

Brain dendritic cells

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Dendritic cells (DCs) are a subset of leukocytes highly specialized in antigen-presentation to T cells, thus promoting the immune response. DCs occur in the meninges and choroid plexus. Brain DCs and brain-derived antigens are drained by cerebrospinal fluid in the afferent lymphatic vessels of cervical lymph nodes (cLNs) for antigen presentation. Information on the role of DCs in intracerebral immune response is still limited.

We recently demonstrated (Laperchia et al., 2013) that in thy1GFP-M transgenic mice, engineered for the expression of green fluorescent protein (GFP) in a proportion of neurons, also myeloid DCs are GFP-tagged. Our *in vivo* analysis by two-photon microscopy on young (3-6 months) thy1GFP-M mice showed DCs floating in the cerebrospinal fluid or static at the pia mater/parenchyma interface. We are using this animal model to study brain DCs trafficking by two-photon microscopy in two different inflammatory conditions. The first concerns chronic encephalitis caused by the extracellular parasite *Trypanosoma brucei*. During the first, hemolympathic stage of this infection, direct interactions between DCs and parasites were seen within meningeal and cortical microvessels. In the second stage, determined by parasite neuroinvasion, DCs invaded the brain parenchyma, exhibiting a random motion for target antigen recognition. With disease progression, intraparenchymal brain DCs were instead mainly arranged in static clusters which incorporated parasites for efficient antigen capture, and extravasated cytotoxic CD8⁺ T cells established contact with parasites. *Ex vivo* analysis on cLNs shown that the subcapsular zone was invaded by migratory DCs, and both migratory and resident DCs preferentially contacted CD8⁺ T cells. The second condition concerns normal aging (18-20 month old mice), which is known to be associated with low-grade chronic inflammation level and with functional impairments of the immune system, also known as immunosenescence. In these mice we observed that DCs infiltrate the brain parenchyma by transmigration from blood vessels and exhibit a motile behavior suggesting a scanning motion. Moreover, some DCs showed a progressive reduction of their motility until convergence, in about 30 minutes, into clusters whose functional significant has yet to be elucidated. Taken together, our studies enlightens key events of the intracerebral immune response both in presence of pathogens and in physiological aging.

References

Laperchia et al. (2013) Two-photon microscopy imaging of thy1GFP-M transgenic mice: a novel animal model to investigate brain dendritic cells subsets *in vivo*. *PLoSOne* 8(2):e56144.

Keywords

Two-photon imaging, *Trypanosoma brucei*, aging, T cells, cervical lymph nodes.