Expanded View Figures

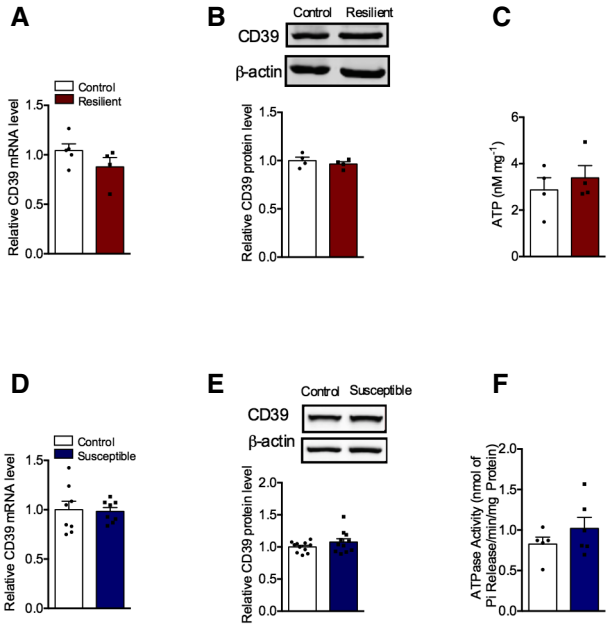

Figure EV1. The CD39 expression and activity in hippocampus of stress resilient mice and in mPFC of stress susceptible mice.

A The CD39 mRNA level in the hippocampus of resilient mice exposure to CSDS (n = 5, 4 mice; resilient versus control, P = 0.1888, Student's t-test).
B The expression of CD39 protein in the hippocampus of resilient mice exposure to CSDS (n = 4 mice/group; resilient versus control, P = 0.4403, Student's t-test).
C The ATP level in the hippocampus of resilient mice exposure to CSDS (n = 4 mice/group; resilient versus control, P = 0.5084, Student's t-test).
D The CD39 mRNA level in the mPFC of susceptible mice after CSDS (n = 8 mice/group; CSDS versus control, P = 0.8592, Student's t-test).
E The expression of CD39 protein in the mPFC of susceptible mice induced by CSDS (n = 11 mice/group; CSDS versus control, P = 0.1194, Student's t-test).
F The ATPase activity in the mPFC of stressed mice (n = 5, 6 mice; CSDS versus control, P = 0.2827, Student's t-test).

Data information: Data are expressed as the means ± SEM.
Source data are available online for this figure.

