Supporting information

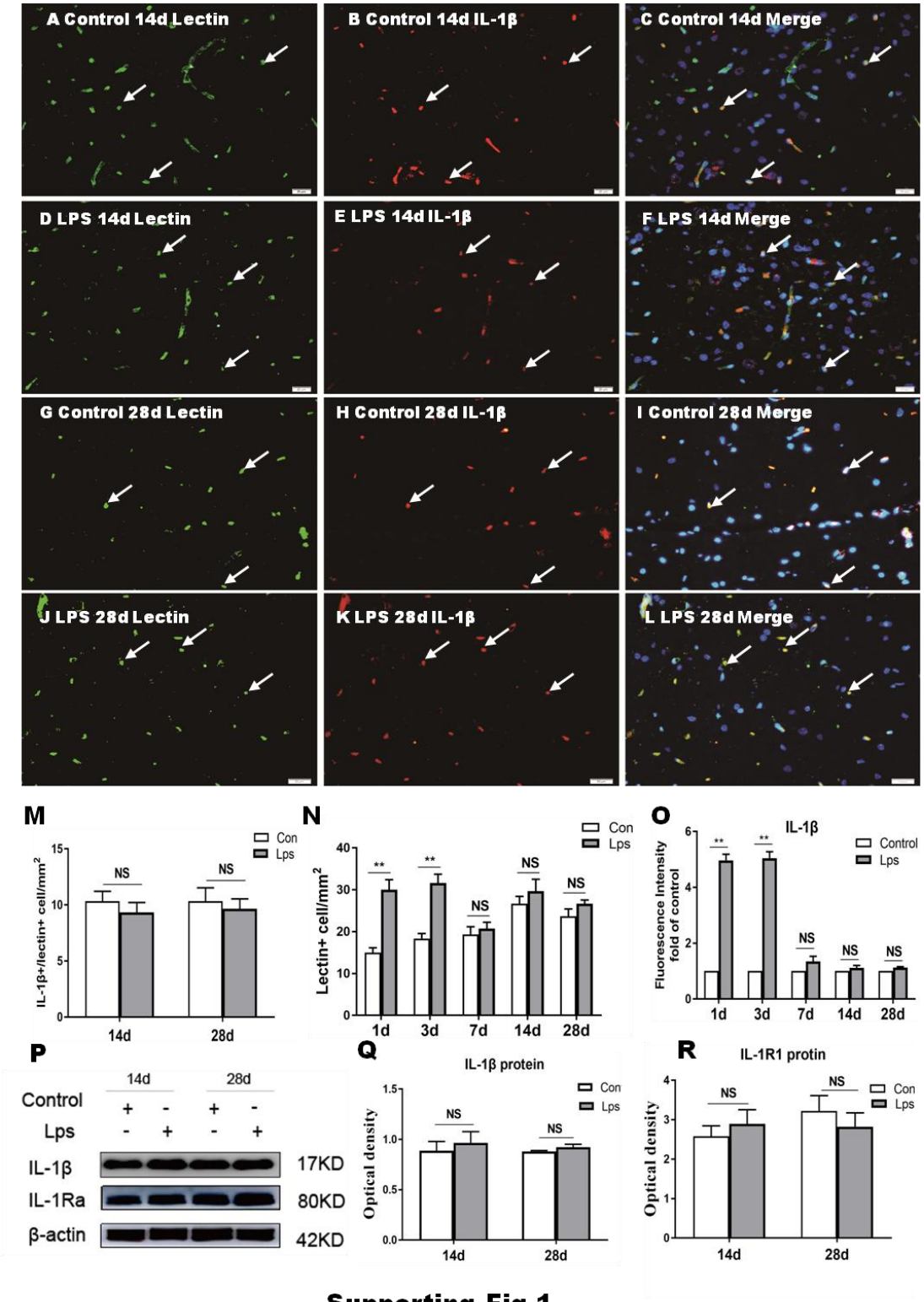
Supporting table 1. Findings as the rationale for dose selection.

