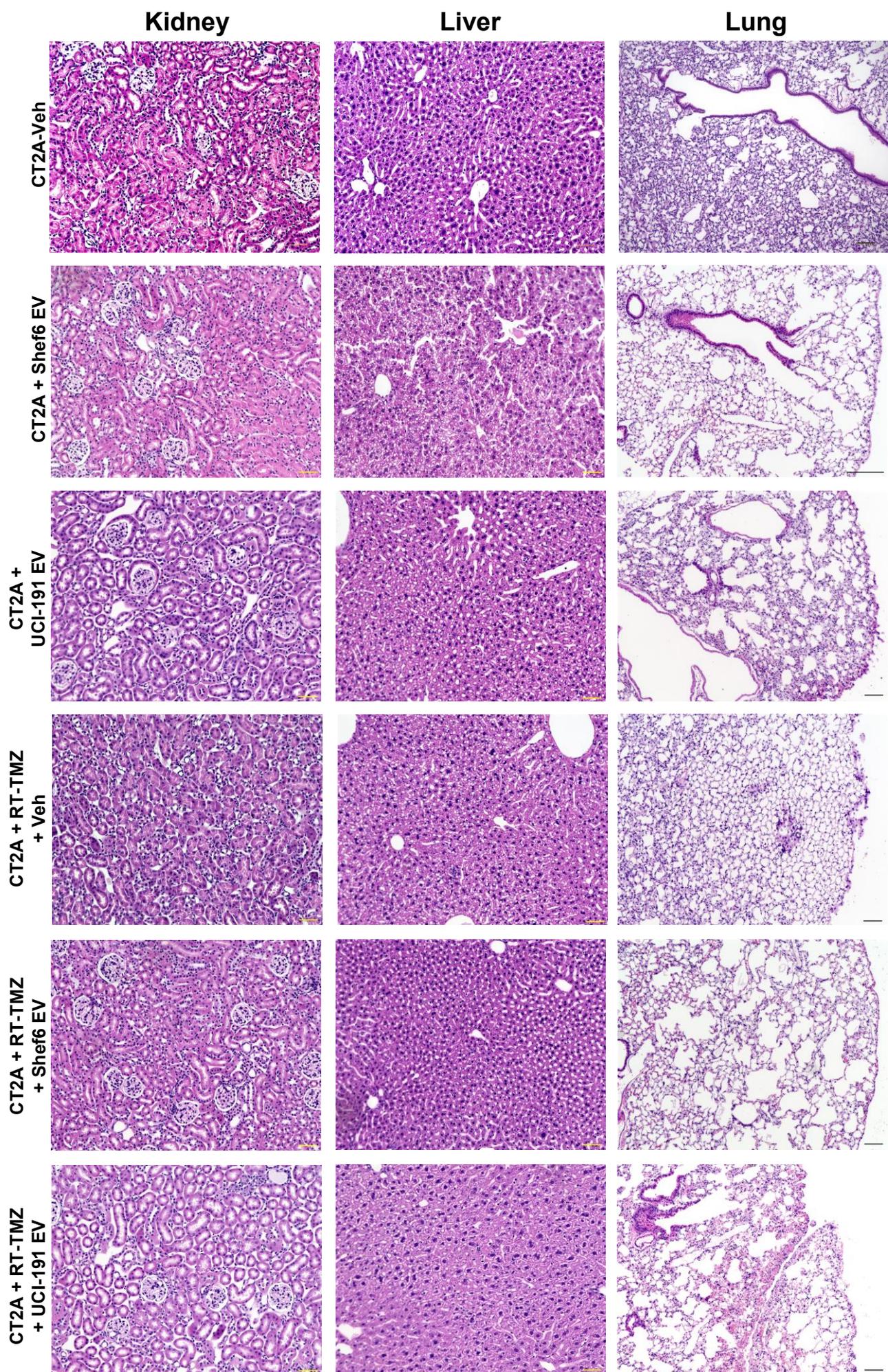
Representative H&E images for non-tumor-bearing male mice. Kidney, liver, and lung tissue specimens were collected and evaluated for gross morphology following hNSC-EV treatment. Paraffin-embedded tissue slices were stained for hematoxylin and eosin (H&E). Kidney and liver were imaged at 20x magnification, and the lung was imaged at 10x magnification. Scale bars, 50  $\mu\text{m}$  for 20x images and 100  $\mu\text{m}$  for 10x.



