

SUPPLEMENTARY INFORMATION

Dendrimer-conjugated glutaminase inhibitor selectively targets microglial glutaminase in a mouse model of Rett syndrome

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1. Compound characterization:

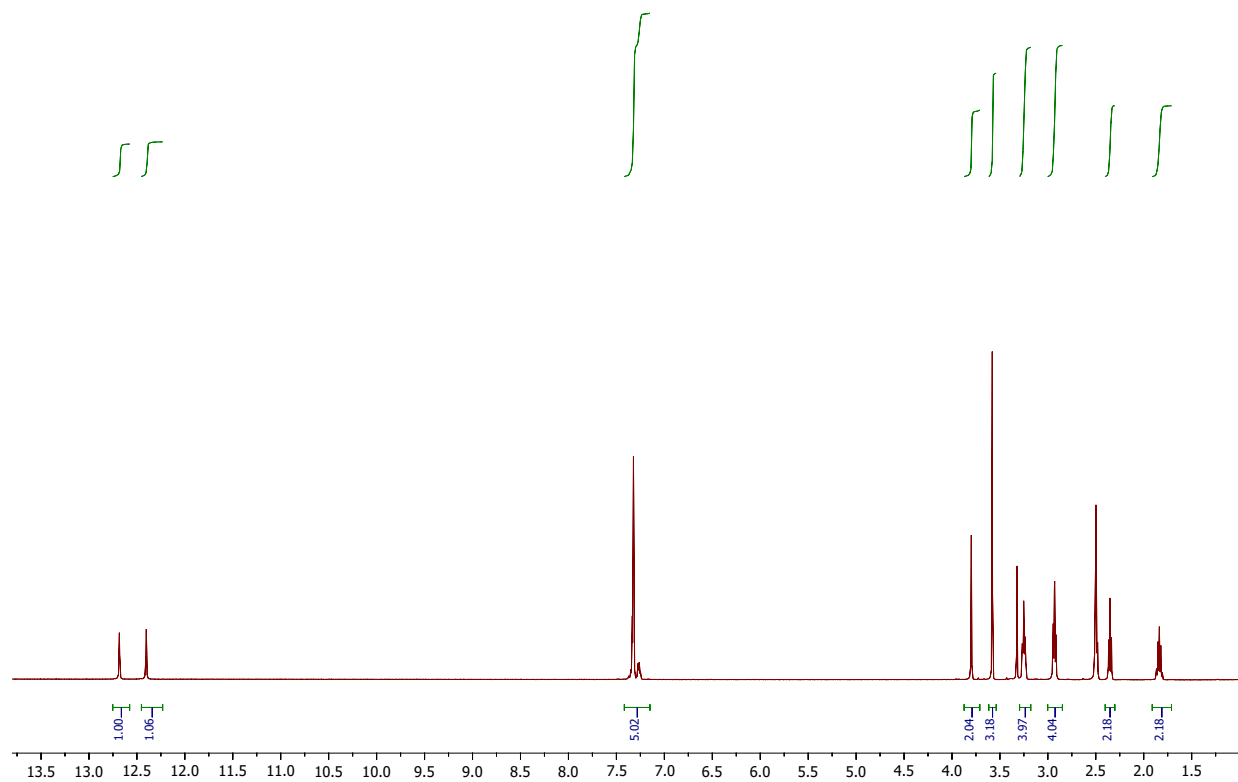


Figure S1. ^1H NMR of compound 3.

