Targeted Project / AY 2024 -2025

Profiling the fates and journeys of innate immune cells after infection in vivo

Project Code: TRG-PDN-MS

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Research area: Innate Immunity, Cell Migration and Development, In Vivo Imaging

BBSRC DTP main strategic theme: Understanding the rules of life

BBSRC DTP secondary strategic theme: Bioscience for an integrated understanding of health

Project outline:

Inflammation is our body's primary response to injury and infection, ensuring tissue defence from invading microbes. Furthermore, dysfunctional inflammation is implicated in many diseases, from autoimmunity to cancer. It is critical therefore to fully understand the migratory response of leukocytes, which is at the heart of inflammation. The first cells to infiltrate damaged tissues are neutrophils and macrophages (collectively referred to here as 'myeloid cells'), which eliminate microbes and promote repair. The function of these cells is often assumed to end at inflammatory lesions. However, recent evidence challenges this view and indicates that myeloid cells disseminate from these sites (i.e. actively spread to other tissues in the body). Such emigration could potentially influence secondary inflammation elsewhere as myeloid cell function can be 'trained' by microbial experience. Given these findings, it is important to discover what happens to myeloid cells post-infection: what journeys they take and what influence they have on inflammation resolution and on subsequent reactions against secondary infection or tumour challenge. This project will exploit infection models in zebrafish, coupled to state-of-the-art microscopy and single cell transcriptomics, to i) map the unexplored journey of myeloid cells after microbial encounter, ii) determine the mechanisms of dissemination iii) elucidate how these experienced myeloid cells shape subsequent inflammatory responses elsewhere in the body.

References

1. Kolaczkowska, E. & Kubes, P. Nat. Rev. Immunol. 13, 159–175 (2013).

2. Wang, J. et al.. Science 358, 111–116 (2017).

5. Netea, M. G. et al. Nat Rev Immunol 20, 375–388 (2020).