## **Supplemental Figure S6**

Histopathology of peripheral organs across treatment groups in females.

Representative H&E images for non-tumor-bearing female mice. Kidney, liver, and lung tissue specimens were collected and evaluated for gross morphology following hNSC-EV treatment. Paraffin-embedded tissue slices were stained for hematoxylin and eosin (H&E). Kidney and liver were imaged at 20x magnification, and the lung was imaged at 10x magnification. Scale bars, 50  $\mu\text{m}$  for 20x images and 100  $\mu\text{m}$  for 10x.



## **Supplemental Figure S7**

Histopathology of peripheral organs across treatment groups in glioma-bearing animals.

Representative H&E images for mice induced with CT2A-glioma. Kidney, liver, and lung tissue specimens were collected and evaluated for gross morphology following hNSC-EV treatment. Paraffin-embedded tissue slices were stained for hematoxylin and eosin (H&E). Kidney and liver were imaged at 20x magnification, and the lung was imaged at 10x magnification. N = 2 females and 4 males. Scale bars, 50  $\mu\text{m}$  for 20x images and 100  $\mu\text{m}$  for 10x.

# Suppl. Table T1

Summary of significant differences for the object recognition memory (ORM) data as presented in **Figure 5E**.

| Compared Groups  | Significance | P-Value  |
|--|--------------|----------|
| <u>Control + Veh</u> vs. CT2A + Veh                      | **           | 0.0053   |
| <u>Control + Veh</u> vs. CT2A + Shef6 EV                 | ***          | 0.0008   |
| <u>Control + Veh</u> vs. CT2A + UCI-191 EV               | ***          | 0.0002   |
| <u>Control + Veh</u> vs. CT2A + RT-TMZ + Veh             | *            | 0.0382   |
| CT2A + Veh vs. <u>CT2A + RT-TMZ + Shef6 EV</u>           | *            | 0.0132   |
| CT2A + Veh vs. <u>CT2A + RT-TMZ- UCI-191 EV</u>          | **           | 0.0017   |
| CT2A + Shef6 EV vs. <u>CT2A + RT-TMZ + Shef6 EV</u>      | **           | 0.0019   |
| CT2A + Shef6 EV vs. <u>CT2A + RT-TMZ- UCI-191 EV</u>     | ***          | 0.0003   |
| CT2A + UCI-191 EV vs. <u>CT2A + RT-TMZ + Shef6 EV</u>    | ***          | 0.0004   |
| CT2A + UCI-191 EV vs. <u>CT2A + RT-TMZ- UCI-191 EV</u>   | ****         | ≤ 0.0001 |
| CT2A + RT-TMZ + Veh vs. <u>CT2A + RT-TMZ- UCI-191 EV</u> | *            | 0.0126   |

ORM data were calculated as a Preference Index as described in the Methods and Materials. Groups that are underlined had a higher Preference Index. Data are presented as mean ± SEM (N = 5-12 animals/group). P values were derived from repeated measures ANOVA and Bonferroni's multiple comparisons.