group	1d[a] (weight/mortality)	3d[a] (weight/mortality)	7d[a] (weight/mortality)
PBS	7-9g/0	12-13g/0	18-20g/0
0.25mg/kg	8-9g/0	12-13g/0	18-20g/0
0.5mg/kg	7-9g/0	11-13g/0	16-19g/0
1.0mg/kg	6-7.5g*/10%	8-10g*/40%	12-13g*/40%
2.0mg/kg	6-7.5g/20%	8-10g/80%	12-13g/80%
4.0mg/kg	6-7.5g/40%	8-10g/100%	-
8.0mg/kg	6-7.5g/80%	8-10g/100%	-

a: d= day/days after LPS/PBS injection. *: weight of 1.0mg/kg LPS group vs. weight of control group, $P < 0.05$.

We conducted a pre-experiment to determine the dose of LPS. The doses of 0.25mg/kg, 0.50mg/kg, 1.0mg/kg, 2.0mg/kg, 4.0mg/kg, 8.0mg/kg were tested. The weight of newborn Sprague-Dawley (SD) rats ranged from 5g to 7g. Postnatal rats at day 1 (P1) were intraperitoneally injected with LPS of different doses or phosphate buffer saline (PBS) (0.01 mol/L). The rats injected with PBS served as the control group. The weight of rats ranged from 7-9g at 1 day (d), 12-13g at 3d and 18-20g at 7d after PBS treatment. The weight of rats from the 0.25mg/kg LPS group ranged from 8-9g at 1d, 12-13g at 3d and 18-20g at 7d after 0.25mg/kg LPS treatment, which was not different from the control group. The weight of rats from the 0.50mg/kg LPS group ranged from 7-9g at 1d, 11-13g at 3d and 16-19g at 7d after 0.50mg/kg LPS treatment, which was not significantly different from the control group. The weight of rats from the 1.0mg/kg LPS group ranged from 6-7.5g at 1d (mortality was 10%), 8-10g at 3d (mortality was 40%) and 12-13g at 7d (mortality was 40%) after 1.0mg/kg LPS treatment, which was significantly different from the control group. The weight of rats from the 2.0mg/kg LPS group ranged from 6-7.5g at 1d (mortality was 20%), 8-10g at 3d (mortality was 80%) and 12-13g (mortality was 80%) at 7d after 2.0mg/kg LPS treatment. The weight of rats from the 4.0mg/kg LPS group ranged from 6-7.5g at 1d (mortality was 40%), 8-10g at 3d (mortality was 100%) after