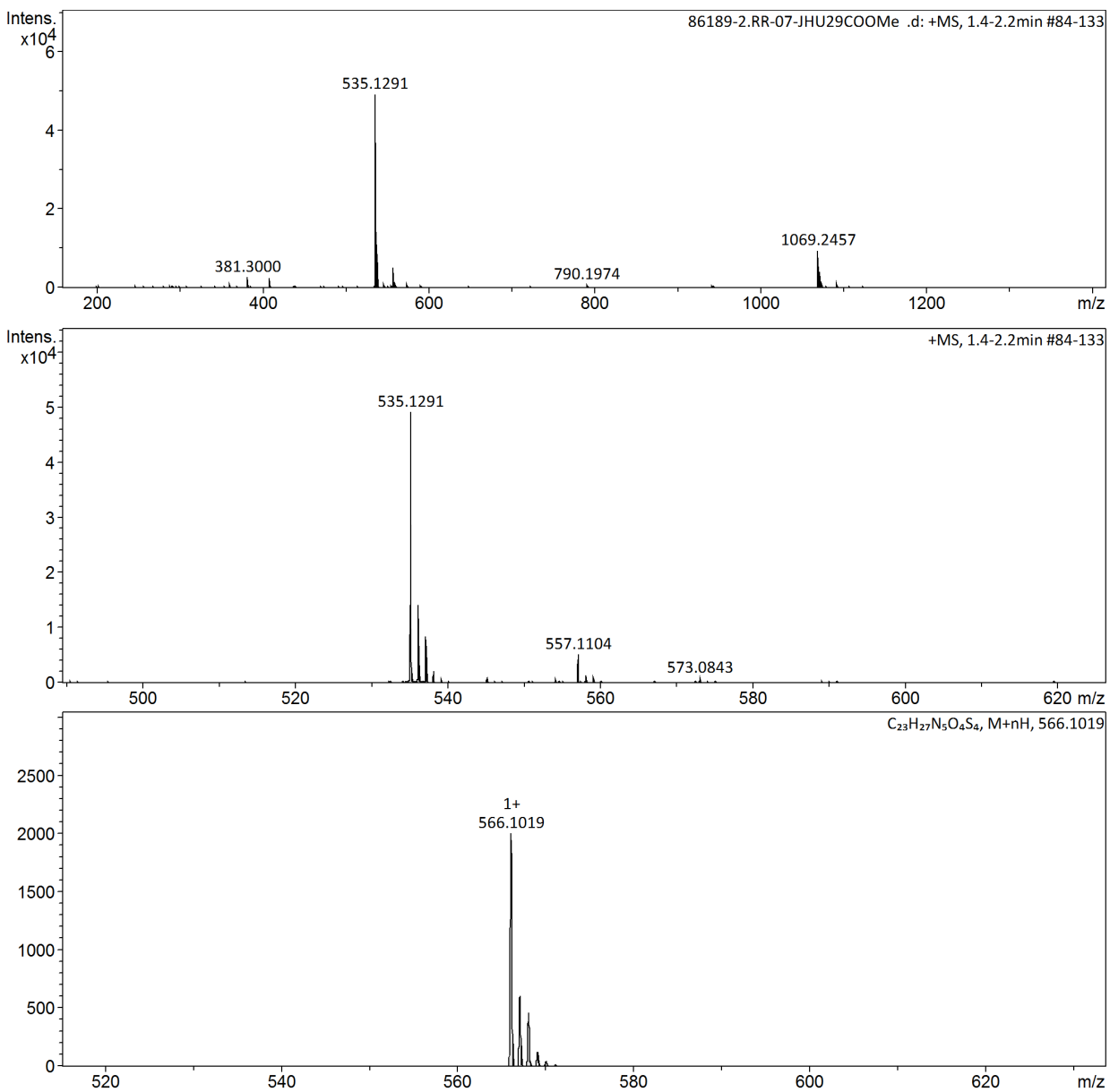


Figure S2. ESI-MS spectrum of compound **3**.