# Suppl. Table T2

Summary of significant differences for the volumetric analysis of the astrocytic glial fibrillary acidic protein (GFAP) as presented in **Figure 6C**.

| Compared Groups   | Significance | P Value  |
|---|--------------|----------|
| Control + Veh vs. <u>CT2A + Veh</u>                     | ****         | ≤ 0.0001 |
| Control + Veh vs. <u>CT2A + UCI-191 EV</u>              | ****         | ≤ 0.0001 |
| Control + Veh vs. <u>CT2A + RT-TMZ + Veh</u>            | *            | 0.0115   |
| <u>CT2A + Veh</u> vs. CT2A + Shef6 EV                   | ****         | ≤ 0.0001 |
| <u>CT2A + Veh</u> vs. CT2A + RT-TMZ + Veh               | ***          | 0.0001   |
| <u>CT2A + Veh</u> vs. CT2A + RT-TMZ + Shef6 EV          | ****         | ≤ 0.0001 |
| <u>CT2A + Veh</u> vs. CT2A + RT-TMZ + UCI-191 EV        | ****         | ≤ 0.0001 |
| CT2A + Shef6 EV vs. <u>CT2A + UCI-191 EV</u>            | ***          | 0.0004   |
| <u>CT2A + Shef6 EV</u> vs. CT2A + RT-TMZ + Shef6 EV     | **           | 0.0013   |
| <u>CT2A + UCI-191 EV</u> vs. CT2A + RT-TMZ + Veh        | *            | 0.0183   |
| <u>CT2A + UCI-191 EV</u> vs. CT2A + RT-TMZ + Shef6 EV   | ****         | ≤ 0.0001 |
| <u>CT2A + UCI-191 EV</u> vs. CT2A + RT-TMZ + UCI-191 EV | ****         | ≤ 0.0001 |
| <u>CT2A + RT-TMZ + Veh</u> vs. CT2A + RT-TMZ + Shef6 EV | ****         | ≤ 0.0001 |

Groups that are underlined had a higher GFAP expression. Data are presented as mean ± SEM (N = 5-12 animals/group). P values were derived from repeated measures ANOVA and Tukey's multiple comparisons tests.

# Suppl. Table T3

Summary of significant differences for the volumetric analysis of the colocalization of the ionized calcium-binding adaptor molecule 1 (Iba1), and lysosomal protein CD68 as presented in **Figure 6F**.

| Compared Groups   | Significance | P Value  |
|---|--------------|----------|
| Control + Veh vs. <u>CT2A + Veh</u>                       | ****         | ≤ 0.0001 |
| Control + Veh vs. <u>CT2A + UCI-191 EV</u>                | ****         | ≤ 0.0001 |
| Control + Veh vs. <u>CT2A + RT-TMZ + Veh</u>              | **           | 0.0026   |
| Control + Veh vs. <u>CT2A + RT-TMZ + Shef6 EV</u>         | *            | 0.0328   |
| <u>CT2A + Veh</u> vs. CT2A + Shef6 EV                     | ****         | ≤ 0.0001 |
| <u>CT2A + Veh</u> vs. CT2A + RT-TMZ + Veh                 | ***          | 0.0001   |
| <u>CT2A + Veh</u> vs. CT2A + RT-TMZ + Shef6 EV            | ****         | ≤ 0.0001 |
| <u>CT2A + Veh</u> vs. CT2A + RT-TMZ + UCI-191 EV          | ****         | ≤ 0.0001 |
| CT2A + Shef6 EV vs. <u>CT2A + UCI-191 EV</u>              | ****         | ≤ 0.0001 |
| <u>CT2A + UCI-191 EV</u> vs. CT2A + RT-TMZ + Veh          | ***          | 0.0002   |
| <u>CT2A + UCI-191 EV</u> vs. CT2A + RT-TMZ + Shef6 EV     | ***          | 0.0002   |
| <u>CT2A + UCI-191 EV</u> vs. CT2A + RT-TMZ + UCI-191 EV   | ****         | ≤ 0.0001 |
| <u>CT2A + RT-TMZ + Veh</u> vs. CT2A + RT-TMZ + UCI-191 EV | *            | 0.0367   |

Groups that are underlined had a higher CD68-Iba1 co-localization. Data are presented as mean ± SEM (N = 5-12 animals/group). P values were derived from repeated measures ANOVA and Tukey's multiple comparisons tests.