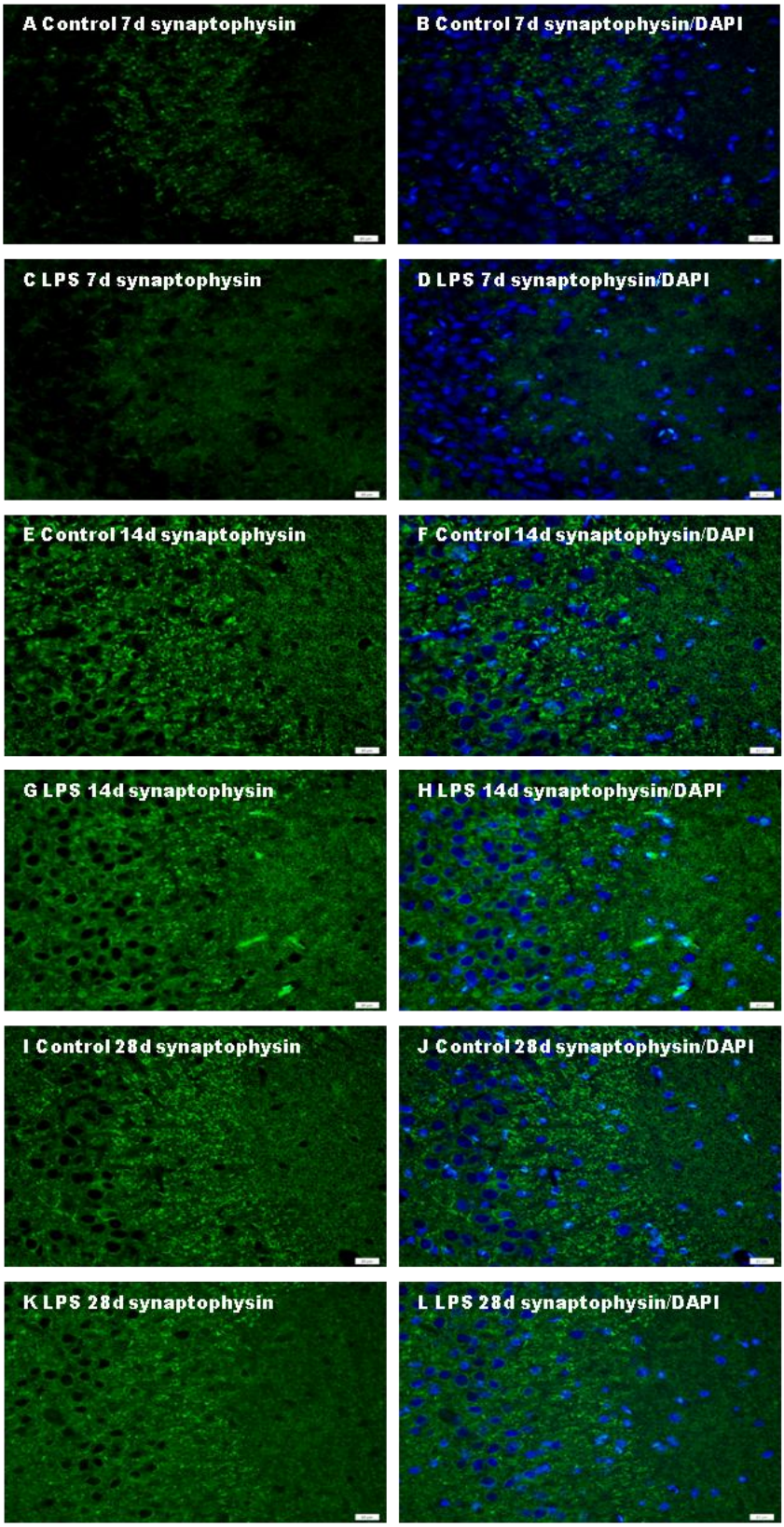
4.0mg/kg LPS treatment. The weight of rats from the 8.0mg/kg LPS group ranged from 6-7.5g at 1d (mortality was 80%), 8-10g at 3d (mortality was 100%) after 8.0mg/kg LPS treatment. According to the weight and mortality of different LPS groups, the protein expression of IL-1β in the hippocampus of 0.25mg/kg, 0.5mg/kg, 1mg/kg LPS groups was measured by western blot. The protein expression of IL-1β in the hippocampus was significantly upregulated at 1d and 3d after 1.0mg/kg LPS treatment compared with the control group, which was not significantly increased in the 0.25mg/kg and 0.5mg/kg groups. The dose of 1mg/kg was adopted for determination of its effects in view of the significantly limited weight gain, acceptable mortality rate and significantly IL-1β upregulation.



Supporting Fig.1

Supporting Fig.1. IL-1β and IL-1R1 protein expression in the hippocampus of postnatal rats at 14 and 28d after LPS administration and their corresponding controls. Double immunofluorescence staining showing the distribution of lectin labeled (A, D, G, J,green), and IL-1β (B, E, H, K, red) immunoreactive microglial cells in the CA1

