Salmonella sneaks past security

Certain gut cells can leave resident bacteria alone but respond selectively to invaders. Satoshi Uematsu, Shizuo Akira, and colleagues (Osaka University, Japan) suggest that gut cells achieve this differentiation by using a special, pathogen-specific receptor called the Toll-like receptor 5 (TLR5). But the pathogenic Salmonella typhimurium turns the situation around: events triggered by the special receptor help the bug to invade its host.

TLRs, which are expressed on professional antigen-presenting cells, recognize common pathogen-associated molecules and trigger innate immunity. TLR5 on dendritic cells recognizes bacterial flagellin protein in vitro, but its function in vivo was previously unknown.

Akira’s team found that TLR5 mRNA was highly expressed in the mouse intestine particularly in a specific subpopulation of antigen-presenting lamina propria cells (CD11c+ LPCs). In these cells, TLR5 was necessary for bacterial flagellin to induce inflammatory cytokines, yet when the team infected TLR5−/− mice with Salmonella, a flagellated bacterium, these mice were unexpectedly resistant to the bug.

It was not, however, invasion of the CD11c+ LPCs that showed a difference. In the gut, Salmonella invaded the CD11c+ LPCs in both TLR5+/+ and TLR5−/− mice. However, in the TLR5−/− mice, fewer bacteria-laden CD11c+ LPCs moved from the intestinal tract to the mesenteric lymph nodes, probably because the LPCs failed to be activated by the bacteria. These mice had more resistance to systemic infection—fewer bacteria reached their livers and spleens—but it is not yet clear whether a similar tactic of TLR5 blocking would work in humans.

Reference: Uematsu, S., et al. 2006. Nat. Immunol. doi:10.1038/ni1362.

Transforming antibiotic treatment

Antibiotic-resistant bacteria are an ever-evolving medical concern. Now, Marc Prudhomme, Laetitia Attaiech, Jean-Pierre Claverys, and colleagues (CNRS, Toulouse, France) report that antibiotics increase genetic exchange and the chance for adaptation in Streptococcus pneumoniae by activating its transformation pathway. The findings highlight the danger of inappropriate antibiotic use.

Transformation (the uptake and genomic integration of exogenous DNA) in S. pneumoniae can only occur when the bacteria are competent. Competence is a transitory state in bacteria. Although its regulation is rather well understood, the signals that trigger it remain elusive. Recent evidence suggests that in S. pneumoniae competence is a stress response to environmental change. Claverys’s team therefore wondered whether antibiotic-induced stress might trigger competence.

Out of the dozen or so antibiotics that the team checked, six up-regulated the competence pathway when used at concentrations that killed approximately 50% of the bacteria. These antibiotics kill bacteria by either damaging DNA, inhibiting protein synthesis, or blocking DNA synthesis. Thus, the mechanism of action of a particular antibiotic cannot be used to predict its ability to induce competence.

Approximately 40% of the human population carry S. pneumoniae asymptomatically in the nose and throat. If the bacteria invade other tissues, however, severe diseases such as pneumonia, meningitis, and osteomyelitis can develop. Two of the antibiotics found to induce competence are commonly used to treat respiratory tract infections. Although the generation of antibiotic-resistant bacteria cannot be completely prevented, choosing antibiotics that do not promote genetic exchange may help to minimize future problems.

Reference: Prudhomme, M., et al. 2006. Science. 313:89–92.