Role of CD4 T cells in brain development

E. Pasciuto,[1,2] O. T. Burton,[3] C. P. Roca, [3] V. Lagou,[1,2] W. D. Rajan,[1,2] T. Theys,[4] R. Mancuso,[1,2] R. Y. Tito,[1,2] L. Kouser,[3] Z. Callaerts-Vegh[2], A. G. de la Fuente,[5] T. Prezzemolo,[1,2] L. G. Mascali,[1,2] A. Brajic,[1,2] C. E. Whyte,[3] L. Yshii,[1,2] A. Martinez-Muriana,[1,2] M. Naughton,[5] A. Young,[5]A. Moudra,[3] P. Lemaitre,[1,2] S. Poovathingal,[1] J. Raes,[1,2] B. De Strooper,[1,2,6] D. C. Fitzgerald,[5] J. Dooley,[3] and A. Liston[1,2,3]

1. VIB, Leuven, Belgium
2. KU Leuven-University of Leuven, Leuven Belgium
3. The Babraham Institute, Cambridge, UK
4. UZ Leuven, Leuven, Belgium
5. The Wellcome-Wolfson Institute for Experimental Medicine, Belfast , UK
6. Dementia Research Institute, University College London, London, UK

The brain is a site of relative immune privilege. While CD4 T cells have been reported in the central nervous system, their presence in the healthy brain remains controversial, and their function largely unknown. Using a combination of imaging, single cell and surgical approaches we identified a $CD69^{+}$ CD4 T cell population in both the mouse and human brain, distinct from circulating CD4 T cells. The brain-resident population is derived through *in situ* differentiation from activated circulatory cells, and shaped by self-antigen and the peripheral microbiome. Single cell sequencing revealed that in the absence of murine CD4 T cells, resident microglia remained suspended between the fetal and adult states. This maturation defect resulted in excess immature neuronal synapses and behavioral abnormalities. Our findings illuminate a role for CD4 T cells in brain development, and a potential interconnected dynamic between the evolution of the immunological and neurological systems.