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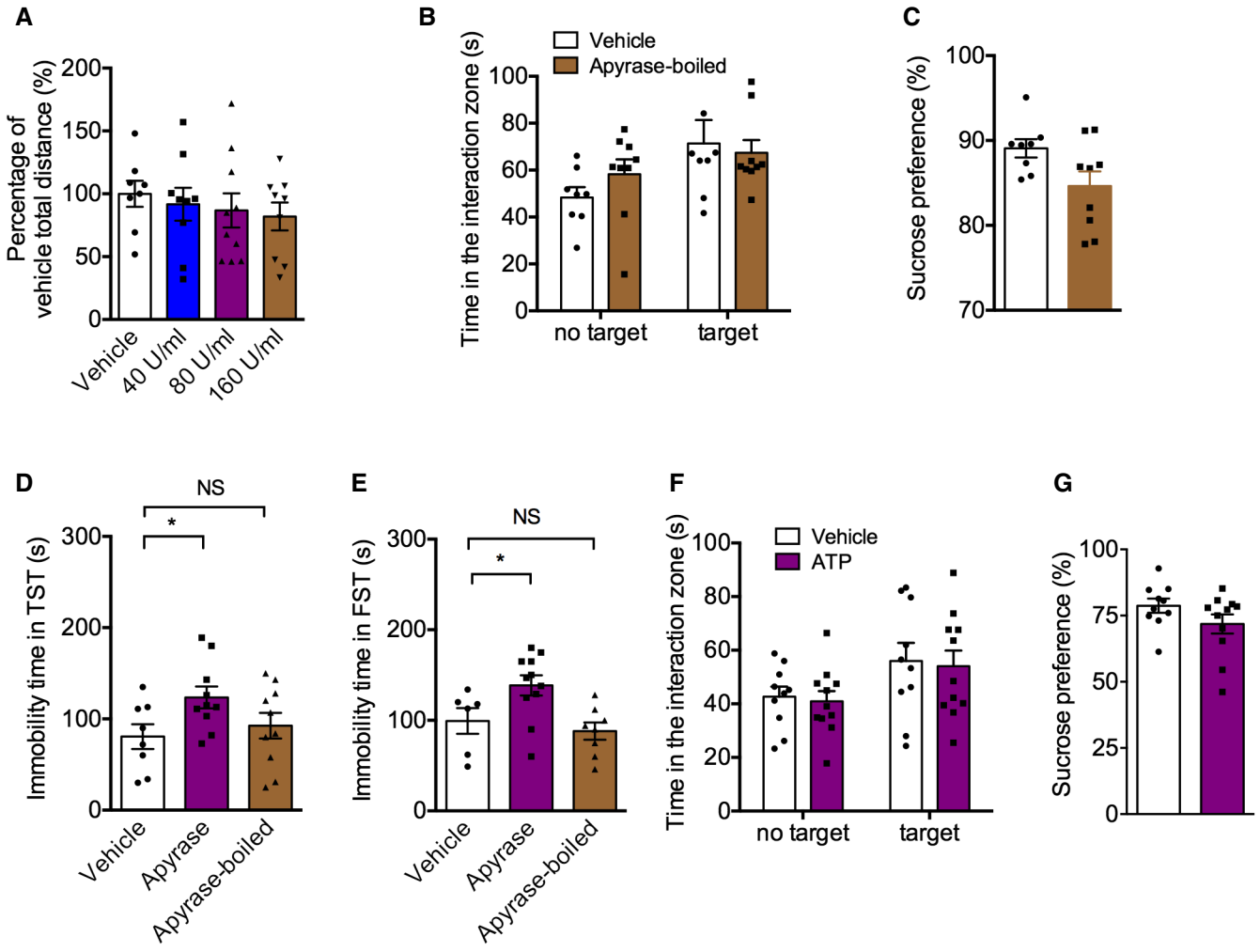

Figure EV2. The effects of apyrase or ATP on locomotor activity and depressive behaviors in normal mice.

A The locomotor activity of mice with apyrase (40, 80, or 160 U/ml) infusion into lateral intracerebroventricular in the open field test (n = 8, 9, 10, 9 mice; Treatment $F_{3,32}$ = 0.37, P = 0.7757, one-way ANOVA with Fisher's LSD test).

B, C Social interaction time (B) and sucrose preference (C) of mice with inactivated apyrase infusion into hippocampus (n = 8, 9 mice; for SI, Interaction $F_{1,30}$ = 1.039, P = 0.3162; Drug $F_{1,30}$ = 5.591, P = 0.0247; Target $F_{1,30}$ = 0.1890, P = 0.6669, two-way ANOVA with Tukey's post-test; for SPT, P = 0.0517, Student's t-test).

D, E Immobility time in the TST (D) and FST (E) of mice with apyrase and boiled-apyrase (for TST, n = 8, 10, 10 mice; Treatment $F_{2,25}$ = 2.766, P = 0.0822; Apyrase versus vehicle, P = 0.0348; Apyrase-boiled versus vehicle, P = 0.5386; for FST, n = 6, 11, 8 mice; Treatment $F_{2,22}$ = 5.92, P = 0.0088; Apyrase versus vehicle, P = 0.0307; Apyrase-boiled versus vehicle, P = 0.5414, one-way ANOVA with Fisher's LSD test).

