Infection alters MHC II− and MHC II+ macrophage populations in the meninges which impairs CNS immunity.

Introduction and objectives
Tissue macrophages have an embryonic origin and can be replenished to some degree under steady-state conditions by blood monocytes. However, little is known about the residency of infiltrating monocytes after an inflammatory challenge. The meninges of the central nervous system (CNS) are inhabited by a dense network of newly identified macrophage populations. They act as immune sentinels and are key to control brain homeostasis and neuroinflammation. Here we studied the functional heterogeneity of those resident macrophages and the becoming of infiltrated monocytes after a microbial challenge. The overarching aim is to understand how episodes of inflammation can permanently affect the macrophage landscape at the surface of the brain and have long-term effects on the immune protection of the CNS.

Methods
To address these questions we used high-throughput transcriptomics, in situ histocytometry, multiparametric flow cytometry, and intravital imaging. We performed lineage tracing experiments and functional assays to investigate the origin, heterogeneity and differential properties of macrophage populations at the surface of the CNS at the steady state and following in vivo infection with lymphocytic choriomeningitis virus.

Results
We studied two populations of resident macrophages: MHC II− and MHC II+ cells which were differentially regulated by immune cytokines at steady-state and differed in their response to microbial challenge, with MHC II+ cells being the less efficient. Following viral infection, both myeloid populations were infected by the virus, and intravital imaging studies revealed that they were targeted by infiltrating virus-specific CD8+ T cells, which promoted their depletion. Concurrently, the meninges were infiltrated by inflammatory monocytes that engrafted the meningeal niche in an interferon-γ-dependent manner. Infiltrated monocytes preferentially differentiated into MHC II+ cells. This engraftment led to an increase in the ratio of MHC II+ MMs, which had functional consequences including loss of bacterial and immunoregulatory sensors.

Conclusion and discussion
Collectively, these data indicate that peripheral monocytes can engraft the meninges after an inflammatory challenge, increasing the proportion of MHC II+ resident macrophage population and imprinting the compartment with long-term defects in immune function.

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