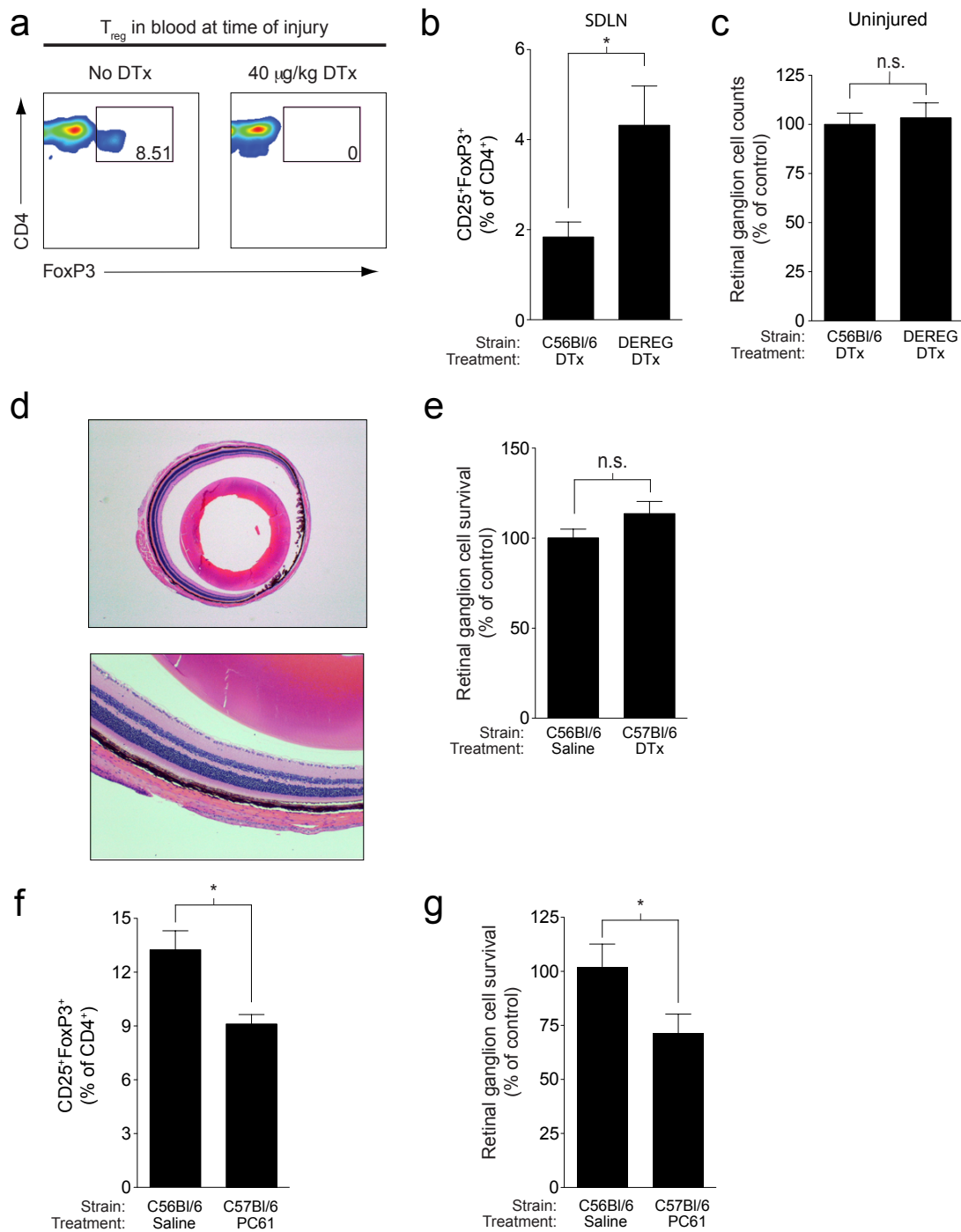
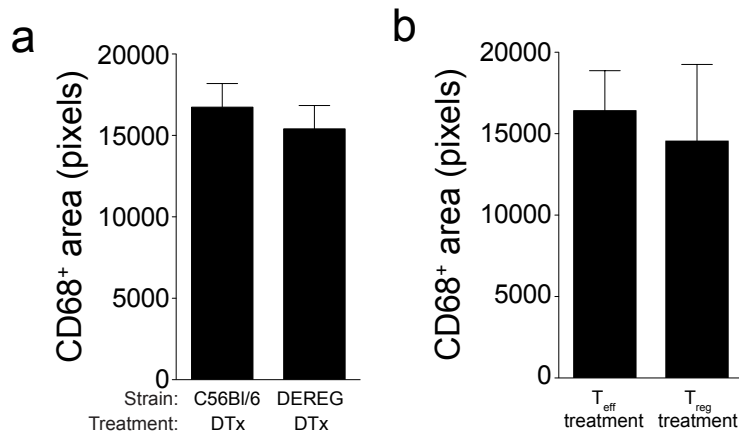