F, G Social interaction time (F) and sucrose preference (G) of normal mice with ATP (25 μM) infusion into hippocampus (n = 10, 11 mice; for SI, Interaction $F_{1,38}$ = 0.0005723, P = 0.9810; Drug $F_{1,38}$ = 6.520, P = 0.0148; Target $F_{1,38}$ = 0.1280, P = 0.7225, two-way ANOVA with Tukey's post-test; for SPT, P = 0.1484, Student's t-test).

Data information: Data are expressed as the means ± SEM. NS $P > 0.05$; *$P < 0.05$.
Source data are available online for this figure.

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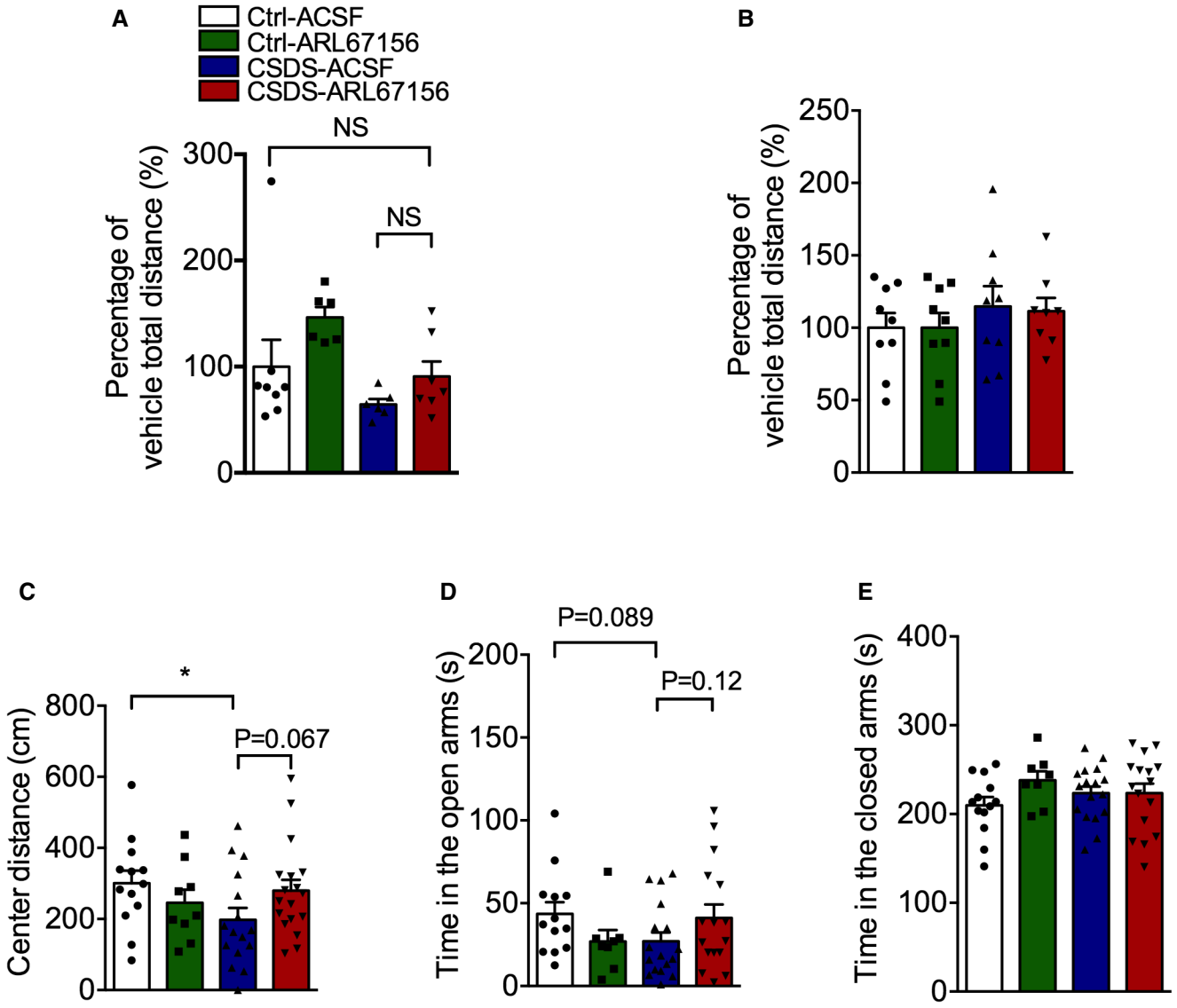

