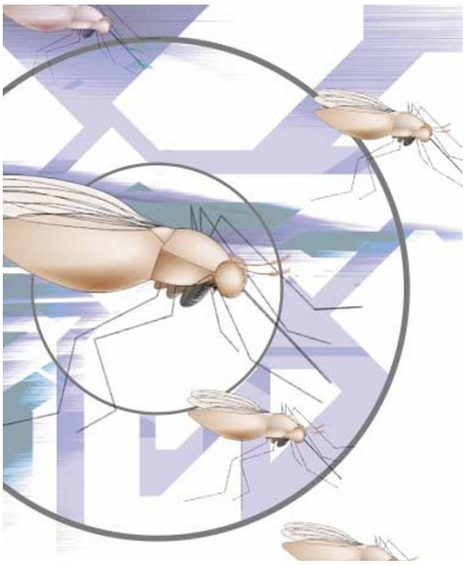

identified *P. falciparum* antigens, for reactivity with peripheral-blood mononuclear cells from volunteers who had been immunized with radiation-attenuated *P. falciparum* sporozoites or from control volunteers. Sixteen of the proteins were recognized as antigens by the volunteers immunized with irradiated sporozoites, but not by the controls. The immune response directed against some of the newly identified antigens was higher that that observed for the previously identified *P. falciparum*-derived protein antigens, indicating that these might be better candidates for vaccine development.

The approach used here shows how complex the immune response to *P. falciparum* is, and also validates this approach for the identification of new target antigens, which could be used in multiantigen vaccines for malaria.

Jenny Buckland

References and links

ORIGINAL RESEARCH PAPER Doolan, D. L. *et al*. Identification of *Plasmodium falciparum* antigens by antigenic analysis of genomic and proteomic data. *Proc. Natl Acad. Sci. USA* 28 July 2003 (DOI: 10.1073/pnas.1633254100)

FURTHER READING Good, M. F. Towards a blood-stage vaccine for malaria: are we following all the leads? *Nature Rev. Immunol.* **2**, 117–125 (2001)

was seen when VDAC2 was re-expressed in these cells. Using haemagglutinin (HA)-tagged VDAC2, endogenous BAK, but not BAX, was coprecipitated. Similarly, HA-tagged BAK, but not BAX, coprecipitated endogenous VDAC2.

BAK in its active, oligomeric conformation is more susceptible to proteolysis than the inactive form, and the absence of VDAC2 increased its susceptibility. So, VDAC2 interacts with BAK, but not BAX, and regulates its conformation.

Next, Korsmeyer and co-workers set out to determine how VDAC2 modulates BAK-dependent apoptosis. Is VDAC2 an inhibitor of BAK-mediated apoptosis, or does it function as a pro-apoptotic factor itself when released from BAK? VDAC2 expression in *BAX*$^{-/-}$ cells inhibited apoptosis, but had no effect in *BAK*$^{-/-}$ cells, which argues against the latter possibility. Also, expression of VDAC2 inhibited BID-induced apoptosis of *BAX*$^{-/-}$ cells, but not *BAK*$^{-/-}$ cells, which indicates that VDAC2 negatively regulates BAK-dependent apoptosis.

Cells deficient for VDAC2 were more sensitive to death stimuli than *VDAC1*$^{-/-}$ and *VDAC3*$^{-/-}$ cells, both of which had similar sensitivities to wild-type cells. By re-expressing VDAC2, the susceptibility to apoptosis of *VDAC2*$^{-/-}$ cells was returned to normal. So, VDAC2 has a physiological role that is distinct from the other VDAC isoforms.

When analysing the apoptosis phenotype of *VDAC2*$^{-/-}$ cells, the authors noted an increased loss of mitochondrial transmembrane potential and the accelerated release of cytochrome *c*, compared with wild-type cells. After treatment with death stimuli, *VDAC2*$^{-/-}$ cells showed caspase activity and BAK oligomerization earlier than wild-type cells.

The authors concluded that VDAC2 is a specific inhibitor of BAK-dependent mitochondrial apoptosis, which, when absent, causes increased susceptibility to apoptotic death.

Arianne Heinrichs, Editor,
Nature Reviews Molecular Cell Biology

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ORIGINAL RESEARCH PAPER Cheng, E. H.-Y. *et al*. VDAC2 inhibits BAK activation and mitochondrial apoptosis. *Science* **301**, 513–517 (2003)

FURTHER READING Cory, S. & Adams, J. M. The BCL2 family: regulators of the cellular life-or-death switch. *Nature Rev. Cancer* **2**, 647–656 (2002)

IN BRIEF

B-CELL RESPONSES

BCL6 controls the expression of the B7-1/CD80 costimulatory receptor in germinal center B cells.

Niu, H. *et al*. *J. Exp. Med*. **198**, 211–221 (2003)

In this study, Dalla-Favera and colleagues looked at the targets of transcriptional repression by BCL6 to gain a better understanding of its involvement in germinal-centre (GC) formation. Previous studies have not been able to distinguish direct targets of BCL6 from secondary effects. This study shows that BCL6 directly inhibits transcription of the *CD80* gene by binding to its promoter enhancer and prevents the upregulation of expression of CD80 in response to CD40–CD40L interactions mediated by nuclear factor-κB (NF-κB). CD80 has a crucial role in T-cell–B-cell interactions required for GC development and T-cell-dependent antibody responses. Therefore, constitutive expression of BCL6 owing to a translocation might lead to lymphomagenesis by disrupting the normal GC differentiation pathway of B cells.

MONOCYTES

Blood monocytes consist of two principal subsets with distinct migratory properties.

Geissmann, F. *et al. Immunity* **19**, 71–82 (2003)

Two subsets of human blood monocytes that differ in their phenotypic and functional characteristics were identified several years ago, but it has proven difficult to characterize any such subsets in mice. Now, Geissmann *et al*. describe two mouse monocyte subsets with distinct chemokine-receptor and adhesion-molecule expression profiles, which correspond to the human subsets. CC-chemokine receptor 2 (CCR2)-positive monocytes are short-lived cells that are recruited to inflamed tissues, whereas the CCR2-negative subset is recruited to non-inflamed tissues and these cells might be the precursors of tissue-resident macrophages and dendritic cells. Both subsets have the capacity to develop into dendritic cells. Further characterization of monocyte subsets in mice should contribute to an increased understanding of the role of monocytes in human diseases.

SPLENIC ARCHITECTURE

A conduit system distributes chemokines and small blood-borne molecules through the splenic white pulp.

Nolte, M. A. *et al. J. Exp. Med.* **198**, 505–512 (2003)

The splenic white pulp is structurally similar to a lymph node, although the spleen receives antigen directly from the blood and not through afferent lymphatics. This paper shows that, similar to the lymph node, the spleen has a conduit system — a kind of structured transport system. The splenic conduit is a tubular network containing collagen fibres that are surrounded by reticular fibroblasts. The white pulp is known to restrict cellular movement to lymphocytes and dendritic cells, but this study shows that the conduit also limits the entry of large molecules. Locally produced chemokines were also found in the conduit system — CC-chemokine ligand 21 (CCL21) in the T-cell area and CXCL13 in the B-cell area.