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Astrocyte gp130-expression is critical for the control of *Toxoplasma* encephalitis

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Toxoplasma (*T.*) *gondii* infects astrocytes, neurons and microglia cells in the CNS and, after acute encephalitis, persists within neurons. Robust astrocyte activation is a hallmark of *Toxoplasma* encephalitis (TE); however, the *in vivo* function of astrocytes is largely unknown. To study their role in TE, we generated C57BL/6 GFAP-Cre gp130$^{fl/fl}$ mice, which lack gp130, the signal transducing receptor for IL-6 family cytokines, in their astrocytes. In TE of wildtype mice, the gp130 ligands IL-6, IL-11, IL-27, LIF, oncostatin M, ciliary neurotrophic factor, B cell stimulating factor, and cardiotrophin-1 were upregulated. In addition, GFAP$^+$ astrocytes of gp130$^{fl/fl}$ control mice were activated, increased in number, and efficiently restricted inflammatory lesions and parasites, thereby, contributing to survival from TE. In contrast, *T. gondii*-infected GFAP-Cre gp130$^{fl/fl}$ mice lost GFAP$^+$ astrocytes in inflammatory lesions resulting in an inefficient containment of inflammatory lesions, impaired parasite control and, ultimately, a lethal necrotizing TE. Production of IFN-gamma and IGTP, which mediate parasite control in astrocytes, were even increased in GFAP-Cre gp130$^{fl/fl}$ mice indicating that instead of the direct anti-parasitic effect the immunoregulatory function of GFAP-Cre gp130$^{fl/fl}$ astrocytes was disturbed. Correspondingly, *in vitro* infected GFAP-Cre gp130$^{fl/fl}$ astrocytes inhibited growth of *T. gondii* efficiently after stimulation with IFN-gamma, whereas neighbouring non-infected and TNF-stimulated GFAP-Cre gp130$^{fl/fl}$ astrocytes became apoptotic. Collectively, these are the first experiments demonstrating a crucial function of astrocytes in CNS infection.