The origins of repopulated microglia in the brain and retina

In February 2018, two research articles were respectively published in *Nature Neuroscience* (2018, 21(4): 530—40) and *Cell Discovery* (2018, 4(1): 9) to decipher the origins of repopulated microglia in the brain and retina. These two studies, supported by the National Natural Science Foundation of China, were led by Dr. Peng Bo (彭勃) at Shenzhen Institutes of Advanced Technology, Chinese Academy of Sciences.

The regenerative capability of the central nervous system (CNS) is largely limited due to the intrinsic properties and external environments. Once the brain gets injured, it is impossible to repair and restore the tissue to the normal situation. This notion has been challenged by a recent study. Microglia can repopulate the whole CNS after acute depletion. However, the origins of repopulated microglia are highly controversial.

Dr. Peng and his colleagues successfully deciphered the origin of repopulated microglia in the brain by a series of fate mapping approaches. They demonstrated that all repopulated microglia in the brain were derived from the proliferation of a few microglia surviving on pharmacological ablation (<1%), and the dividing microglia transiently expressed Nestin (Figure A). The results thus provided solid evidence that repopulated microglia were solely derived from residual microglia rather than *de novo* progenitors, indicating the absence of microglial progenitor cells in the adult brain.

Moreover, Dr. Peng and his colleagues found that inhibition of CSF1R eliminated all resident microglia in the retina (100%) and new microglia emerged and rapidly repopulated the whole retina after removal of CSF1R inhibition. They further found that repopulated retinal microglia have two populations of distinct origins: the center-emerging microglia were solely derived from residual microglia in the optic nerve, whereas the periphery-emerging microglia were derived from macrophages in the ciliary body/iris (Figure B). By using the microglial repopulation model, the authors thus for the first time observed a robust and massive cell regeneration in the adult mammalian retina. Furthermore, they first identified extra-retinal origins of microglia in the adult retina, shedding new light on the origins and maintenance of microglia in the retina.

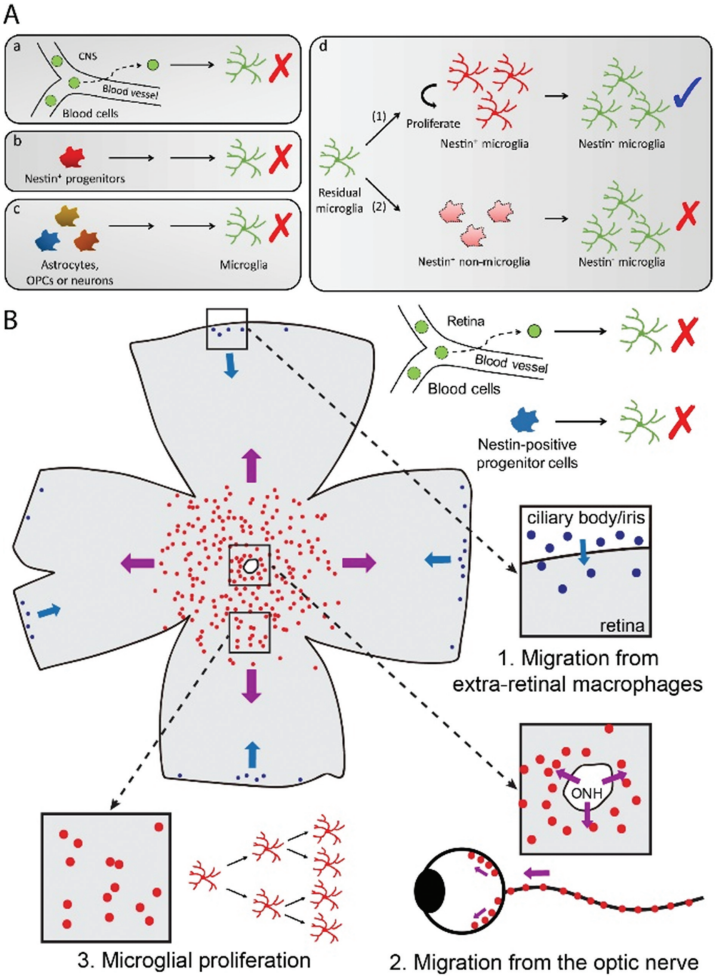

Figure The origins of repopulated microglia in the brain (A) and retina (B).