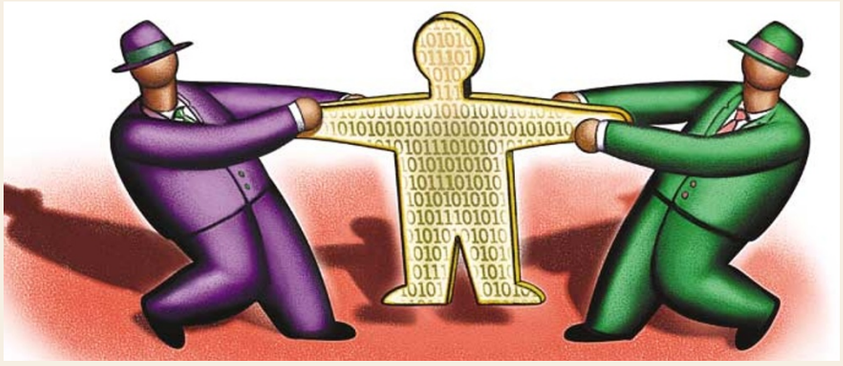
HAEMATOPOIESIS

For or against?



The ETS-family transcription factor PU.1 and the GATA-family transcription factor GATA1 have been shown to antagonize each other's function during haematopoiesis. Work from Walsh *et al.* in *Immunity* shows that PU.1 can antagonize the function of GATA2 by blocking its expression, but, surprisingly, these transcription factors can also cooperate to specify mast-cell fate.

Studies with *PU.1*$^{-/-}$ mice have shown that this transcription factor is essential for the generation of myeloid and lymphoid, but not erythroid or megakaryocytic, lineages. Here, the authors establish that PU.1 is required for the survival and differentiation of mast-cell progenitors. Mast cells are absent in *PU.1*$^{-/-}$ mice, and the low number of mast-cell progenitors that are present are blocked at an early stage of development. Retroviral expression of PU.1 in *PU.1*$^{-/-}$ haematopoietic progenitors, however, allows the development of both mast cells and macrophages.

To investigate how PU.1 regulates the mast-cell versus macrophage cell-fate decision, the authors generated a *PU.1*$^{-/-}$ progenitor cell-line that conditionally expressed an activatable form of PU.1. In this setting, active PU.1 resulted in the development of macrophages, but not mast cells. Cells that express the active form of PU.1 lacked *Gata2* expression, whereas *PU.1*$^{+/-}$ and *PU.1*$^{-/-}$ cells expressed this gene, indicating that PU.1 negatively regulates the expression of *Gata2*.

Further experiments showed that, in the absence of Gata2, PU.1 promotes the differentiation of myeloid progenitors into macrophages — but not into mast cells — and that the re-expression of *Gata2* in these progenitors resulted in the generation of mast cells. The authors propose that, during macrophage differentiation, PU.1 antagonizes *Gata2* expression and function, but that PU.1 and Gata2 work together during mast-cell development.

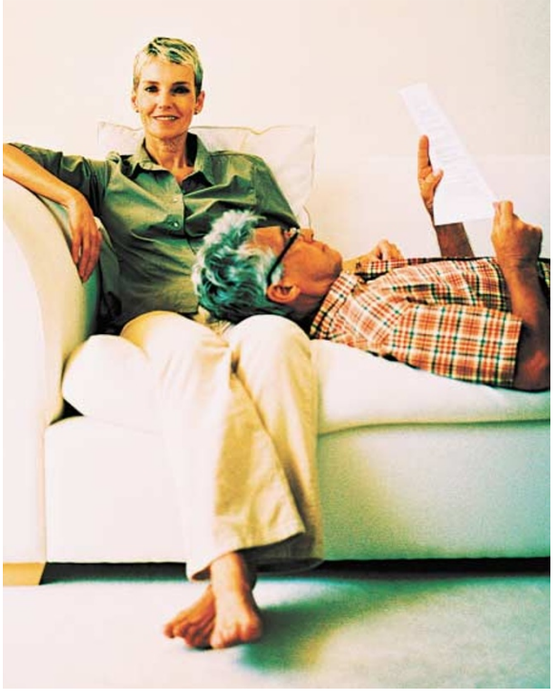
Jenny Buckland

References and links

ORIGINAL RESEARCH PAPER Walsh, J. C. *et al.* Cooperative and antagonistic interplay between PU.1 and GATA2 in the specification of myeloid cell fates. *Immunity* **17**, 665–676 (2002)

IMMUNE EVASION

Make yourself at home



If *Legionella pneumophila* — an aquatic bacterium that infects protozoan hosts in freshwater ecosystems — is inhaled by humans, it causes a severe form of pneumonia known as Legionnaires' disease. Once in the lungs, *L. pneumophila* is internalized into the phagosomes of alveolar macrophages. However, rather than being degraded by the macrophage lysosome, this bacterium makes itself at home. It hijacks host vesicle trafficking to make an endoplasmic reticulum (ER)-derived vacuole that supports its replication. So, how does it do it?

New insights are now reported by Kagan and Roy in *Nature Cell Biology*. They began by showing that *L. pneumophila*-containing phagosomes mature into ER-derived vacuoles in a biphasic manner. First, they interact with early secretory vesicles — vesicles travelling from the ER to the ER–Golgi intermediate compartment (ERGIC); then, they acquire markers that are concentrated in the ER. But, how do they get to the ER?

Cholera and Shiga toxins are known to reach the ER using a pathway that takes them through the Golgi, but Kagan and Roy show that *L. pneumophila*-containing phagosomes do not interact with intermediate compartments (the Golgi or ERGIC). Instead, they found that these phagosomes interact directly with transitional ER (tER) sites — dynamic sites where early secretory vesicles exit the ER — and that *L. pneumophila* forms an ER-derived vacuole by subverting vesicular transport from these sites. In addition, they showed that the subversion of early secretory vesicles is required to make a stable vacuole that is kept sequestered from the endocytic pathway.

Therefore, Kagan and Roy have shown that *L. pneumophila* subverts host cellular processes in a new way, and they suggest that understanding the mechanisms that are used by this bacterium to interact with tER sites and to recruit ER-derived vesicles might help us to identify host factors that regulate vesicular transport at these sites.

Rachel Smallridge Associate Editor, Nature Reviews Molecular Cell Biology

References and links

ORIGINAL RESEARCH PAPER Kagan, J. C. & Roy, C. R. *Legionella* phagosomes intercept vesicular traffic from endoplasmic reticulum exit sites. *Nature Cell Biol.* **4**, 945–954 (2002)

FURTHER READING Roy, C. R. Exploitation of the endoplasmic reticulum by bacterial pathogens. *Trends Microbiol.* **10**, 418–424 (2002)

WEB SITE

Craig Roy's lab:
http://info.med.yale.edu/micropath/fac_roy.html