GLIA

Anchored at the axon

Perineuronal satellite microglia are closely associated with neuronal cell bodies and are thought to promote plasticity or provide trophic support to neurons. Whether these microglia interact directly with the axon initial segment (AIS) — the site at which action potentials are generated in neurons — is not known. However, Baalman *et al.* now identify a subset of satellite microglia in the cortex that associate specifically with the AIS in a select sub-population of neurons.

The authors examined microglia–neuron interactions in the cortex of transgenic mice with green fluorescent protein-labelled microglia. They found that satellite microglia were associated with a small proportion of cortical neurons, and the majority of these glia were localized to the axonal side of the neuron's cell body. Approximately half of the axonal side satellite microglia had a single process that overlapped extensively with the AIS, as demonstrated by co-staining for ankyrin G, a cytoskeletal scaffold protein that is essential for AIS assembly and function. By contrast, using transgenic mice expressing yellow fluorescent protein in cortical layer V pyramidal neurons,

and co-staining for a marker of microglia, the authors showed that microglial process overlap is rare on apical dendrites.

AIS-associated microglia were also observed in the cortex of wild-type mice and in the cortex of rats and non-human primates. Importantly, CNS knockout of ankyrin G in mice decreased the number of neurons that had AIS-associated microglia, which suggests that AIS–microglia associations are not random and require intact AIS components.

Interestingly, cortical areas contained a higher proportion of AIS-associated microglia than the thalamus and striatum. Furthermore, in the motor cortex, AIS-associated microglia were more often found at non-GABAergic neurons than GABAergic neurons, and were more frequently associated with pyramidal neurons in cortical layer V than with the total cortical neuron population. This suggests that AIS–microglia interactions are specific to functional subtypes of neuron and particular brain regions.

Microglial processes are continuously extending and retracting in the normal CNS environment, and

microglia undergo further morphological changes upon activation in response to injury. Using a mouse model of mild traumatic brain injury, the authors investigated whether AIS–microglia interactions change after microglial activation. They found that the number of AIS-associated microglia decreased in the cortex 3–72 hours after injury, which suggests that activated microglia are less likely to form associations with the AIS. AIS-associated microglia may therefore have more prominent functions in the healthy brain than in modulating response to injury.

These findings suggest that AIS-associated microglia are a distinct subset of satellite microglia found in the cortex of the healthy brain, and support the notion that microglia have region- and neuronal-subtype-specific functions in the CNS.

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ORIGINAL RESEARCH PAPER Baalman, K. *et al.*
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