Figure EV3. The effects of ARL67156 on locomotor activity and anxiety behaviors of mice.

A The locomotor activity of susceptible mice with ARL67156 (100 μM) infusion into the right cerebral ventricle in the open field test (n = 8, 6, 6, 7 mice; Interaction $F_{1,23}$ = 0.3174, P = 0.5786; Group $F_{1,23}$ = 6.619, P = 0.0170; Drug $F_{1,23}$ = 4.226, P = 0.0513, two-way ANOVA with Tukey's post-test).

B The locomotor activity of mice with ARL67156 (100 μM) infusion into the hippocampus in the open field test (n = 9, 9, 9, 8 mice; Interaction $F_{1,31}$ = 0.1670, P = 0.6856; Group $F_{1,31}$ = 0.8477, P = 0.3643; Drug $F_{1,31}$ = 0.01314, P = 0.9095, two-way ANOVA with Tukey's post-test).

C The distance spent in center zone of stressed mice with ARL67156 (100 μM) in the OFT (n = 13, 9, 16, 18 mice; Treatment $F_{3,52}$ = 1.880, P = 0.1444; CSDS – ACSF versus Ctrl – ACSF, P = 0.0346; CSDS – ARL67156 versus CSDS – ACSF, P = 0.0671, one-way ANOVA with Fisher's LSD test).

D, E The anxiety behaviors of stressed mice with ARL67156 (100 μM) accessing by the open arms (D) and the closed arms (E) in the EPM test (n = 13, 8, 17, 16 mice; for the open arms, Treatment $F_{3,50}$ = 1.569, P = 0.2086; CSDS – ACSF versus Ctrl – ACSF, P = 0.0891; CSDS – ARL67156 versus CSDS – ACSF, P = 0.1234; for the closed arms, Treatment $F_{3,50}$ = 1.063, P = 0.3731, one-way ANOVA with Fisher's LSD test).

Data information: Data are expressed as the means ± SEM. NS $P > 0.05$; *$P < 0.05$. Ctrl, control.
Source data are available online for this figure.