# Suppl. Table T4

Summary of significant differences for the volumetric analysis of synaptic vesicle glycoprotein 2A (SV2a) in the pyramidal cell layer (*pyr*) and stratum radiatum (*sr*) of CA1 in the hippocampus as presented in **Figure 7E**.

| Compared Groups   | Significance | P Value  |
|---|--------------|----------|
| <u>Control + Veh</u> vs. CT2A + Veh                       | ****         | ≤ 0.0001 |
| <u>Control + Veh</u> vs. CT2A + Shef6 EV                  | ****         | ≤ 0.0001 |
| <u>Control + Veh</u> vs. CT2A + UCI-191 EV                | ****         | ≤ 0.0001 |
| <u>Control + Veh</u> vs. CT2A + RT-TMZ + Veh              | ****         | ≤ 0.0001 |
| <u>Control + Veh</u> vs. CT2A + RT-TMZ + Shef6 EV         | *            | 0.015    |
| CT2A + Veh vs. <u>CT2A + Shef6 EV</u>                     | ****         | ≤ 0.0001 |
| <u>CT2A + Veh</u> vs. CT2A + UCI-191 EV                   | **           | 0.0095   |
| CT2A + Veh vs. <u>CT2A + RT-TMZ + Veh</u>                 | **           | 0.0047   |
| CT2A + Veh vs. <u>CT2A + RT-TMZ + Shef6 EV</u>            | ****         | ≤ 0.0001 |
| CT2A + Veh vs. <u>CT2A + RT-TMZ + UCI-191 EV</u>          | ****         | ≤ 0.0001 |
| <u>CT2A + Shef6 EV</u> vs. CT2A + UCI-191 EV              | ****         | ≤ 0.0001 |
| CT2A + Shef6 EV vs. <u>CT2A + RT-TMZ + Shef6 EV</u>       | ****         | ≤ 0.0001 |
| CT2A + Shef6 EV vs. <u>CT2A + RT-TMZ + UCI-191 EV</u>     | ****         | ≤ 0.0001 |
| CT2A + UCI-191 EV vs. <u>CT2A + RT-TMZ + Veh</u>          | ****         | ≤ 0.0001 |
| CT2A + UCI-191 EV vs. <u>CT2A + RT-TMZ + Shef6 EV</u>     | ****         | ≤ 0.0001 |
| CT2A + UCI-191 EV vs. <u>CT2A + RT-TMZ + UCI-191 EV</u>   | ****         | ≤ 0.0001 |
| CT2A + RT-TMZ + Veh vs. <u>CT2A + RT-TMZ + Shef6 EV</u>   | ****         | ≤ 0.0001 |
| CT2A + RT-TMZ + Veh vs. <u>CT2A + RT-TMZ + UCI-191 EV</u> | ****         | ≤ 0.0001 |

Groups that are underlined had a higher SV2a expression. Data are presented as mean ± SEM (N = 5-12 animals/group). P values were derived from repeated measures ANOVA and Tukey's multiple comparisons tests.

# Suppl. Table T5

Summary of significant differences for the volumetric analysis of synaptic vesicle glycoprotein 2A (SV2a) in the molecular layer (*ml*) and dentate gyrus (*dg*) in the hippocampus, as presented in **Figure 7F**.