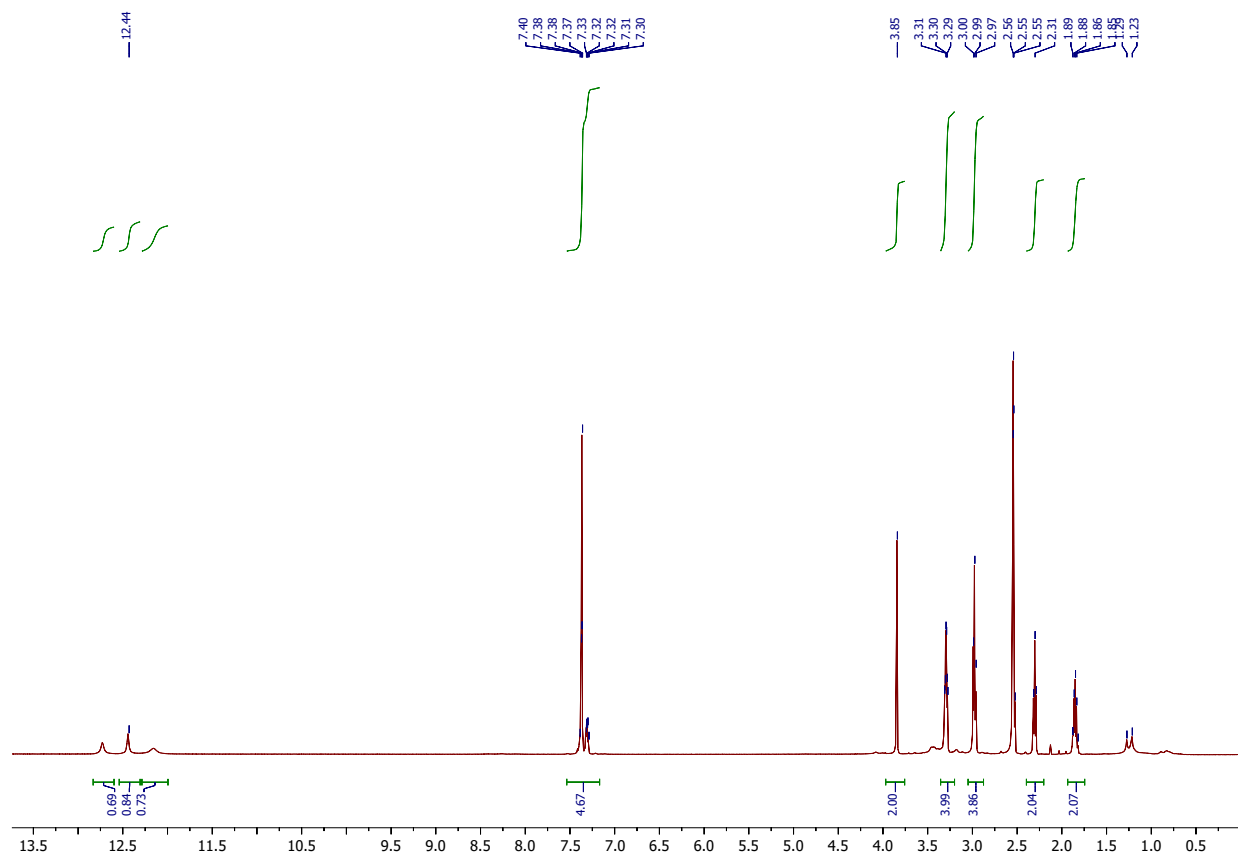


Figure S3. ^1H NMR of compound 4.