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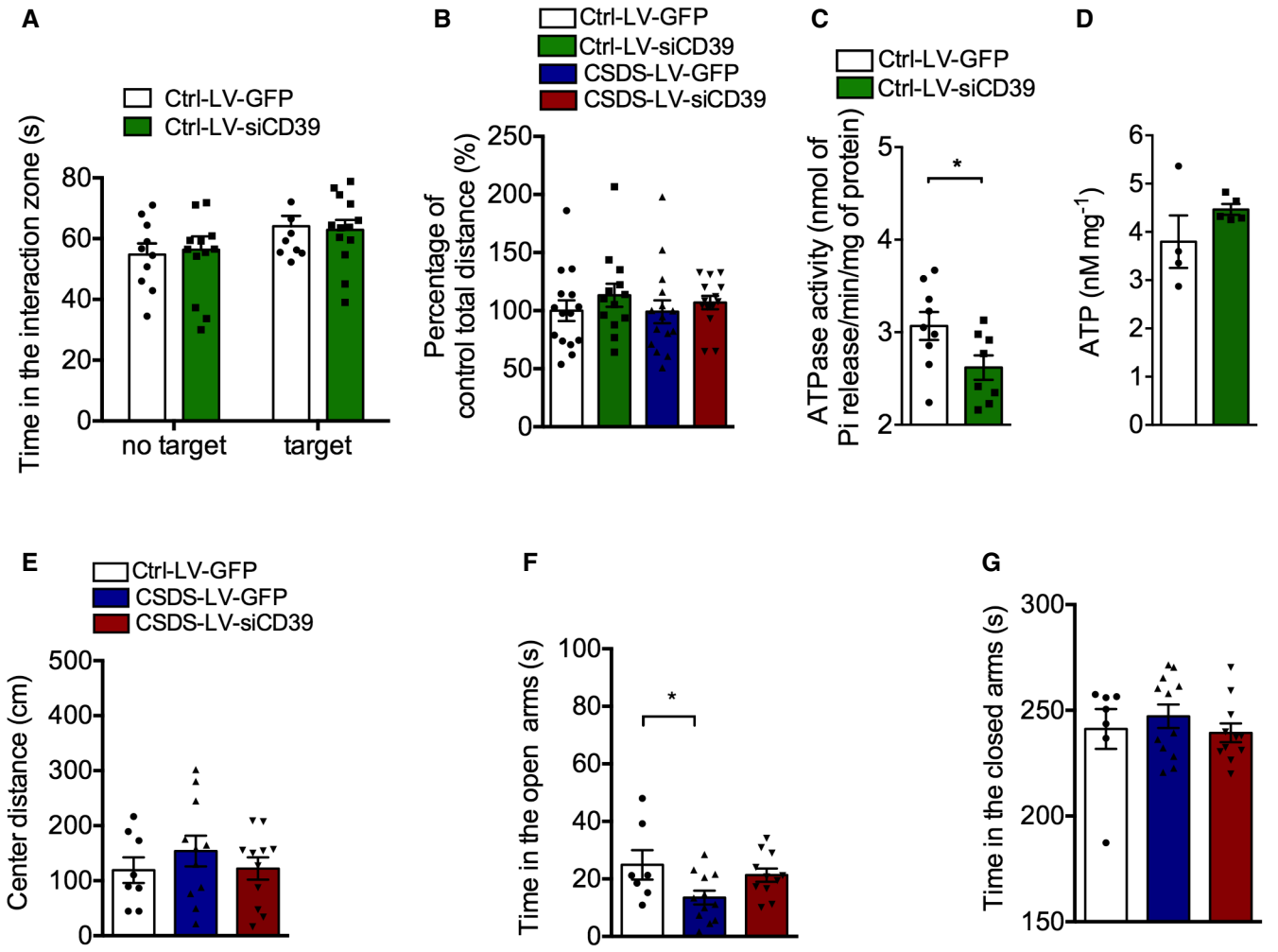

Figure EV4. The effect of LV-siCD39 on locomotor activity and anxiety behaviors of mice exposure to chronic stress.

A The social interaction time of control mice after knocking down CD39 (n = 10, 13 mice; Interaction $F_{1,42}$ = 0.1334, P = 0.7167; Group $F_{1,42}$ = 4.366, P = 0.0428; Drug $F_{1,42}$ = 0.002565, P = 0.9598, two-way ANOVA with Tukey's post-test).

B The locomotor activity of mice with LV-siCD39 infusion into hippocampus in the open field test (n = 15, 13, 15, 14 mice; Interaction $F_{1,53}$ = 0.09372, P = 0.7607; Group $F_{1,53}$ = 0.1669, P = 0.6845; Drug $F_{1,53}$ = 1.450, P = 0.2339, two-way ANOVA with Tukey's post-test).

C The ATPase activity of control mice with LV- siCD39 intra-hippocampal infusion (n = 9, 8 mice; P = 0.043, Student's t-test).

D The ATP level of control mice with LV-siCD39 intra-hippocampal infusion (n = 4, 5 mice; P = 0.2181, Student's t-test).