| Compared Groups  | Significance | P Value  |
|--|--------------|----------|
| <u>Control + Veh</u> vs. CT2A + Veh                            | ****         | ≤ 0.0001 |
| <u>Control + Veh</u> vs. CT2A + Shef6 EV                       | ****         | ≤ 0.0001 |
| <u>Control + Veh</u> vs. CT2A + UCI-191 EV                     | *            | 0.0181   |
| <u>Control + Veh</u> vs. CT2A + RT-TMZ + Veh                   | ****         | ≤ 0.0001 |
| CT2A + Veh vs. <u>CT2A + Shef6 EV</u>                          | **           | 0.0043   |
| CT2A + Veh vs. <u>CT2A + UCI-191 EV</u>                        | ****         | ≤ 0.0001 |
| CT2A + Veh vs. <u>CT2A + RT-TMZ + Shef6 EV</u>                 | ****         | ≤ 0.0001 |
| CT2A + Veh vs. <u>CT2A + RT-TMZ + UCI-191 EV</u>               | ****         | ≤ 0.0001 |
| CT2A + Shef6 EV vs. <u>CT2A + UCI-191 EV</u>                   | ***          | 0.0003   |
| CT2A + Shef6 EV vs. <u>CT2A + RT-TMZ + Shef6 EV</u>            | ****         | ≤ 0.0001 |
| CT2A + Shef6 EV vs. <u>CT2A + RT-TMZ + UCI-191 EV</u>          | ****         | ≤ 0.0001 |
| <u>CT2A + UCI-191 EV</u> vs. CT2A + RT-TMZ + Veh               | ****         | ≤ 0.0001 |
| CT2A + UCI-191 EV vs. <u>CT2A + RT-TMZ + UCI-191 EV</u>        | ****         | ≤ 0.0001 |
| CT2A + RT-TMZ + Veh vs. <u>CT2A + RT-TMZ + Shef6 EV</u>        | ****         | ≤ 0.0001 |
| CT2A + RT-TMZ + Veh vs. <u>CT2A + RT-TMZ + UCI-191 EV</u>      | ****         | ≤ 0.0001 |
| CT2A + RT-TMZ + Shef6 EV vs. <u>CT2A + RT-TMZ + UCI-191 EV</u> | **           | 0.0011   |

Groups that are underlined had a higher SV2a expression. Data are presented as mean ± SEM (N = 5-12 animals/group). P values were derived from repeated measures ANOVA and Tukey's multiple comparisons tests.

# Suppl. Table T6

Summary of significant differences for the volumetric analysis of postsynaptic density protein 95 (PSD95) in the pyramidal cell layer (*pyr*) and stratum radiatum (*sr*) of CA1 in the hippocampus, as presented in **Figure 7G**.

| Compared Groups   | Significance | P Value  |
|---|--------------|----------|
| <u>Control + Veh</u> vs. CT2A + Veh                       | ****         | ≤ 0.0001 |
| <u>Control + Veh</u> vs. CT2A + Shef6 EV                  | ****         | ≤ 0.0001 |
| <u>Control + Veh</u> vs. CT2A + UCI-191 EV                | ****         | ≤ 0.0001 |
| <u>Control + Veh</u> vs. CT2A + RT-TMZ + Veh              | ****         | ≤ 0.0001 |
| <u>CT2A + Veh</u> vs. CT2A + RT-TMZ + Shef6 EV            | ****         | ≤ 0.0001 |
| <u>CT2A + Veh</u> vs. CT2A + RT-TMZ + UCI-191 EV          | ****         | ≤ 0.0001 |
| <u>CT2A + Shef6 EV</u> vs. CT2A + UCI-191 EV              | *            | 0.0338   |
| CT2A + Shef6 EV vs. <u>CT2A + RT-TMZ + Shef6 EV</u>       | **           | 0.001    |
| CT2A + Shef6 EV vs. <u>CT2A + RT-TMZ + UCI-191 EV</u>     | **           | 0.0056   |
| CT2A + UCI-191 EV vs. <u>CT2A + RT-TMZ + Shef6 EV</u>     | ****         | ≤ 0.0001 |
| CT2A + UCI-191 EV vs. <u>CT2A + RT-TMZ + UCI-191 EV</u>   | ****         | ≤ 0.0001 |
| CT2A + RT-TMZ + Veh vs. <u>CT2A + RT-TMZ + Shef6 EV</u>   | **           | 0.0013   |
| CT2A + RT-TMZ + Veh vs. <u>CT2A + RT-TMZ + UCI-191 EV</u> | **           | 0.006    |

Groups that are underlined had a higher PSD95 expression. Data are presented as mean ± SEM (N = 5-12 animals/group). P values were derived from repeated measures ANOVA and Tukey's multiple comparisons tests.