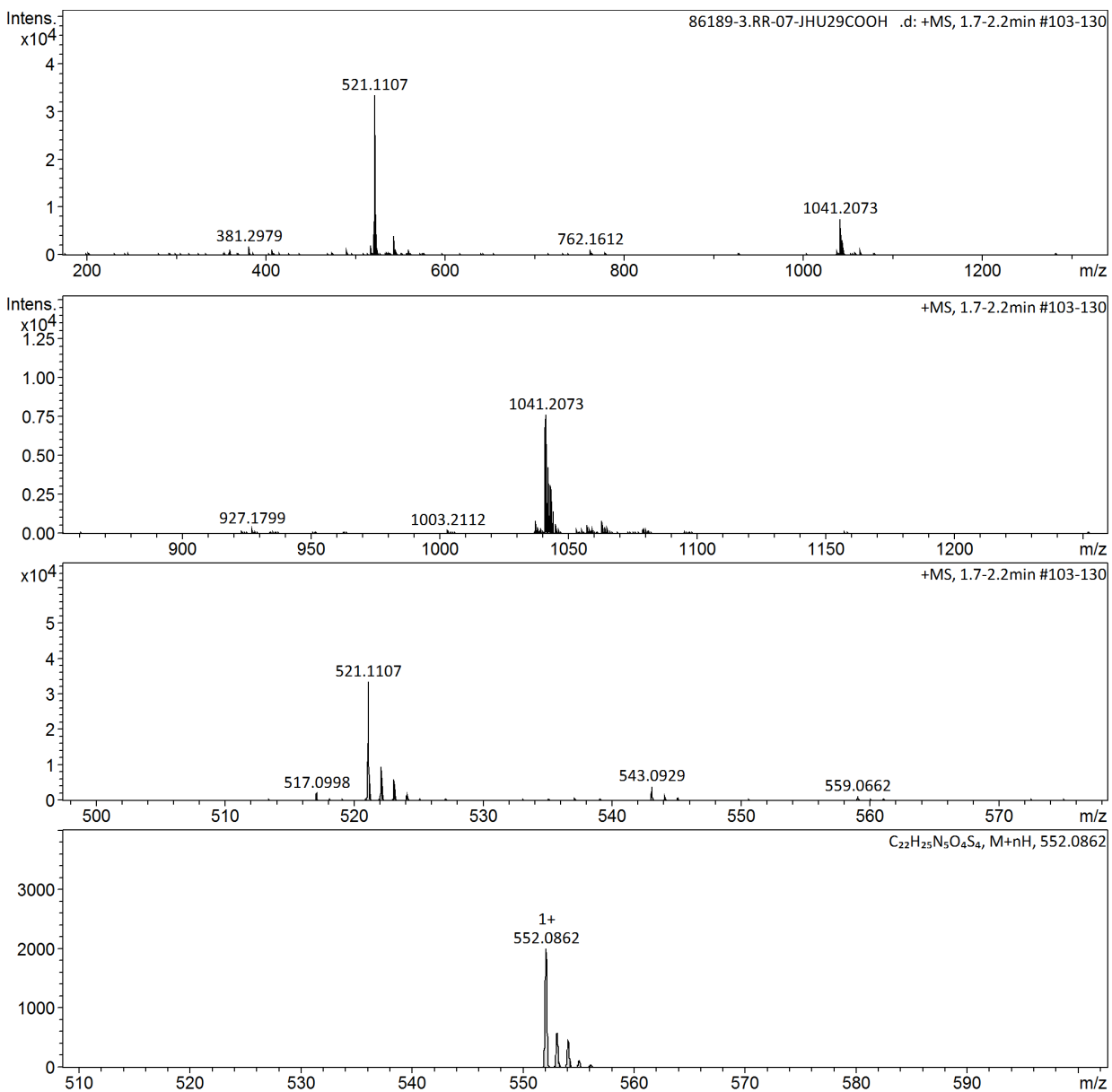


Figure S4. ESI-MS spectrum of compound 4.

