

IN BRIEF

 MACROPHAGES**Interleukin-4 boosts macrophage numbers**

Tissue-resident macrophage populations are maintained or expanded by local proliferation and, in nematode infection, this requires interleukin-4 (IL-4). This study shows that the expression of IL-4 receptor- α (IL-4R α) by macrophages confers a competitive advantage, allowing higher and more sustained proliferation of IL-4R α^+ compared with IL-4R α^- resident macrophages. Early during nematode infection, proliferation is IL-4R α independent and is controlled by colony-stimulating factor 1 (CSF1). As the immune response progresses, proliferation and alternative activation become dependent on IL-4. The authors suggest that the IL-4 pathway allows the outgrowth of resident macrophages when CSF1 is limiting without a coincident increase in monocyte recruitment.

ORIGINAL RESEARCH PAPER Jenkins, S. J. *et al.* IL-4 directly signals tissue-resident macrophages to proliferate beyond homeostatic levels controlled by CSF-1. *J. Exp. Med.* <http://dx.doi.org/10.1084/jem.20121999> (2013)

 MUCOSAL IMMUNOLOGY**Linking ER stress, autophagy and colitis**

New research provides a mechanism that links autophagy and the endoplasmic reticulum (ER) stress response with Crohn's disease, and suggests that Paneth cells are the origin of inflammation in the intestines. Mice that were unable to mount an ER stress response in intestinal epithelial cells (IECs) showed increased autophagy induction, most notably in Paneth cells. Conversely, mice with an IEC autophagy defect had evidence of ER stress and inflammation. The absence of both pathways in IECs or specifically in Paneth cells led to severe ileitis that depended on commensal bacteria and that resulted from increased IEC death. Mechanistic studies indicate that the failure to remove ER stress-induced activated inositol-requiring enzyme 1 α (IRE1 α) by autophagy promotes inflammation through nuclear factor- κ B activation and tumour necrosis factor signalling.

ORIGINAL RESEARCH PAPER Adolph, T. E. *et al.* Paneth cells as a site of origin for intestinal inflammation. *Nature* <http://dx.doi.org/10.1038/nature12599> (2013)

 MACROPHAGES**The shape of things to come**

Differences in the cell morphology of macrophages in either pro-inflammatory (M1)-polarizing or pro-healing (M2)-polarizing conditions have been previously observed. As described in this study, M1-polarizing stimuli (LPS plus IFN γ) cause cells to flatten into a round, pancake-like shape, whereas M2-polarizing stimuli (IL-4 and IL-13) induce an elongated cell shape. The extent of cell elongation was shown to correlate with the expression levels of the M2 phenotype marker arginase 1. Using engineered cell culture substrates to control cell shape, the authors found that cell elongation itself promotes macrophage polarization towards the M2 phenotype. Elongation of cells enhanced cytokine-induced M2 polarization and reduced the expression of induced nitric oxide synthase in response to M1-polarizing stimuli. Although cell elongation itself was not affected, inhibition of cytoskeletal contractility abrogated the upregulation of arginase 1 expression by cells elongated on the substrates but not in cytokine-polarized M2 macrophages. Together, these data indicate that cell shape has an important role in modulating M2 macrophage polarization.

ORIGINAL RESEARCH PAPER McWhorter, F. Y. *et al.* Modulation of macrophage phenotype by cell shape. *Proc. Natl Acad. Sci. USA* <http://dx.doi.org/10.1073/pnas.1308887110> (2013)