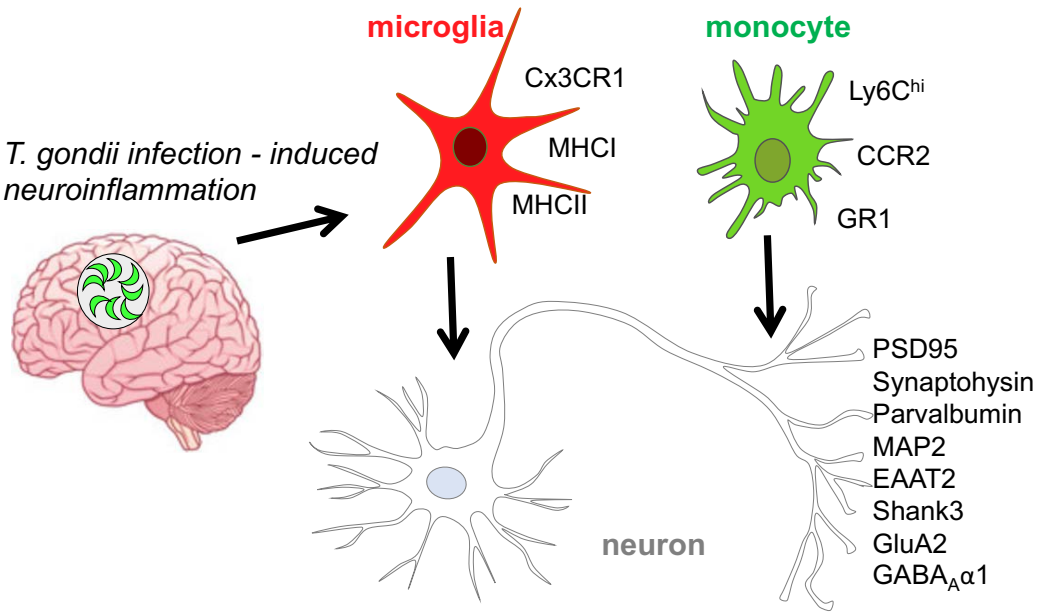
TP5: The effect of immunosenescence on synapse composition in a chronic neuroinflammation model (Ildiko R. Dunay)

Age-related impairments in the immune system, referred to as immunosenescence, contribute to increased susceptibility to infection in the older population. It has been reported that aging in microglia and macrophages impacts on many processes including toll-like receptor signaling, polarization, phagocytosis, and wound repair (Rawji et al., 2016, Raj et al., 2017). An important factor that contributes to such age-related changes is the infection with *Toxoplasma gondii (T. gondii),* as the seropositivity of this infection increases significantly with age (Parlog et al., 2015). Using a well-established murine model, we have recently detected distinct alterations in neuronal morphology (by DT-MRI, MAP 2 Immunofluorescence and Sholl analysis) and in the expression of synaptic proteins (e.g. PSD95, synaptophysin, EAAT2, Shank3, GluA2 by WB and mass spectrometry) upon chronic cerebral *T. gondii* infection. The underlying alterations in synaptic composition and plasticity as well as consequences for neuronal connectivity are likely to involve the parallel development of neuroinflammation (Parlog et. al., 2014, Lang et al. 2018). In fact, latent *T. gondii* infection is associated with basal neuroinfammation, where resident microglia become activated and produce specific cytokines and chemokines. We have recently reported, that myeloid derived innate immune cells enter the CNS and contribute to the development of neuroinflammation as well as host defense (Biswas et al., 2016, Möhle et al., 2014). While both microglia and macrophages display diminished phagocytic capacity and chemotaxis upon aging, the effects manifest differently with regards to cytokine production.

Hypothesis: We propose that chronic *T. gondii* infection-induced immune cell activation and myeloid cell recruitment contribute to synaptic changes during aging. We define the Aims:

1. To elucidate age-dependent microglia activation upon infection-induced neuroinflammation, and correlate these to the alterations in synapse composition and function during the course of infection.
2. To unravel differences in innate immune cells recruitment and function in the aging mice brain, and their communication with neuronal synapses during chronic cerebral Toxoplasmosis.



Infection-induced neuroinflammation alters synaptic proteins.

Collaborations: **TP1/9** Dieterich and **TP8** Gundelfinger/Seidenbecher (alterations in the synaptic proteins). **TP11** Leßmann (LTP on hippocampal slices from young and old mice after adoptive transfer of immune cells) **TP6** Dityatev (analyzing microglia and monocyte migration). **TP12** Düzel (characterizing blood monocytes in patients with mild cognitive decline).

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