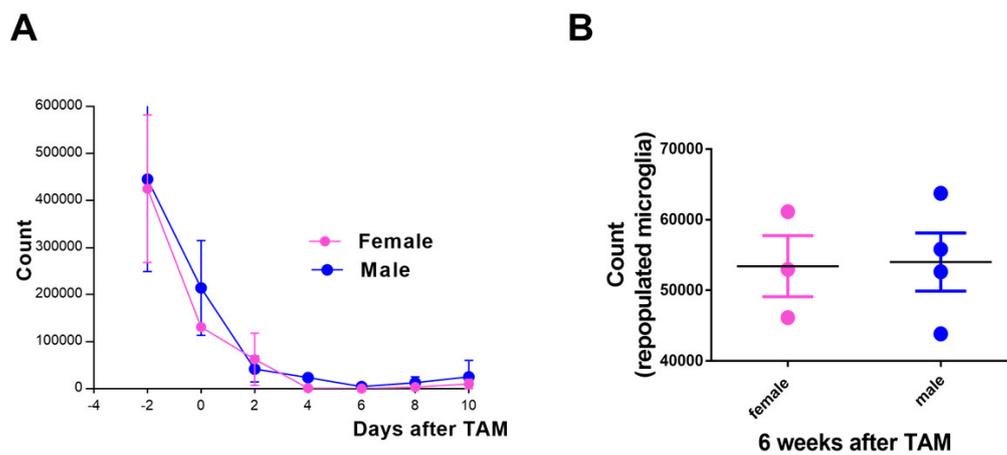
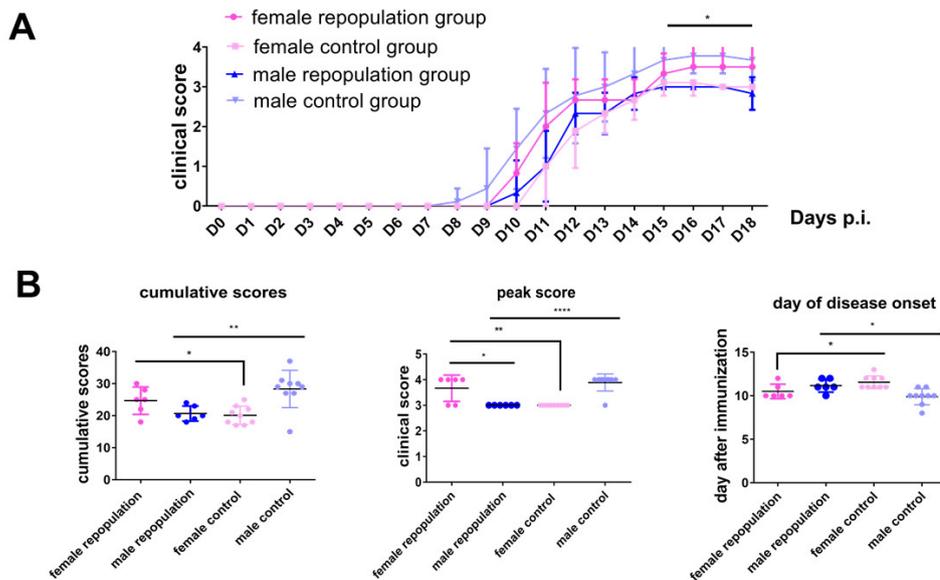


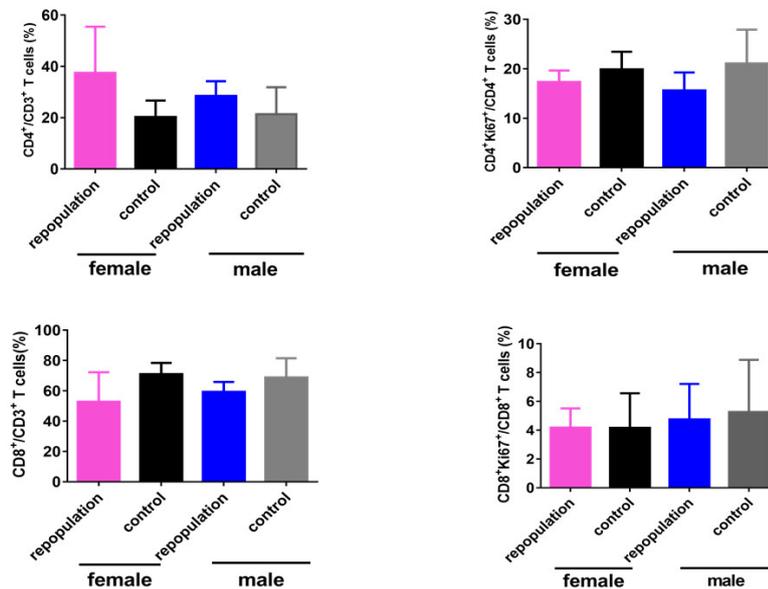
**Supplementary Figure 1: Gating strategy for flow cytometric analysis** (A) Gating strategy of brain myeloid cells in normal  $Cx3cr1^{CreER/+}Rosa26^{DTA/+}$  mice without microglial depletion and repopulation. (B) Gating strategy of brain myeloid cells during MOG-induced EAE in  $Cx3cr1^{CreER/+}Rosa26^{DTA/+}$  mice with newly repopulated microglia. (C) Gating strategy of spinal cord myeloid cells in  $Cx3cr1^{CreER/+}Rosa26^{DTA/+}$  mice without microglial depletion and repopulation. (D) Gating strategy of spinal cord myeloid cells in MOG-induced EAE  $Cx3cr1^{CreER/+}Rosa26^{DTA/+}$  mice with newly repopulated microglia.



**Supplementary Figure 2:** (A) Microglial depletion follows similar dynamics between male and female  $Cx3cr1^{CreER/+}Rosa26^{DTA/+}$  mice at relevant time points. (B) There are no differences regarding the overall numbers of repopulating microglia 6 weeks after tamoxifen injections.



**Supplementary Figure 3:** Sex-specific effects of microglia-like cell engraftment during the acute EAE phase. (A) Clinical scores of neurological deficits post-immunization up to 18 days are indicated. (B) Cumulative scores, peak disease score and day of disease onset in both male and female groups are depicted.



**Supplementary Figure 4:** No differences of infiltrating T cells between sexes during acute EAE (18 days post-immunization of EAE) were recorded in *Cx3cr1<sup>CreER/+</sup>Rosa26<sup>DTA/+</sup>* mice with repopulated microglia and *Cx3cr1<sup>CreER/+</sup>* mice with resident microglia.  $n = 6$  mice/group in female repopulation, female control and male repopulation groups, and  $n = 7$  mice in male control group.