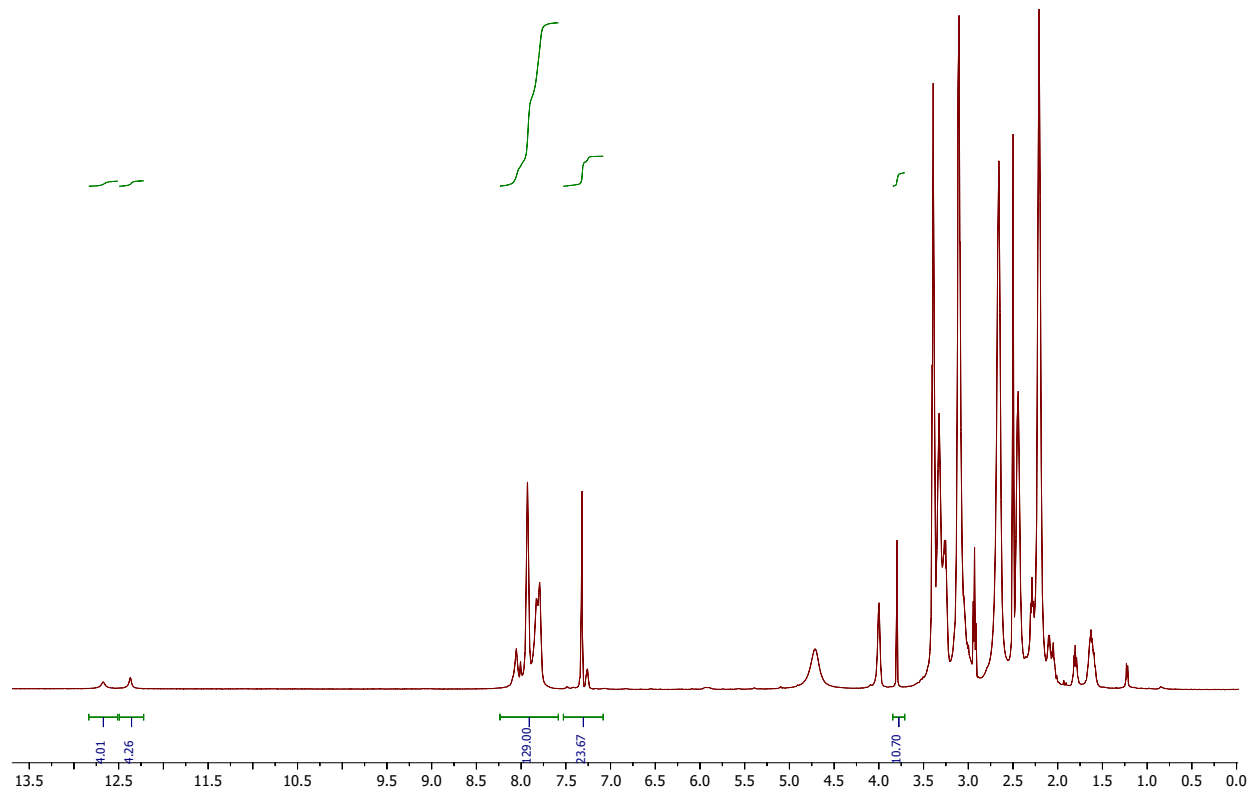


Figure S5. ^1H NMR of compound 6 (D-JHU29).

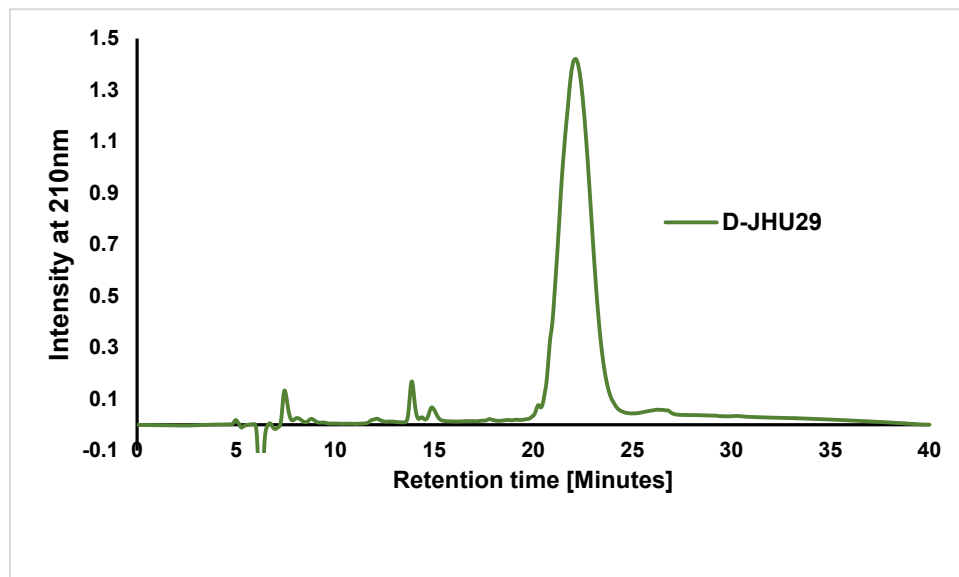


Figure S6. HPLC chromatogram of compound 6 (D-JHU29).

