T-CELL ACTIVATION

T-cell–APC interactions

In the past few years, studies based on suspension cultures have revealed the existence of long-lived immunological synapses between T cells and antigen-presenting cells (APCs). Now, Matthias Gunzer and colleagues use a three-dimensional collagen-matrix system and intravital imaging to show that T cells can interact with different APCs in both short- and long-lived interactions and that the nature of these contacts depends on the type of APC.

Gunzer and colleagues propose that the three-dimensional collagen-matrix system is a better mimic of the reticular-cell scaffolding structure of lymph nodes than suspension cultures. Using this system, they have previously shown the existence of short-lived interactions between T cells and dendritic cells (DCs). But what determines whether the T-cell contacts are long-lived, as occurs in the suspension-culture system, or short-lived, as occurs in the collagen-matrix model? To address this, the authors compared the kinetics of T-cell activation by different types of APC. As described previously, DCs engaged T cells for short periods, but T cells interacted with resting B cells in stable, long-lived interactions. In these T-cell–B-cell pairs, the B cell was sessile, but the T cell maintained motile function and was observed to push the B cell through the matrix. However, despite a lack of long-lived encounters, DCs and pre-activated B cells were more-efficient inducers of T-cell activation than resting B cells.

These results show that short-lived, dynamic interactions of T cells with DCs and activated B cells are more efficient at activating T cells than long-lived synapse-like interactions with resting B cells. Whether this interaction between T cells and resting B cells resembles a conventional immune synapse or a new type of structure, and the physiological relevance of this interaction, remains to be determined.

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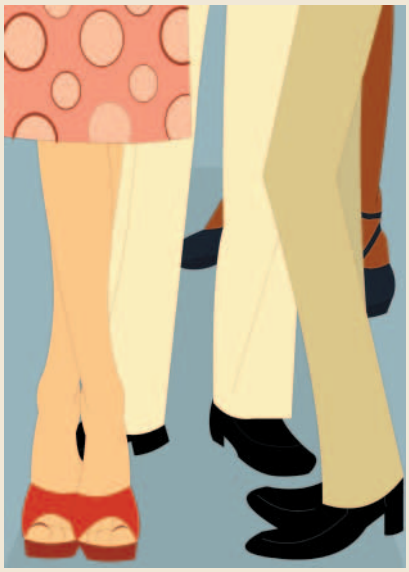

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INNATE IMMUNITY

The fight for iron

Bacterial survival and growth depends on iron, much of which is acquired from the host by siderophores that scavenge iron and transport it into the pathogen. However, as described in a recent *Nature* paper, the innate immune system of the host can prevent bacteria from obtaining iron by producing lipocalin-2, which sequesters bacterial siderophores, in response to Toll-like receptor (TLR) triggering.

In this report, Flo *et al.* show that stimulation of macrophages through TLRs induces marked upregulation of transcription of the lipocalin-2 gene. They confirm these results *in vivo*, showing that injection of mice with the TLR4 ligand lipopolysaccharide induces increased expression of lipocalin-2 in a TLR4-dependent manner. So, the authors generated lipocalin-2-deficient mice to assess the role of lipocalin-2 in bacterial infection. Although these mice remain healthy in specific-pathogen-free conditions, when challenged with *Escherichia coli* (strain H9049), they develop marked bacteraemia, have high bacterial loads in the blood, liver and spleen, and have accelerated morbidity at high doses, indicating that lipocalin-2 has an important role in innate defence against bacterial infection.

In the serum, the concentration of free iron is tightly regulated by iron-binding proteins such as transferrin, so invading pathogens must acquire iron by secreting siderophores, which effectively compete for iron. The authors have previously shown that lipocalin-2 can bind catecholate-type siderophores (such as enterochelin) but not other types of siderophore (such as ferrichrome). As *E. coli* strain H9049 depends on enterochelin for importing iron, its growth was inhibited when cultured in acute-phase serum from wild-type mice but not from lipocalin-2-deficient mice. By contrast, the *in vitro* growth of *Staphylococcus aureus*, which does not depend on enterochelin, was not affected by the presence of lipocalin-2.

The specificity of the protective effect of lipocalin-2 against enterochelin-dependent bacterial infection was then examined *in vivo*. Mice were challenged with *E. coli* either with or without co-injection of ferrichrome, which allows bacteria to acquire iron in an enterochelin-independent manner. Similar to lipocalin-2-deficient mice, wild-type mice that received bacteria and ferrichrome showed markedly increased morbidity, indicating that lipocalin-2 confers resistance to bacterial infection by abrogating enterochelin-dependent iron uptake by bacteria.

Lucy Bird

References and links

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WEB SITE
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