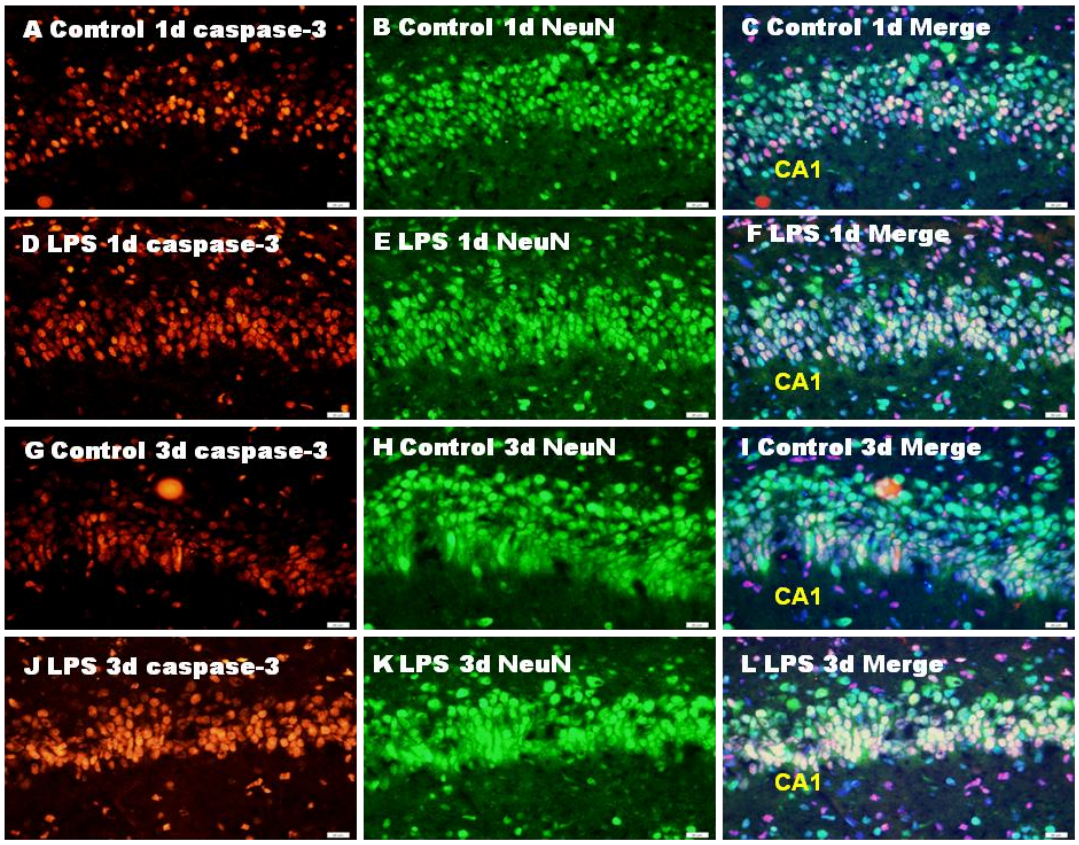
area of hippocampus at 14 and 28d after the LPS injection and in the corresponding control rats. The co-localized expression of lectin and IL-1β in microglia can be seen in C, F, I and L. IL-1β immunofluorescence in microglia at 14 and 28d is comparable to the corresponding controls. Bar graph in **M** summarizes the frequency of IL-1β^+/lectin$^+$ cells/mm^2 at 14 and 28d from three independent experiments (n=3). Bar graph in **N** summarizes lectin$^+$ cells/mm^2 at 1, 3, 7, 14 and 28d from three independent experiments (n=3). Bar graph in **O** shows quantification of fluorescence intensity ratio (LPS vs. Control) of IL-1β in the CA1 area of hippocampus at 1, 3, 7, 14 and 28d from three experiments (n=3). Quantification by immunoblot (**P**) showing no significant difference in IL-1β and IL-1R1 protein expression at 14 and 28d after LPS treatment when compared with controls. Graphs **Q** and **R** show optical density changes of IL-1β and IL-1R1, respectively, relative to β-actin of each group from three independent experiments (n=3). Scale bars: **A-L** 20 μm. * P<0.05, ** P<0.01