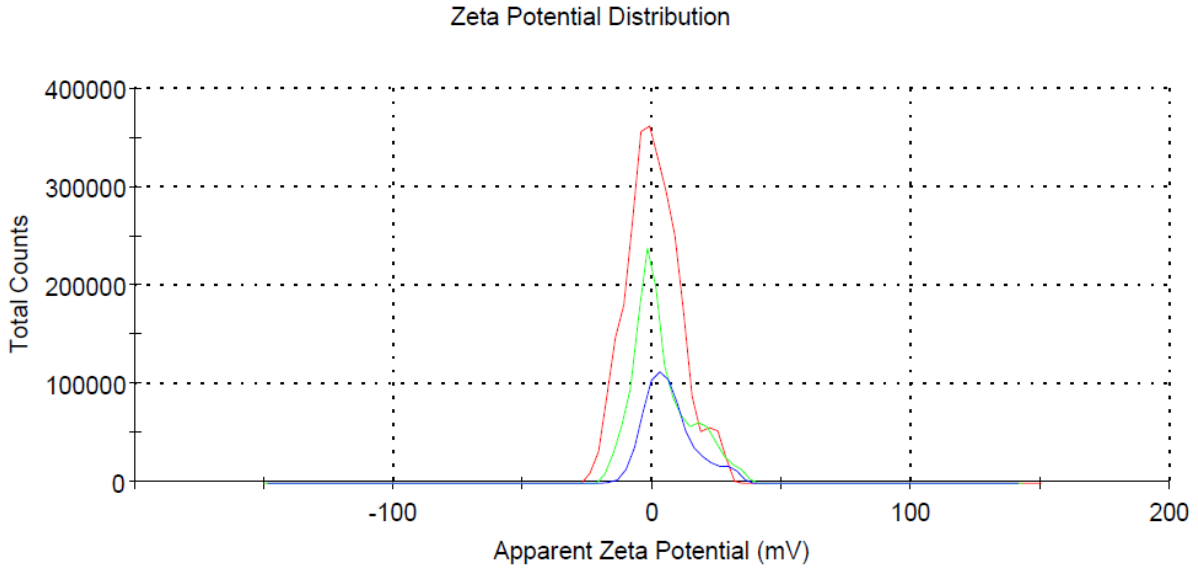


Figure S7. The zeta potential distribution of D-JHU29.

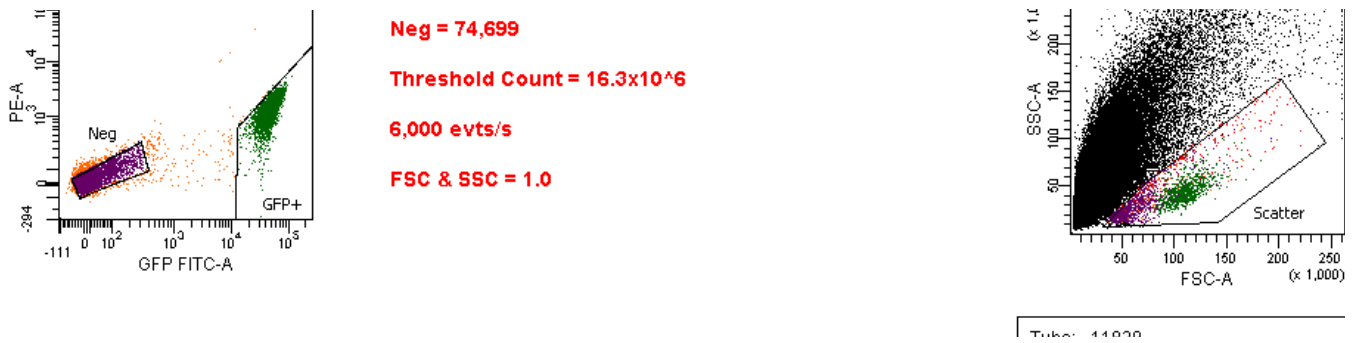


Figure S8. Flow cytometry gating scheme. Approximately 8.0×10^4 GFP+ and GFP- cells were collected per sample. Events were processed at a rate of 6,000 events/s and with a threshold count of 16.3×10^6 .