# Suppl. Table T7

Summary of significant differences for the volumetric analysis of postsynaptic density protein 95 (PSD95) in the molecular layer (*ml*) and dentate gyrus (*dg*) in the hippocampus, as presented in **Figure 7H**.

| Compared Groups   | Significance | P Value  |
|---|--------------|----------|
| <u>Control + Veh</u> vs. CT2A + Veh                       | ***          | 0.0002   |
| Control + Veh vs. <u>CT2A + UCI-191 EV</u>                | **           | 0.009    |
| Control + Veh vs. <u>CT2A + RT-TMZ + UCI-191 EV</u>       | *            | 0.0301   |
| CT2A + Veh vs. <u>CT2A + Shef6 EV</u>                     | *            | 0.0321   |
| CT2A + Veh vs. <u>CT2A + UCI-191 EV</u>                   | ****         | ≤ 0.0001 |
| CT2A + Veh vs. <u>CT2A + RT-TMZ + Veh</u>                 | *            | 0.0117   |
| CT2A + Veh vs. <u>CT2A + RT-TMZ + Shef6 EV</u>            | ****         | ≤ 0.0001 |
| CT2A + Veh vs. <u>CT2A + RT-TMZ + UCI-191 EV</u>          | ****         | ≤ 0.0001 |
| CT2A + Shef6 EV vs. <u>CT2A + UCI-191 EV</u>              | ***          | 0.0001   |
| CT2A + Shef6 EV vs. <u>CT2A + RT-TMZ + UCI-191 EV</u>     | ***          | 0.0005   |
| <u>CT2A + UCI-191 EV</u> vs. CT2A + RT-TMZ + Veh          | **           | 0.0011   |
| CT2A + RT-TMZ + Veh vs. <u>CT2A + RT-TMZ + UCI-191 EV</u> | **           | 0.0038   |

Groups that are underlined had a higher PSD95 expression. Data are presented as mean ± SEM (N = 5-12 animals/group). P values were derived from repeated measures ANOVA and Tukey's multiple comparisons tests.

