



CDB SEMINAR

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15:00~16:00 C1F CDB Auditorium

Fate mapping studies reveal that adult microglia derive from primitive macrophages

Summary

Microglia are the resident macrophages of the central nervous system (CNS) and have been implicated in the pathogenesis of many neurodegenerative and brain inflammatory diseases. Despite its potentially key role in CNS diseases, much controversy remains regarding the nature of microglial progenitors, their time of appearance during development, whether adult and embryonic microglia share similar origins and how microglial homeostasis is maintained during adult life. The most consensual hypothesis to date is that multiple haematopoietic waves of microglial recruitment and differentiation occur in the CNS. However their exact contribution to the adult microglial pool in the steady state remains unclear. Here, we examined the contribution of primitive and definitive haematopoiesis to the adult microglial population that populate the CNS during the steady state. Our results establish that post-natal haematopoietic progenitors do not contribute to microglial homeostasis. We also show that in contrast to many macrophage populations, microglia develop in osteopetrotic (*Csf1^{op/op}*) mice that lack colony stimulating factor 1 (CSF-1), but are absent in CSF-1 receptor-deficient (*Csf1r^{-/-}*) mice. Strikingly, using a lineage tracing system to genetically label yolk sac haematopoietic cells, we established that adult microglia that populate normal brains derive from primitive macrophage precursors that arise before embryonic day 8 (E8.0). These results provide the first evidence of the major contribution of primitive macrophages to an adult haematopoietic cell compartment and identify microglia as a unique and ontogenically distinct population among tissue macrophages. These results should have major implications in the use of embryonically-derived microglial progenitors for the treatment of brain inflammatory diseases.

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