**Supplementary Figure 1:** *Uninjured optic nerves have few GFP<sup>+</sup> Iba1<sup>+</sup> microglia and little arginase-1, but arginase-1 staining is greatly increased after injury. (a)* Immunohistochemical staining of arginase-1 (green) and CD68 (red) in the uninjured and injured optic nerve (scale bar = 100  $\mu$ m). **(b)** Immunohistochemical staining of an optic nerve in a C57Bl/6 mouse that was lethally irradiated and transplanted with GFP bone marrow showing sparse transplanted GFP<sup>+</sup> cells (green) among plentiful resident Iba1<sup>+</sup> microglia (red). Image is from uninjured nerve 6 weeks post-transplantation (scale bar = 100  $\mu$ m).

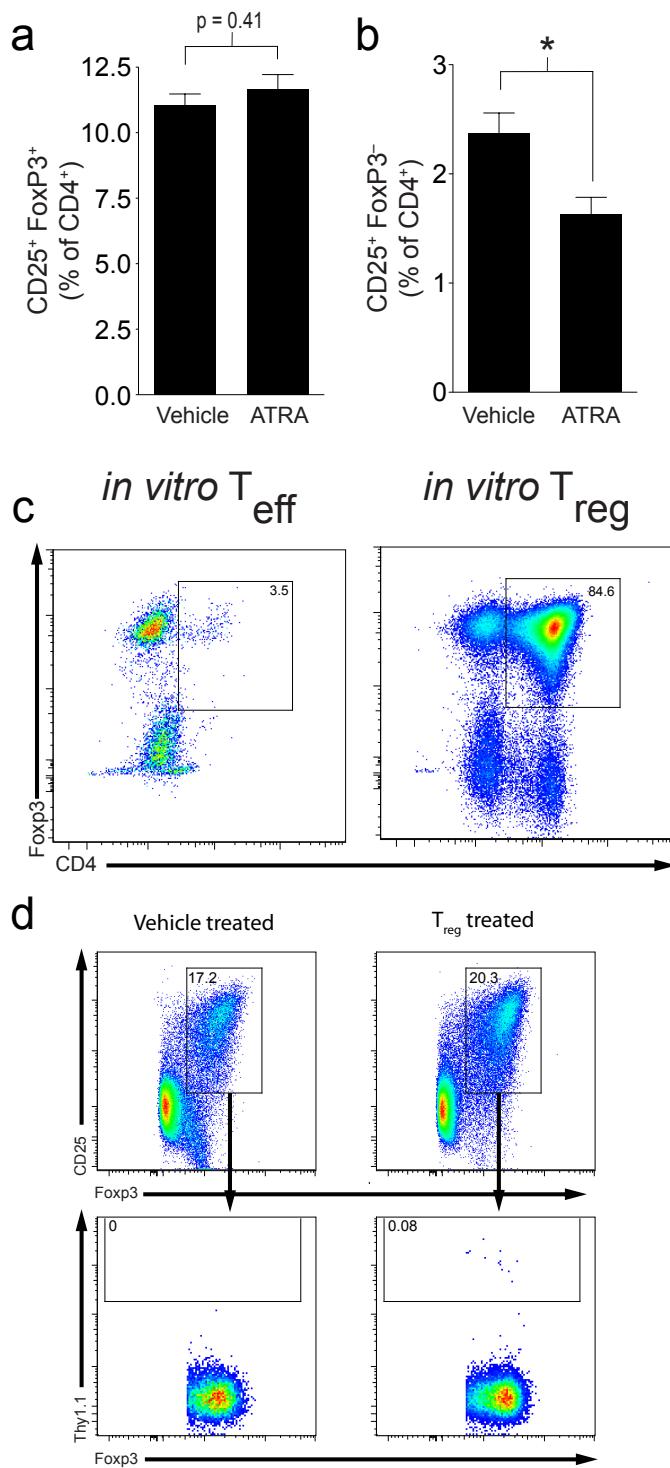


**Supplementary Figure 2: Characterization of 40  $\mu\text{g}/\text{kg}$  DTx. treatment.** (a) Flow cytometry on the day of injury of CD4 and FoxP3 in peripheral blood of DERE mice treated with vehicle or 40  $\mu\text{g}/\text{kg}$  DTx. (b) Flow cytometry in the skin-draining lymph nodes of DEREg or wild type littermates treated with DTx two days before injury and on

