Figure 1 Toll-like receptor proteins in immunity and autoimmunity. **a, b,** Bacterial lipopolysaccharides (components of the cell wall) or CpG base pairs (a feature more common in microbial than mammalian DNA) can induce T-cell-independent proliferation of, and antibody production by, B cells by stimulating certain Toll-like receptors (TLRs). Simultaneous recognition of the lipopolysaccharide or DNA by specific B cells through cell-surface antigen receptors and TLRs results in synergistic signalling by the receptors. The signals, 1 and 2, lead to the production of bacteria-targeted circulating antibodies. **c,** Bacterial capsular polysaccharides stimulate specific B cells through their ability to cluster many antigen receptors. For *Neisseria* species, the response can be enhanced¹⁰ by stimulation of TLR2. **d,** According to Leadbetter *et al.*¹, the binding of complexes containing self-IgG2a and self-DNA (or, presumably, bacterial DNA) to antigen receptors and TLR9 induces B-cell proliferation and the secretion of autoantibodies (rheumatoid factors) against IgG2a.

TLR9 on B cells and prompting the production of autoantibodies against IgG.

Although Toll-like receptors are generally thought to be crucial for sensing pathogens by recognizing structural motifs that distinguish microbes from our own tissues, there are precedents for their binding to self-antigens. As cells die they release various antigens, including heat-shock protein 60 and mitochondrial and nuclear molecules, which can bind to TLR4 and TLR2 on macrophages and trigger these cells to clear up dying cells and thereby help repair damaged tissues⁹. So it is conceivable that B cells, too, may simultaneously recognize these self-antigens by cell-surface antigen receptors and Toll-like receptors, provoking other autoantibodies to nuclear antigens such as self-DNA itself, in diseases that are characterized by prominent tissue damage or the impaired removal of dying cells and DNA. For example, such a process might promote the formation of anti-DNA autoantibodies in systemic lupus erythematosus.

Finally, the finding that Toll-like receptors can drive the production of autoantibodies by their ability to activate B cells single-handedly, without needing T-cell help, should shift some of the clinical focus in

autoimmune diseases towards T-cell-independent processes of antibody production. Leadbetter *et al.*¹ raise the possibility that the drug chloroquine, which inhibits TLR9-mediated signalling, might be effective in some patients with systemic autoimmune diseases. Drugs that specifically target Toll-like-receptor signalling pathways could be promising new treatments for antibody-mediated autoimmune diseases or their complications.

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Daedalus

Meteoric heating

Many satellites have examined the heat of the atmosphere as a means of predicting the weather. Daedalus now wants to look at the heat of the Earth. The best infrared 'window' through the atmosphere is perhaps 10 micrometres wavelength. Changes in the weather pattern can cause great differences in heat and are not very interesting. Daedalus is looking for small thermal effects. Thermal imaging cameras can be sensitive to a thousandth of a degree centigrade or less. Anomalies of this order on the Earth's surface, sustained local changes from one point to another nearby, demand explanation.

The obvious source of excess local heat is an underground nuclear blast. An unexplained or unacknowledged hotspot in some desert or waste area would show an evasion of the anti-nuclear treaty, and could even give an estimate of its yield. Wider regions of sustained heat might show where coal mines had caught fire. And an earthquake would release energy and warm the ground over a wide area. Indeed, a quake might give a useful thermal signature ahead of time, allowing it to be predicted. Geologists could later map the intensity of the disturbance, independently of seismological records.

The most interesting search, however, would be for meteorite impact sites. On hitting the Earth, a meteorite or comet dumps a lot of thermal energy, which is released for many thousands of years. If it fragments the local crust, heat from within the Earth escapes more copiously thereafter. Many geologists feel that such 'astroblemes' drive evolution. Accordingly, the statistics of meteorite or asteroid descent is a hot topic: will there be another soon? We need to find and date the remains of old ones.

The Barringer crater in Arizona is a famous astrobleme: the site should still be warm. The extinction of the dinosaurs has been blamed on a meteorite that shaped the Yucatán Peninsula of Central America — is that region warmer than it should be? Hudson Bay and James Bay in Canada may be astroblemes — how warm are they? Indeed, all the meteorites that fell into the sea and left unrecorded craters may still be warming the water over the site of their fall. Even human clusters, such as a crowd on a pilgrimage, might be detected.

But the first spot for study must be the Tunguska region of Siberia, where a meteorite fell in 1908. Local heating was intense enough to knock trees over or ignite them. Thermal evidence must still be there.

David Jones