|   | MHCII | Ly6G   | Ly6G-C  | Ly6C   |
|---|-------|--------|---------|--------|
|   | ![Image](image1) | ![Image](image2) | ![Image](image3) | ![Image](image4) |
|   | Ki67  | F4-80  | CX3CR1  | CD172  |
|   | ![Image](image5) | ![Image](image6) | ![Image](image7) | ![Image](image8) |
|   | CD49  | CD45   | CD19    | CD11c  |
|   | ![Image](image9) | ![Image](image10) | ![Image](image11) | ![Image](image12) |
|   | CD8a  | CD4    | CD3e    | CD11b  |
|   | ![Image](image13) | ![Image](image14) | ![Image](image15) | ![Image](image16) |
|   | CD44  | CD24   | CD14    | NK1.1  |
|   | ![Image](image17) | ![Image](image18) | ![Image](image19) | ![Image](image20) |
Figure S1. Mice exposed to foot-shocks developed PTSD-like behavior. (A) Schematic representation of treatment schedules and the order of behavior tests. As shown, foot-shocks (FS) were delivered to mice at day 1 and day 2, contextual freezing paradigm were measured at day 3, day 8, day 15, and open field (OF) test were performed at day 16. FS: foot-shocks, CFP: contextual freezing paradigm, OF: open field test. (B-D) Foot-shocks exposure increased mice contextual freezing, sertraline administration reduced freezing time percent. (E) Representative image of mice track plot in OF test. (F-H) Statistical analysis of mice performance in OF test. n=9, Data are expressed as means ± SEM. * p<0.05, **p<0.01, ***p<0.001 (ANOVA).

Figure S2. High-dimensional characterization of brain lymphocytes. (A) viSNE plots show the expression pattern of representative markers in all brain lymphocytes.

Figure S3. Decreased the density of dendritic spines of pyramidal neurons in CA1 region in PTSD mice brain. (A) Representative images of third order dendrites in the CA1 regions of the hippocampus. scale bar = 10 μm (B) Statistic graph displaying spine density of third order dendrites in CA1 region.

Figure S4. Microglia depletion alleviates foot-shocks induced PTSD-like behaviors. (A) IHC staining shows microglia restored after DT administration. (B) Statistic data shows microglia number restored after DT administration. **p<0.01, ***p<0.001 (ANOVA) (C) IHC staining shows microglia depletion efficiency after elevated plus maze test with PLX3397 treatment. (D) Statistic data shows microglia number decreased after elevated plus maze test with PLX3397 treatment. (E-G) PLX3397 administration decreased mice freezing behavior. (H-K) PLX3397 administration increased mice activity in center area in OF test. (L-O) PLX3397 administration increased mice activity in open arm in EPM test. n=8, Data are expressed as means ± SEM. * p<0.05, **p<0.01, ***p<0.001 (Student’s t test).

Figure S5. Minocycline treatment alleviates PTSD-like phenotype after long term foot-shocks exposure. (A) Schematic representation of experimental procedure. (B-C) Effect of minocycline on PTSD mice in fear freezing test. (D-G) Effect of minocycline on
PTSD mice in open field test. (H-K) Effect of minocycline on PTSD mice in EPM test; n = 10, data are expressed as means ± SEM, * p < 0.05, ** p < 0.01, *** p < 0.001 (ANOVA).
## Supplementary Table 1. List of antibody panel used in CytoF

| List | mark          | List | mark          |
|------|---------------|------|---------------|
| 1    | CD45          | 22   | F4/80         |
| 2    | CD3e          | 23   | CD274(PD-L1)  |
| 3    | CD44          | 24   | iNOS          |
| 4    | CD24          | 25   | CD69          |
| 5    | MHC II        | 26   | CD25          |
| 6    | B220(CD45R)   | 27   | CD103         |
| 7    | FceRIα        | 28   | NK1.1         |
| 8    | Ly6G/C        | 29   | Argnase I     |
| 9    | CD38          | 30   | CD49b         |
| 10   | Ly6G          | 31   | Foxp3         |
| 11   | Ly6C          | 32   | CD115(CSF-1R) |
| 12   | CX3CR1        | 33   | CD49a         |
| 13   | CD14          | 34   | CD23          |
| 14   | CD62L         | 35   | CD127         |
| 15   | CD11c         | 36   | CD172a(SIRPα) |
| 16   | SiglecF       | 37   | CD152(CTLA-4) |
| 17   | Ki67          | 38   | TCR-b chain   |
| 18   | CD80          | 39   | IgM           |
| 19   | BST2          | 40   | CD4           |
| 20   | CD27          | 41   | CD8a          |
| 21   | CD19          | 42   | CD11b         |
| Gene symbol | NCBI Gene ID | Forward | Reverse |
|-------------|--------------|---------|---------|
| TNF-α       | 21926        | CAGGCGGTGCCTATG TCTC | CGATCACCCCGAAGT TCAGTAG |
| IL-6        | 16193        | GCTACCAAACCTGGATATAATCAGGA | CCAGGATGCTATGGA ACTCCAGAA |
| Il-4        | 16189        | GGTCTCAACCCACAGCTAGT | GCCGATGATCTCTCT CAAGTGAT |
| Il-10       | 16153        | GCTCTTACTGACTGACTGAGCATG | CGCAGCTCTAGGAGC ATGTG |
| CD206       | 17533        | CTCTGTTTCAGCTATTGGACGC | CGGAATTTCTGGGATTCAGCTTC |
| β-actin     | 11461        | GGCTGTATTCCCCTCCATCG | CCAGTTGGTAACAATGCCATGT |
| IFNγ        | 15978        | GATGCATTCATGAGATTGCCAAGT | GTGGACCACTCGGATGAGCTC |
| IL-1β       | 16176        | GCAACTGTTTCCTGAACTCAACT | ATCTTTTGGGGTCCGTCAACT |