Breaking the route of immune cells from lung to brain

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The migration of immune cells from one organ to another is critical for their differentiation and function. T cells play critical roles in multiple sclerosis, a human disease characterized by the demyelination of neurons and detrimental damage to the nervous system. The lung is involved in this process by accumulating myeloid cells and educating myelin-reactive T cells to be more susceptible to disease development. However, it remains to be explored whether processes in the lung can be used for therapeutic interference. Here, we report that [Pyr1]-Apelin 13 (A13) treatment leads to reduced disease development and lethality in experimental autoimmune encephalomyelitis (EAE), an animal model of multiple sclerosis. Following A13 treatment, T cell entry into the brain is strongly reduced, whereas immune cells accumulate in lung. Further arguing for a primary effect of A13 in the lung, the receptor for Apelin, APJ, shows strong expression in the adult pulmonary endothelium but not in the brain vasculature.
Trans-endothelial cell migration of T cells is significantly impaired by A13 treatment, which reduces inflammatory gene expression of ECs in vitro and in vivo. In addition, APJ-expressing ECs show weaker VE-Cadherin+ junctions than other ECs, whereas A13 treatment increases junctional VE-Cadherin together with the internalization of the APJ. Ablation of APJ expression in ECs in vivo and vitro recapitulates both the downregulation of inflammatory gene expression and the reduction of EAE severity. Based on the sum of our data, we propose a beneficial effect of A13 treatment in the development of autoimmune disease through the alteration of immune cell clustering and trans-endothelial cell migration in lung.