E The center distance of stressed mice with LV-siCD39 in the OFT (n = 8, 11, 11 mice; Treatment, $F_{2,27}$ = 0.6317, P = 0.5394, one-way ANOVA with Fisher's LSD test).

F, G Time spent in the open arms (F) and closed arms (G) of stressed mice with LV-siCD39 in EPM test (n = 7, 12, 11 mice; for open arms, Treatment, $F_{2,27}$ = 3.650, P = 0.0395; CSDS – LV-GFP versus Ctrl – LV-GFP, P = 0.0183; for closed arms, Treatment, $F_{2,27}$ = 0.5164, P = 0.6024, one-way ANOVA with Fisher's LSD test).

Data information: Data are expressed as the means ± SEM. *P < 0.05, **P < 0.05.
Source data are available online for this figure.

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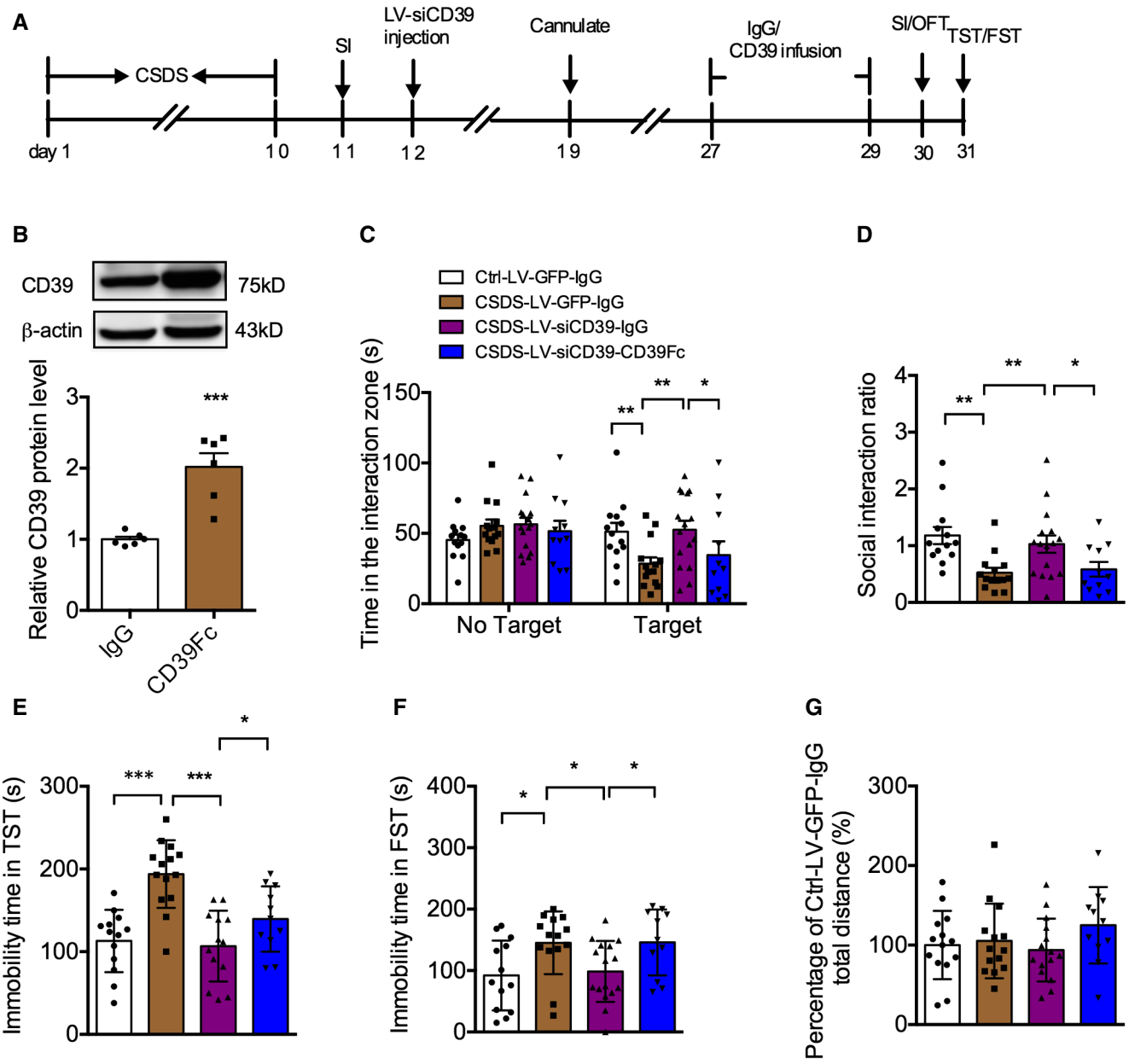