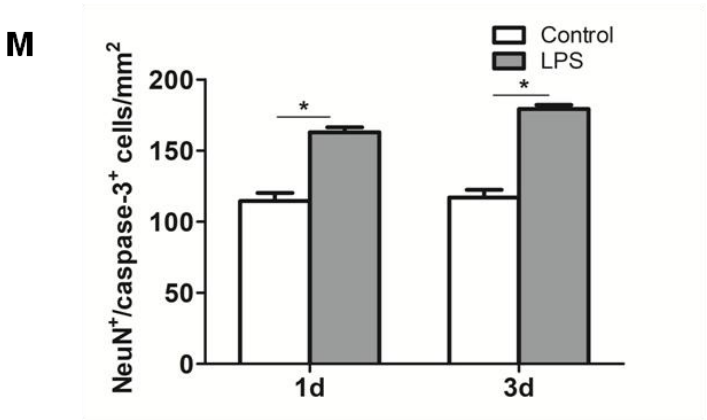


Supporting Fig.2

Supporting Fig.2. Synaptic protein expression in the CA3 of hippocampus at 7, 14 and 28d following LPS/PBS treatment. By immunostaining, synaptophysin (green)

mainly distributed in the CA3 was decreased at 7 (**C**), 14 (**G**) and 28d (**K**) after LPS treatment compared with controls (**A**, **E**, **I**). (n=3) Scale bars: A-L 20 μm.

