"Multi-omic approaches reveal a dynamic crosstalk between plasma cells and *Cx3cr1*+ microglia in the brain during chronic *Trypanosoma brucei* infection"

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Chronic infections with the parasite *Trypanosoma brucei*, the causative agent of Human African trypanosomiasis, lead to severe neuroinflammation and death if left untreated. However, a detailed understanding of the cellular and molecular interactions that mediate this severe pathology is lacking. Using single cell and spatial transcriptomics, we have identified for the first time, a unique population of CD138$^+$ plasma cells in the brain ventricles of infected animals compared to naïve controls. These plasma cells express a robust innate-like, regulatory transcriptional profile, characterised by the expression of pathogen-sensing molecules (*Tlr4),* anti-inflammatory cytokines *(Il10)* and pro-survival receptor molecules such as *Tnfrsf17 (*B cell maturation antigen, BCMA). Additionally, we detected a subpopulation of *Cx3cr1*$^+$ microglia that express a wide range of factors associated with B cell recruitment and survival, such as *Cxcl12* and *Tnfsf13b* (B cell activating factor). Interestingly, *Cx3cr1*$^+$ microglia are the only cells in our dataset expressing both *Il10ra* and *Il10rb*, suggesting that they are primed to respond to IL-10. Further *in vitro* studies demonstrated that these regulatory, innate-like plasma cells can stimulate microglia polarisation towards an anti-inflammatory state *via* IL-10 signalling. We propose a model in which unresolved brain infections induce the activation of *Cx3cr1*$^+$ microglia, leading to the recruitment and survival of plasma cells mediated by CXCL12 and BAFF-BCAM signalling, respectively. In turn, these regulatory plasma cells alleviate inflammation by dampening *Cx3cr1*$^+$ activation *via* IL-10 signalling, limiting pathology. This work provides novel insights into the mechanisms of B cell-stromal interactions in the brain during infection.