## SUPPLEMENTAL RESOURCE TABLE

| REAGENT or RESOURCES                                 | SOURCE                     | IDENTIFIER                           |
|--|----------------------------|--------------------------------------|
| <b>Antibodies</b>                                    |                            |                                      |
| Rat anti-Mouse CD68                                  | Bio-Rad                    | Cat: MCA1957<br>RRID: AB_322219      |
| Rabbit anti-IBA1                                     | FUJIFILM Wako              | Cat: 019-19741<br>RRID: AB_839504    |
| Goat anti-Rat AF 647                                 | Abcam                      | Cat: ab150159<br>RRID: AB_2566823    |
| Goat anti Rabbit AF 488                              | FisherSci                  | Cat: a11008<br>RRID: AB_143165       |
| Mouse anti-SV2A                                      | DHSB                       | Cat: SV2<br>RRID: AB_2315387         |
| Goat anti-Mouse AF 568                               | Abcam                      | Cat: ab175473<br>RRID: AB_2895153    |
| Mouse anti-PSD-95                                    | FisherSci                  | Cat: MA1-045<br>RRID: AB_325399      |
| Goat anti-Mouse AF 647                               | Abcam                      | Cat: ab150115<br>RRID: AB_2687948    |
| Mouse anti-GFAP                                      | Milipore                   | Cat: AB5804<br>RRID: AB_11212597     |
| DAPI   | FisherSci                  | Cat: D1306<br>RRID: AB_2629482       |
| <b>Experimental Model: Cell lines</b>                |                            |                                      |
| CT2A-Luc astrocytoma cells                           | Sigma-Aldrich              | Cat: SCC195<br>RRID: CVCL_ZJ60       |
| Human neural stem cells UCI-191                      | Univ. of California Irvine | Dr. Aileen Anderson (PI)             |
| Human neural stem cells Shef6                        | Univ. of California Irvine | Dr. Brian Cummings (PI)              |
| Contd.   |                            |                                      |
| <b>Experimental Model: Organisms/strains</b>         |                            |                                      |
| C57BL/6J mice  | Jackson Labs               | Cat: 000664<br>RRID: IMSR_JAX:000664 |
| <b>Chemicals, peptides, and recombinant proteins</b> |                            |                                      |
| Gibco™ DMEM (1X) + GlutaMAX™-I                       | FisherSci                  | Cat: 10-569-010                      |
| Gibco™ FBS   | FisherSci                  | Cat: 10-082-147                      |
| Gibco™ Hibernate™-A Medium                           | FisherSci                  | Cat: A1247501                        |
| Gibco™ TrypLE™ Express Enzyme                        | FisherSci                  | Cat: 12-605-010                      |
| CTS™ TrypLE™ Select Enzyme                           | ThermoFisher               | Cat: A1285901                        |
| Isospire™ (isoflurane) Inhalation Anesthetic         | Dechra                     | Cat: 26675-46-7                      |
| Betadine® Surgical Scrub                             | Patterson Veterinary       | Cat: 07-836-3379                     |
| Hydrogen Peroxide, 30% (Certified ACS)               | FisherSci                  | Cat: H325-500                        |
| Normal Saline (Sodium Chloride) 0.9%                 | Patterson Veterinary       | Cat: 07-800-9424                     |
| Buprenorphine HCl (0.3 mg/ml)                        | MWI Health                 | Cat: 78949214                        |
| VECTASHIELD® Antifade Mounting Medium                | VectaShield                | Cat: H-1000-10                       |
| D-Luciferin, sodium salt                             | GoldBio                    | Cat: eLUCNA                          |
| Gibco™ DPBS (no magnesium, no calcium)               | FisherSci                  | Cat: 14-190-144                      |
| Normal Goat Serum                                    | Jackson ImmunoResearch     | Cat: 005-000-121<br>RRID: AB_2336990 |
| Bovine Serum Albumin                                 | Sigma-Aldrich              | Cat: 05470                           |
| Virkon, premixed spray bottle                        | Lanxess                    | Cat: RSL_31/Virks                    |
| Heparin sodium salt from porcine intestinal mucosa   | Sigma-Aldrich              | Cat: H3149-25KU                      |