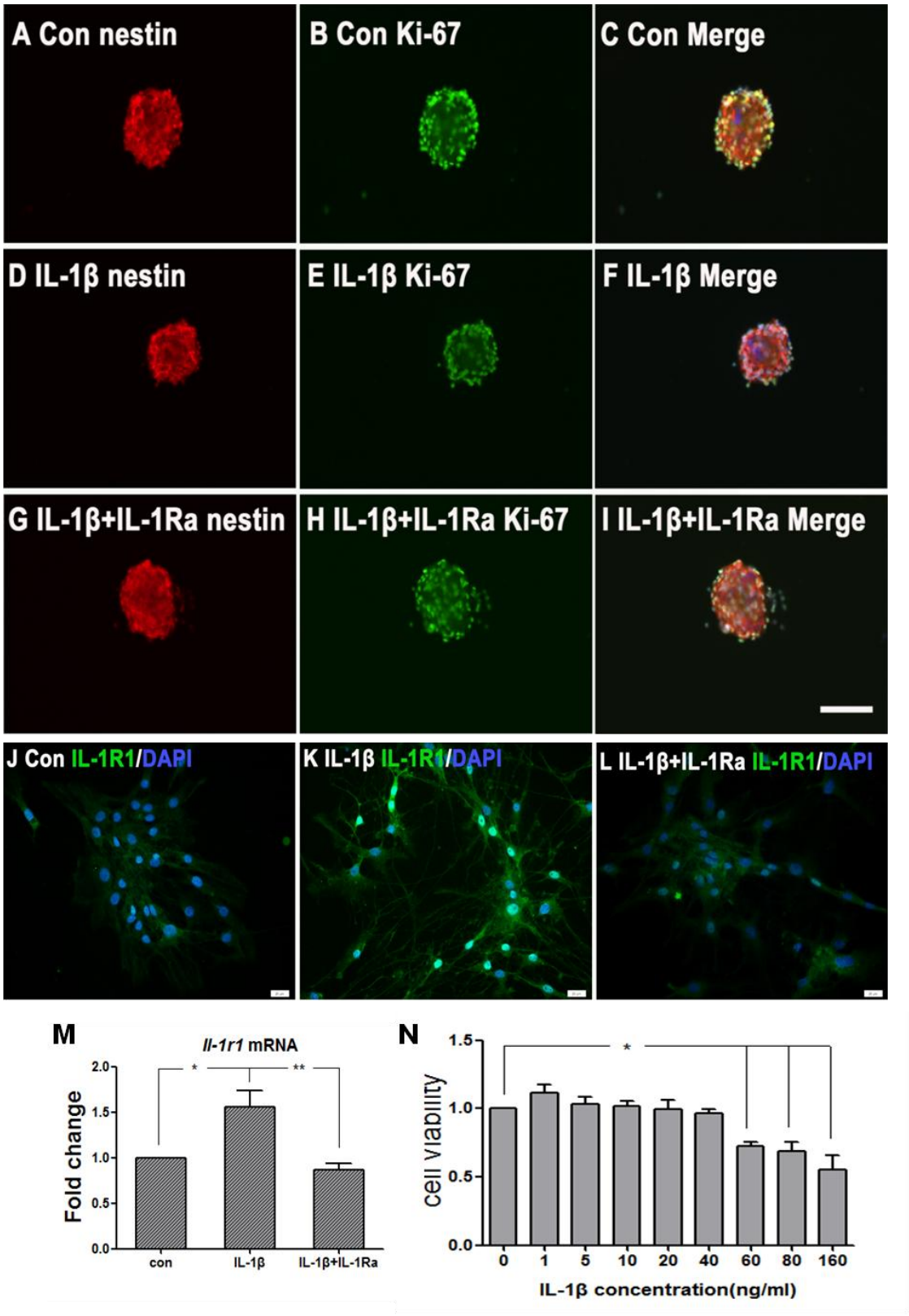




Supporting Fig.3

Supporting Fig.3. Apoptosis of neurons in CA1 of hippocampus. The incidence of apoptotic neurons colabeled by caspase-3 (*red*) and NeuN (*green*) was markedly increased at 1 (**D-F**) and 3d (**J-L**) in CA1 of hippocampus when compared with controls (**A-C**, **G-I**). Scale bars: **A-X** 20 μm. Bar graph **M** summarized the frequency

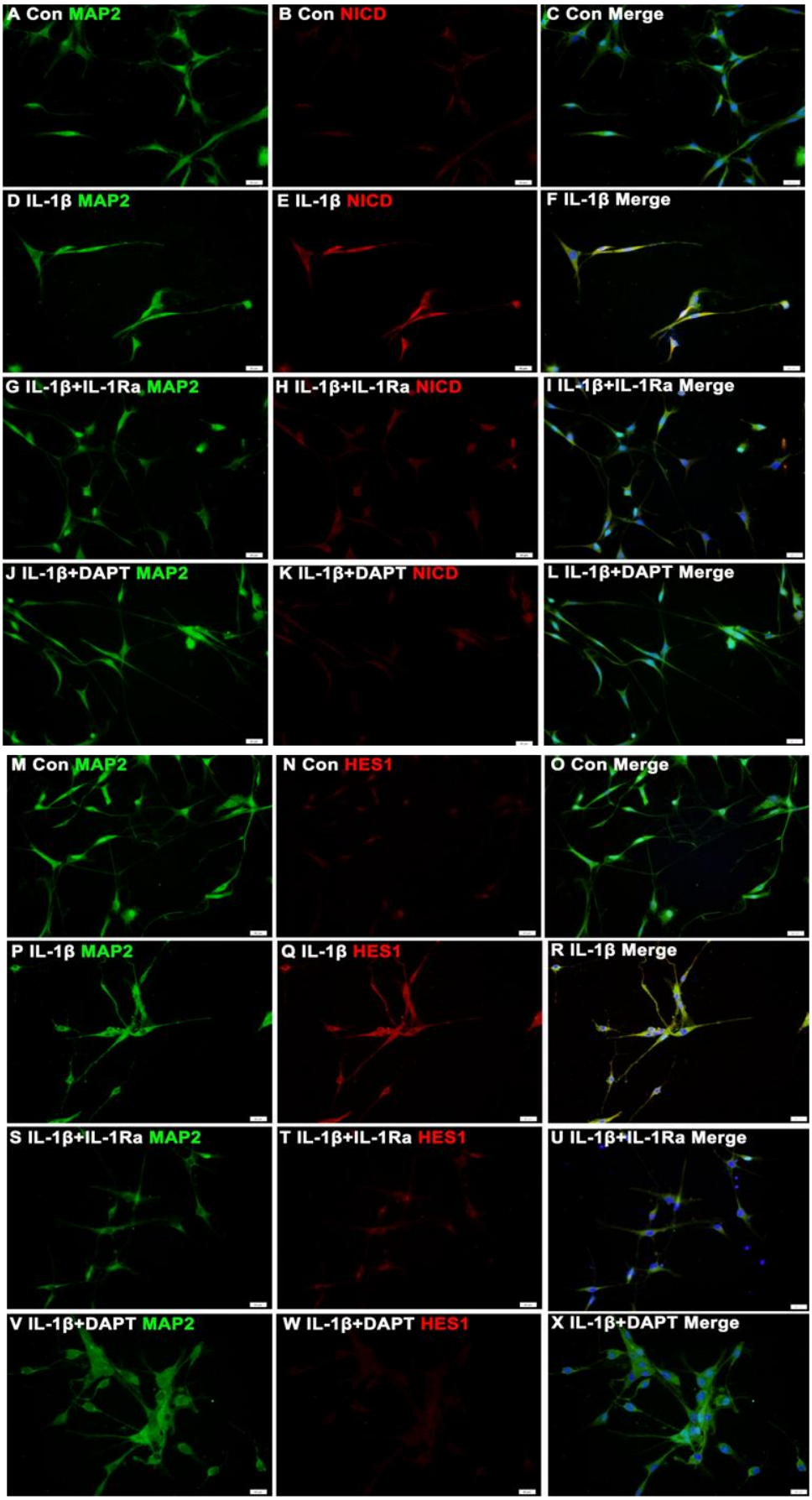
of $NeuN^+/Caspase3^+$ cells/mm^2 at 1 and 3d after LPS injection when compared with their corresponding controls from three independent experiment s (n=3). * $P<0.05$



