

If **microglial** debris is not removed in a timely manner, accumulated debris may influence **CNS function**. Clearance of microglial debris is crucial for CNS **homeostasis**. However, underlying mechanisms remain obscure. Zhou et al. investigated how dead **microglia** are removed. They find that although microglia can phagocytose microglial debris **in vitro**, the territory-dependent competition hinders the microglia-to-microglial debris engulfment **in vivo**. In contrast, microglial debris is mainly phagocytosed by **astrocytes** in the brain, facilitated by **C4b opsonization**. The engulfed microglial fragments are then degraded in astrocytes via RUBICON-dependent **LC3**-associated phagocytosis (LAP), a form of noncanonical autophagy. Interference with C4b-mediated engulfment and subsequent LAP disrupt the removal and degradation of microglial debris, respectively. Together, we elucidate the cellular and molecular mechanisms of microglial debris removal in mice, extending the knowledge on the maintenance of CNS homeostasis ¹⁾.

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Zhou T, Li Y, Li X, Zeng F, Rao Y, He Y, Wang Y, Liu M, Li D, Xu Z, Zhou X, Du S, Niu F, Peng J, Mei X, Ji SJ, Shu Y, Lu W, Guo F, Wu T, Yuan TF, Mao Y, Peng B. Microglial debris is cleared by astrocytes via C4b-facilitated phagocytosis and degraded via RUBICON-dependent noncanonical autophagy in mice. Nat Commun. 2022 Oct 24;13(1):6233. doi: 10.1038/s41467-022-33932-3. PMID: 36280666.

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