|   |                       |                       |
|---|-----------------------|-----------------------|
| Gibco™ DPBS (10X), no calcium, no magnesium                 | FisherSci             | Cat: 14-190-144       |
| Gibco™ DPBS (10X), with calcium and magnesium               | FisherSci             | Cat: 14-040-117       |
| Temozolomide  | Selleck Chemicals     | Cat: S1237            |
| Human FGF-acidic (FGF-1) Recombinant Protein                | ThermoFisher          | Cat: PHG0014          |
| Human EGF Recombinant Protein                               | ThermoFisher          | Cat: PHG0311          |
| CTS™ N-2 Supplement   | Invitrogen            | Cat: A13707-01        |
| Leukemia Inhibitory Factor (LIF)                            | Sigma-Aldrich         | Cat: LIF1010          |
| N-acetylcysteine  | Sigma-Aldrich         | Cat: A9165-5G         |
| X-VIVO™ 15 Serum-Free Medium                                | Lonza                 | Cat: 04-481Q          |
| CELLStart™ Substrate  | ThermoFisher          | Cat: A1014201         |
| Methanol  | FisherSci             | Cat: A412500          |
| Paraformaldehyde  | Sigma-Aldrich         | Cat: 158127           |
| Sodium azide  | Sigma-Aldrich         | Cat: S2002            |
| Sucrose   | Sigma-Aldrich         | Cat: S7903            |
| Tissue-Tek* O.C.T. Compound                                 | VWR                   | Cat: 25608-930        |
| Tris-buffered Salin (10X TBS)                               | Bioland Scientific    | Cat: TBS01-03         |
| Triton™ X-100 Surfact-Amps™ Detergent Solution              | FisherSci             | Cat: 85111            |
| TWEEN® 20   | Sigma-Aldrich         | Cat: 9005-64-5        |
| FineFIX   | Milestone Medical     | Cat: 70147G           |
| <b>Critical commercial assays</b>                           |                       |                       |
| RNeasy Plus Universal Mini Kit                              | Qiagen                | Cat: 73404            |
| Nanostring nCounter Mouse Neuroinflammation                 | Nanostring            | Cat: XT-CSO-MNROI1-12 |
| <b>Software and algorithms</b>                              |                       |                       |
| Living Image Software                                       | Revvity               | Cat: 128110           |
| IVIS Lumina III Imaging System                              | Revvity               | Cat: CLS136334        |
| Noldus EthoVisionXT 18 Tracking Software                    | Noldus                | RRID: SCR_000441      |
| FreezeFrame v6 (ActiMetrics)                                | Coulbourn Instruments | RRID: SCR_014429      |
| Imaris 9.1  | Oxford Instruments    | RRID: SCR_007370      |
| nSolver software version 4.0                                | Nanostring            | N/A                   |
| nSolver Advanced Analysis                                   | Nanostring            | N/A                   |
| NanoSight 300   | Malvern Panalytical   | Cat: NS300            |
| <b>Other</b>  |                       |                       |
| Ultra Precise Digital Just for Mouse Stereotaxic Instrument | Stoelting             | Cat: 51730UD          |
| Sterile Alcohol Prep Pads                                   | FisherSci             | Cat: 06-669-62        |
| Feather™ Single-Use Scalpels, size #11                      | FisherSci             | Cat: 08-927-5B        |
| 10 µL Microliter Syringe Model 701 N                        | Hamilton              | Cat: 80300            |
| Pivotal® WebCryl™ Sutures                                   | Patterson Veterinary  | Cat: 07-891-0161      |
| 3M™ Vetbond™ Tissue Adhesive Bottle                         | Patterson Veterinary  | Cat: 07-805-5031      |
| Fisherbrand™ Superfrost™ Plus Microscope Slides             | FisherSci             | Cat: 22-037-246       |
| SmART+ irradiator   | Precision X-Ray       | RRID: SCR_021996      |
| Noldus EthoVisionXT 18 Video Capture Hardware System        | Noldus                | RRID: SCR_000441      |
| Nanodrop  | FisherSci             | Cat: 13-400-525       |
| Bone Drill  | Cell Point Scientific | Cat: 67-1024          |
| Anesthesia System   | Vet Equip             | Cat: 922100           |
| Optima XE-90 Ultracentrifuge                                | Beckman Coulter       | Cat: A94471           |
| 0.2 µm Nalgene™ Rapid-Flow™ Sterile Filter Unit             | ThermoFisher          | Cat: 566-0020         |
| 0.2 µm Nylon Filter   | ThermoFisher          | Cat: 13-1001-00       |
| 70 mL ultracentrifuge tubes                                 | Beckman Coulter       | Cat: 355655           |
| 26 mL ultracentrifuge tubes                                 | Beckman Coulter       | Cat: 355654           |
| Transmission Electron Microscope                            | JOEL TLD              | Cat: Jem-1400 Plus    |

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| UCSD Cellular and Molecular Medicine<br>Electron Microscopy Core | University of California, San<br>Diego | RRID: SCR_022039 |
| UCI Genomics Research and Technology<br>Hub                      | Univ. of California, Irvine            | RRID: SCR_026615 |
| UCI Experimental Tissue Resources                                | Univ. of California, Irvine            | RRID: SCR_024622 |
| Cryostat Hm 525 NX   | Cryostat MX                            | Cat: 95-664-0EC  |