the day of injury, showing percent of CD25<sup>+</sup>Foxp3<sup>-</sup> T<sub>eff</sub> cells, graphed as a percentage of TCRβ<sup>+</sup>CD4<sup>+</sup> cells (n = 12 wild type and 9 DEREg treated mice; \*, p < 0.05, Student's t-test; representative of three experiments). (c) Representative images of H&E staining in eyes of DEREg mice treated with 40 μg/kg DTx. Abnormal architecture or immune cell infiltration was found in 0/17 C57Bl/6 and 0/21 B6AF1 mice. (d) Retinal ganglion cell counts from DEREg and wild type mice injected with 40 μg/kg DTx two days before injury and on the day of injury (n = 19 wild type and 25 DEREg; Student's t-test; representative of three experiments). (e) No difference was observed in RGC survival of C57Bl/6 mice treated with 40 μg/kg DTx or saline 2 days before injury and on the day of injury (n = 10 mice per group; Student's t-test; representative of 2 experiments). (f) Flow cytometry in the skin-draining lymph nodes of wild type mice treated with 250μg anti-CD25 or IgG 8 days before injury, showing percent of CD25<sup>+</sup>Foxp3<sup>+</sup> T<sub>reg</sub> cells, graphed as a percentage of TCRβ<sup>+</sup>CD4<sup>+</sup> cells (n = 4 per group; \*, p < 0.05, Student's t-test; representative of three experiments). (g) RGC survival of C57Bl/6 mice treated with 250 μg anti-CD25 or IgG 8 days before injury (n = 6 IgG and 7 anti-CD25; \*, p < 0.05, Student's t-test; representative of 2 experiments).



**Supplementary Figure 3:** *There is no change in CD68<sup>+</sup> area after injury with T<sub>reg</sub> manipulation.* (a) Quantification of CD68<sup>+</sup> area in immunohistochemical staining of injured optic nerves of C57Bl/6 treated with DTx or DEREg mice treated with DTx (n = 3 C57Bl/6 treated with DTx and 9 DEREg treated with DTx Student's t-test; representative of two experiments). (b) Quantification of CD68<sup>+</sup> area in immunohistochemical staining of injured optic nerves of C57Bl/6 mice injected with 1x10<sup>6</sup> T<sub>eff</sub> or T<sub>reg</sub> cells 2 days before injury and on the day of injury (n = 9 T<sub>eff</sub> injected and 6 T<sub>reg</sub> injected; Student's t-test; representative of two experiments).



**Supplementary Figure 4:** ATRA treatment leads to decreased  $T_{eff}$  proportion in the skin-draining lymph nodes and to increased  $T_{reg}$  proportion *in vitro*. **(a, b)** Flow cytometry in the skin-draining lymph nodes of wild type treated with vehicle or ATRA showing percent of CD25<sup>+</sup>Foxp3<sup>+</sup> T<sub>reg</sub> cells **(a)** and of CD25<sup>+</sup>Foxp3<sup>-</sup> T<sub>eff</sub> cells **(b)**, graphed as a percentage of TCRβ<sup>+</sup>CD4<sup>+</sup> cells (n = 7 vehicle treated and n = 9 ATRA treated; \*, *p* <

0.05, Student's t-test; representative of two experiments). **(c)** Representative flow cytometry plots of viable cells in lymph node cultures that have been treated with 10 nM ATRA, 5 ng/mL TGF $\beta$ , 250 U/mL IL-2, 1  $\mu$ g/mL anti-CD3, and 1  $\mu$ g/mL anti-CD28 ( $T_{reg}$ ) or only 1  $\mu$ g/mL anti-CD3, and 1  $\mu$ g/mL anti-CD28 ( $T_{eff}$ ) for 5 days. The boxes denote the CD4<sup>+</sup>Foxp3<sup>+</sup>  $T_{reg}$  population, and numbers represent percent of viable cells that are CD4<sup>+</sup>Foxp3<sup>+</sup>. **(d)** Representative flow cytometry plots of viable cells in the deep cervical lymph node cultures after injection of 1 X 10<sup>6</sup> Thy1.1  $T_{reg}$  cells or vehicle. The gates on the top plots denote the CD4<sup>+</sup>Foxp3<sup>+</sup>  $T_{reg}$  cells, and the gates on the bottom denote the Thy1.1<sup>+</sup> fraction of  $T_{reg}$  cells.