Figure EV5. The effect of extracellular recombinant CD39 protein (CD39Fc) on depressive behaviors of stressed mice infusion with LV-siCD39.

A Experimental timelines.

B Expression of CD39 in the hippocampus of mice injected with CD200Fc (n = 6 mice/group; CD39Fc versus IgG, P = 0.0004, Student's t-test).

C Time in the interaction zone of mice infusion with CD39Fc after knockdown of CD39 in SI test (n = 13, 14, 16, 11 mice; Interaction, $F_{3,100}$ = 2.977, P = 0.0352; Target, $F_{1,100}$ = 6.175, P = 0.0146; Drug, $F_{3,100}$ = 2.028, P = 0.1148; for target, CSDS-LV-GFP-IgG versus Ctrl-LV-GFP-IgG, P = 0.0077; CSDS-LV-siCD39-IgG versus CSDS-LV-GFP-IgG, P = 0.0031; CSDS-LV-siCD39-CD39Fc versus CSDS-LV-siCD39-IgG, P = 0.0378, two-way ANOVA with Tukey's post-test).

D Social interaction ratio of mice infusion with CD39Fc after knockdown of CD39 in SI test (n = 13, 14, 16, 11 mice; Treatment, $F_{3,50}$ = 5.690, P = 0.0020; CSDS-LV-GFP-IgG versus Ctrl-LV-GFP-IgG, P = 0.0012; CSDS-LV-siCD39-IgG versus CSDS-LV-GFP-IgG, P = 0075; CSDS-LV-siCD39-CD39Fc versus CSDS-LV-siCD39-IgG, P = 0.0263, one-way ANOVA with Fisher's LSD test).

E, F Infusion with CD39Fc into hippocampus abolished the decreased immobility time of stressed mice injection with LV-siCD39 in the TST (E) and FST (F) (for TST, n = 13, 14, 13, 11; Treatment, $F_{3,47}$ = 13.22, P < 0.0001; CSDS-LV-GFP-IgG versus Ctrl-LV-GFP-IgG, P < 0.0001; CSDS-LV-siCD39-IgG versus CSDS-LV-GFP-IgG, P < 0001; CSDS-LV-siCD39-CD39Fc versus CSDS-LV-siCD39-IgG, P = 0.05; for FST, n = 13, 14, 16, 11; Treatment, $F_{3,50}$ = 4.047, P = 0.0119; CSDS-LV-GFP-IgG versus Ctrl-LV-GFP-IgG, P = 0.0116; CSDS-LV-siCD39-IgG versus CSDS-LV-GFP-IgG, P = 0191; CSDS-LV-siCD39-CD39Fc versus CSDS-LV-siCD39-IgG, P = 0.0261, one-way ANOVA with Fisher's LSD test).

G Total distance of mice in the OFT (n = 14, 14, 15, 11 mice; Treatment, $F_{3,50}$ = 1.136, P = 0.3437, one-way ANOVA with Fisher's LSD test).

Data information: Data are expressed as the means ± SEM. *P < 0.05, **P < 0.01, ***P < 0.001.
Source data are available online for this figure.

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