Supporting Fig.4

Supporting Fig.4. IL-1β inhibits the proliferation of NPCs' neurosphere and induces IL-1R1 expression in differentiated NPCs *in vitro*. Immunofluorescence

staining shows expression of nestin (A, D, G, red) and Ki-67 (B, E, H, green). The co-localized expression of nestin and Ki-67 can be seen in panels C, F, I. IL-1β exposure for 1d induced a decrease in NPCs proliferation (**D-F**) when compared with controls (**A-C**). IL-1Ra reversed these changes induced by IL-1β (**G-I**). Immunofluorescence staining (**J-L**) shows increased expression of IL-1R1 on differentiated NPCs exposed to IL-1β (40 ng/ml) for 1d. Panel **M** shows bar graph depicting significant increase in IL-1R1 mRNA expression in differentiated NPCs treated with IL-1β for 1d. The upregulated mRNA expression of IL-1R1 was counteracted by IL-1Ra. Panel **N** shows the viability of differentiated NPCs treated with different concentrations of IL-1β. The viability of differentiated NPCs was significantly decreased when the cells were treated with IL-1β at a dose exceeding 40ng/mL (**N**). Data were derived from three independent experiments (n=3). Scale bars: **A-I** 50 μm, **J-L** 20 μm. * $P<0.05$, ** $P<0.01$



Supporting Fig.5

Supporting Fig.5. Protein expression of NICD and Hes1 in differentiated NPCs exposed to IL-1β for 1d *in vitro*. Immunofluorescence images of cultured NPCs show expression of NICD (B, E, H, K, *red*), MAP2 (A, D, G, J, M, P, S, V, *green*), Hes1 (N, Q, T, W, *red*) and DAPI (C, F, I, L, O, R, U, X, blue) at 1d after IL-1β, or IL-1β+IL-1Ra or IL-1β+DAPT treatment when compared with the corresponding control. IL-1β exposure for 1d induced increased expression of NICD (**E**) and Hes1 (**Q**) when compared with the controls (**B**, **N**). However, NICD and Hes1 immunofluorescence was attenuated in differentiated NPCs pretreated with IL-1Ra (**H**, **T**) or DAPT (**K**, **W**)(n=3). Scale bars: A-X 20 μm.