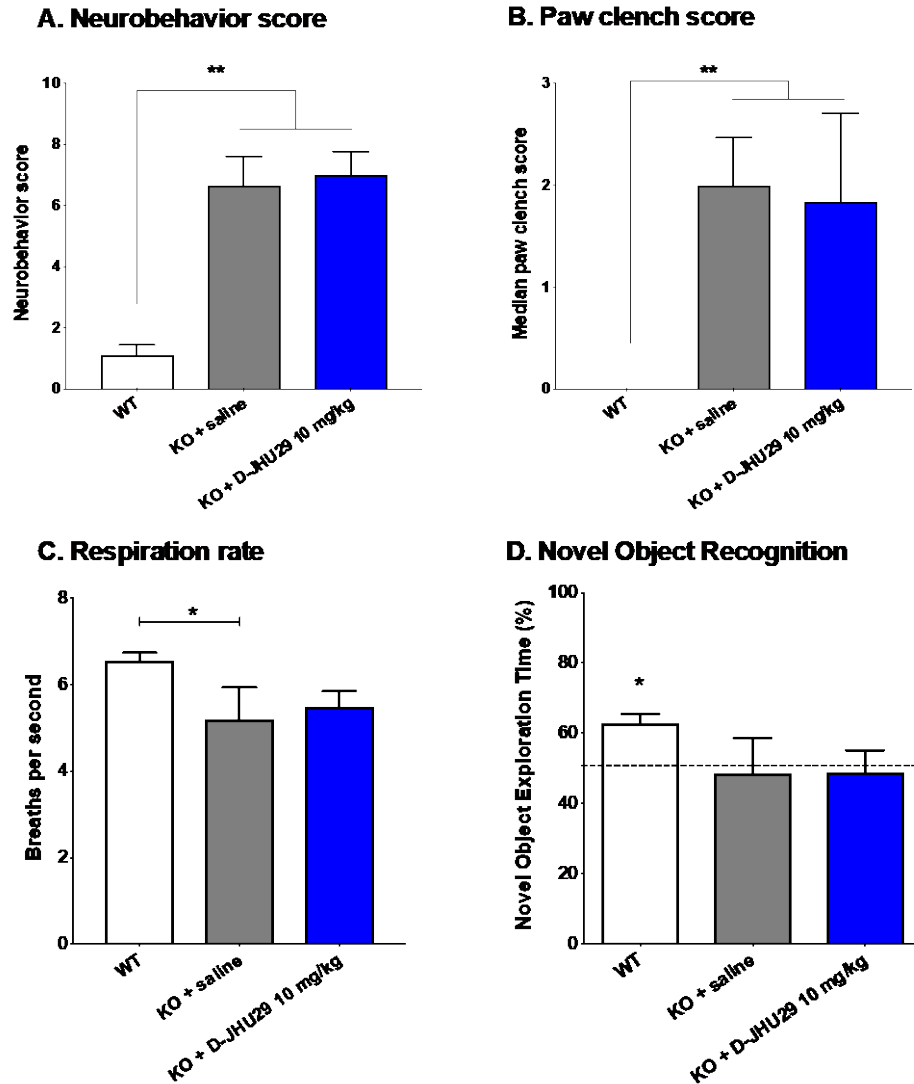


Figure S9. Non-motor phenotypic assessments in *Mecp2*-KO mice after twice weekly D-JHU29 treatment. **A.** Neurobehavioral assessment is significantly greater in *Mecp2*-KO mice indicating significant phenotypic changes in these mice and there is no significant improvement with treatment. **B.** The predominant neurobehavior subscore, paw clench also shows no improvement change with D-JHU29 treatment. **C.** Respiration rate is significantly decreased in *Mecp2*-KO mice (gray bars) but is not recovered with D-JHU29 administration (blue bars). **D.** No improvements in novel object recognition were observed at D-JHU29 treatment. Only wild type (WT) mice (white bars) show on average more time spent with the novel object than what would be expected at chance (50%). * $p < 0.05$, ** $p < 0.01$

Neurobehavior Rubric:

Neurobehavioral phenotype was scored using the following measures by a blinded observer. All subscores were added to create an overall/composite neurobehavior score.

Subscore:

Mobility

- 0 normal, active
- 1 decreased spontaneous movement
- 2 no spontaneous movement, only moves when prodded
- 3 no movement

Gait

- 0 walks normally
- 1 waddling
- 2 waddling, walks on toes (paws not flat on ground)
- 3 waddling, feet displaced outward, paws clenched when walking

Tremors

- 0 none
- 1 sporadic
- 2 intermittent
- 3 continuous

Paw Clenching

- 0 none
- 1 1-2 paws
- 2 3 paws or both fore limbs/hind limbs
- 3 all paws

Clench time

- 0 none
- 1 sporadic
- 2 intermittent (patterned)
- 3 continuous

Paw wringing

- 0 none
- 1 some front paw
- 2 some front and back paw
- 3 continuous

Respiration

- 0 regular
- 1 irregular
- 2 too fast or too slow
- 3 apnic

Composite Score: addition of all sub-scores