WEB WATCH

Developing-world focus

- http://www.scidev.net

Advances in science and technology could be of profound benefit to people in developing countries; yet, these are often the people who have the least access to such information. *SciDev.Net* is a free-access web resource, launched in December 2001, that is dedicated to covering scientific and technology issues that are relevant to the needs of developing countries. *SciDev.Net* is a non-profit-making organization that is supported financially by several international agencies. It is run by a board of trustees, many of whom are based in developing countries, and the goal of the site is to provide, "informed debate on ways of applying science and technology to social and economic development in an environmentally responsible way". The site is sponsored by *Nature* and *Science*, both of which have agreed to provide free access to several articles each week.

The site contains news, feature articles, opinions, editorials and book reviews, as well as a section called 'How do I…?', which provides guidelines on topics such as writing research grants or becoming a science journalist. You can also search for meetings, and check for available jobs and grants from various agencies. The 'Dossier' section provides introductory material and resource guides. Future 'Dossier' topics to watch out for include AIDS/HIV, gender and science, GM crops and food, malaria, and technology transfer. The 'Links' section provides access to scientific organizations, news sources and journals, as well as aid and funding agencies. Future plans include regional gateways, with the possibility of some material being published in the appropriate language for that region.

Elaine Bell

TRANSPLANTATION

Mismatch advantages

Allogeneic bone-marrow (BM) transplantation has greatly improved the treatment of leukaemia. Conventionally, BM transplants are performed between individuals that are matched at their MHC loci (but differ with respect to 'minor' antigens). Donor T cells that recognize recipient minor antigens mediate a graft-versus-leukaemia (GVL) effect, but can also cause graft-versus-host disease (GVHD). However, an MHC-matched donor can be found for only a proportion of patients. Full MHC-haplotype-mismatched BM grafts have been made possible by depleting T cells from the graft (which reduces the otherwise lethal GVH reactions across the MHC barrier), but this leads to a higher incidence of relapse due to a decrease in the GVL effect, and a greater risk of graft rejection. Now, Ruggeri and colleagues report in *Science* that certain MHC mismatches between BM donors and recipients might, in fact, be advantageous — donor natural killer (NK)-cell alloreactivity correlates with the elimination of leukaemia relapses and graft rejection, and protects patients against GVHD.

NK cells, unlike T cells, are activated when they recognize an absence of MHC class I molecules. When MHC class I ligands are present, killer inhibitory receptors (KIRs) on the NK cells are engaged and the cells are not activated. Ruggeri *et al.* reasoned that mismatched BM transplants might, therefore, trigger NK-cell alloreactivity. To assess the effect of

AUTOIMMUNITY

Mistaken identity

The long-standing puzzle of why nuclear antigens are targeted in systemic autoimmune diseases might have been resolved. Elizabeth Leadbetter and co-workers, reporting in *Nature,* show that autoreactive B cells can be triggered by self-antigens that look foreign to innate receptors.

All of us have potentially autoreactive B cells in our circulation, but these are normally kept in check. When tolerance breaks down, antibodies that are specific for DNA, RNA, nucleoproteins and immunoglobulins dominate the autoimmune response. But, it has never been clear why these specificities are selected.

Previous studies had indicated that transgenic B cells that are specific for IgG2a (a common autoantigen in systemic lupus erythematosus; SLE) can be activated by immune complexes but not monomeric antibodies. The authors have now shown that only certain immune complexes are effective — IgG2a–nucleosome complexes stimulate the B cells, but IgG2a–hapten complexes do not. Moreover, digestion with DNAse ablated the activating potential of IgG2a–nucleosome complexes, which showed that DNA was the key. It was predicted that the immune complexes activate B cells by simultaneously engaging the B-cell receptor (BCR) and a co-receptor.

Complement receptors — the most obvious co-receptor candidates — were ruled out, so the authors looked to the Toll-like receptors (TLRs). TLRs recognize conserved molecular signatures that are characteristic of microorganisms, such as hypomethylated CpG motifs in DNA. Importantly, mammalian DNA contains some CpG motifs, so it is possible that IgG2a–nucleosome immune complexes might co-ligate the IgG2a-specific BCR and a TLR.

To test this idea, the transgenic mice were crossed with mice that were deficient in Myd88, an adaptor molecule that is essential for most Tlr signalling pathways. Strikingly, *Myd88*$^{-/-}$ transgenic B cells were unresponsive to IgG2a–chromatin immune complexes.

The receptor that recognizes CpG motifs, Tlr9, is unique in that it requires endosome acidification for signalling, and specific inhibitors of endosome acidification, such as chloroquine, were shown to block the transgenic B-cell responses to IgG2a–chromatin complexes.