NEUROSCIENCE

Microfetti: a fate-mapping system for microglia

A multicolor reporter mouse model enables monitoring of the fate and dynamics of microglia in health and disease.

Microglia are long-lived tissue-resident macrophages of the central nervous system (CNS) and play a critical role in sculpturing developing neural circuits, maintaining the normal functions of the brain, and mediating immune responses in CNS diseases. Microglia originate from progenitors in the yolk sac during embryogenesis and can self-replenish during steady state or disease. However, fate-mapping studies have relied on unicolor reporter mouse lines, which do not distinguish long-lived cells from the continuously renewing population. Consequently, questions such as the existence of proliferative niches or microglial stem cell populations remain largely unanswered.

To address this limitation, Marco Prinz and colleagues at the University of Freiburg developed a microglia-focused multicolor

fate-mapping system based on the 'Confetti' system; they named their system 'Microfetti'. In these mice, individual microglia can randomly express one of four possible fluorescent proteins. Daughter cells from a dividing microglia express the same fluorescent protein as the mother cell and so give rise to a cluster of clonally related microglia.

Using the Microfetti system, the authors observed limited microglial proliferation in the mouse hippocampus and cerebellum and almost no division in the cerebral cortex. They found no evidence for a specialized microglial niche, as proliferation seemed to occur at random locations. Thus, the microglial network in the healthy adult mouse brain is largely stable, and microglial self-renewal is likely a stochastic process.

They then examined microglial dynamics during CNS pathology by subjecting Microfetti mice to unilateral facial nerve axotomy (FNX). A few days after FNX,

proliferating microglia appeared in the pons facial nucleus. In the following weeks, microglia underwent clonal expansion, and the clonal clusters distributed randomly throughout the facial nucleus. The excess microglia then egressed to nearby regions or underwent apoptosis, restoring the homeostatic microglial network.

By harnessing the power of multicolor genetic labeling, this study reveals insights into the fate and dynamics of microglia in the adult mouse brain under normal and diseased conditions. The Microfetti system may also be used to study microglial dynamics during development, as well as in other disease models.

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RESEARCH PAPERS

Tay, T.L. *et al.* A new fate mapping system reveals context-dependent random or clonal expansion of microglia. *Nat. Neurosci.* <http://dx.doi.org/10.1038/nn.4547> (2017).