What doesn't kill you. . .

Low doses of antibiotics can have an unintended effect—instead of killing bacteria, some antibiotics promote the formation of biofilms, slimy aggregates of bacteria that resist drug treatment (*Nature* **435**, 1171–1175).

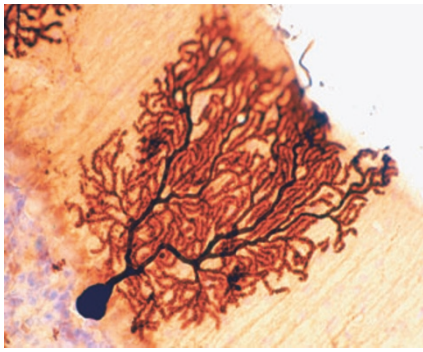
Lucas Hoffman *et al.* examine *in vitro* biofilm formation by the Gram-negative bacteria *Escherichia coli* and *Pseudomonas aeruginosa*, the latter an opportunistic pathogen that causes respiratory infections in people with cystic fibrosis. Tobramycin, an antibiotic frequently used to treat cystic fibrosis, induced biofilm formation of both bacteria at one-third the dose required to kill them.

The researchers found that the bacterial protein aminoglycoside response regulator (encoded by the gene *arr*) mediates biofilm formation by degrading a bacterial inhibitor of cell adhesion. The protein also seems to mediate other aspects of drug resistance—preformed biofilms from *arr* mutant bacteria were 100 times more sensitive to killing by tobramycin than wild-type biofilms.

Notably, *arr* is not found in all clinical isolates, which may explain the variable sensitivity to tobramycin of individuals with cystic fibrosis. The research, although performed *in vitro*, suggests that antibiotic use could foster the development of biofilms and drug resistance *in vivo* in individuals with cystic fibrosis and other diseases, such as tuberculosis. —*AA*

Paying attention to fragile X

Synaptic plasticity, in which synaptic activity modifies neuronal communication, mediates learning and memory. Abnormalities in this process underlie deficits in attention and motor learning in fragile X syndrome, according to two studies.



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Cerebellar Purkinje cells such as this show abnormal plasticity in fragile X syndrome.

Mental retardation in fragile X syndrome is caused by lack of expression of FMRP, a protein important for the formation of synapses. Previous studies have shown that fragile X model mice have abnormal synaptic plasticity in the hippocampus, a brain structure important for spatial learning. But it was unclear why humans with fragile X syndrome also had attention deficits and difficulties in learning motor tasks.

In the 10 August *Journal of Neuroscience* (25, 7385–7392), Ming-Gao Zhao *et al.* report that fragile X mice show dysfunctional synaptic plasticity in brain areas important for attention, the lateral amygdala and anterior cingulate gyrus. Trace fear conditioning, a measure of memory that requires attention and is dependent on these brain areas, was reduced in fragile X mice. Likewise, in the 4 August *Neuron* (47, 339–352), Sebastiaan Koekkoek *et al.* find that synaptic plasticity in the cerebellum, which controls motor learning, is affected in fragile X. Classical delay eyeblink conditioning, a cerebellum-dependent task, was abnormal in both mice and humans with fragile X, suggesting that cerebellar dysfunction may be involved in the cognitive deficits of this syndrome. —*EC*

Written by Allison Alcivar, Eva Chmielnicki and Charlotte Schubert

Gut response to radiation

Many cancer patients who receive radiation treatment in areas near the abdomen suffer from intestinal damage and radiation enteritis. Clinical trials with antibiotics were attempted several decades ago based on a curious finding in mice: killing off intestinal microflora protected the animals from radiation enteritis. The trials went nowhere, but new data from Peter Crawford and Jeffrey Gordon published in the *Proceedings of the National Academy of Sciences* now dissect the molecular underpinnings of the phenomenon (doi:10.1073/pnas.0504830102).

As in previous studies, the researchers found that germ-free mice were resistant to radiation enteritis. The germ-free mice also had fewer apoptotic endothelial cells in their intestine than normal mice, consistent with the notion that endothelial cells regulate radiation enteritis.

The researchers next examined a secreted protein, fasting-induced adipose factor (Fiaf), that is known to be turned on in the intestine of germ-free mice. The data suggest that Fiaf protects gut endothelial cells from apoptosis in response to radiation. But exactly how it does this remain unknown, and other factors that cooperate in protecting from damage remain to be discovered. That line of inquiry could lead to agents that shield patients from radiation enteritis. —*CS*

Gut response to chemotherapy

Crypt cells, highly proliferative cells in the intestine, often do not function well during cancer chemotherapy and in various intestinal ailments. One approach to the problem has been to identify molecules that regulate crypt cell proliferation: in the 19 August *Science,* Kyung-Ah Kim *et al.* do just that (309, 1256–1259).

The researchers found that the secreted molecule human R-spondin1 (HRSpo1) has powerful effects on crypt cells. For instance, when they injected mice with the protein, the crypt cells began to proliferate within 3 hours. The effect was reversible—after the protein was withdrawn, crypt cell proliferation returned to normal.

Next the investigators tested the protein in a tumor model, in which mouse colon cancer cells are inoculated into mice. The mice were administered chemotherapy, inducing diarrhea and weight loss. HRSpo1 treatment reduced these side effects.

HRSpo1 seems to influence the function of β-catenin, which regulates cell proliferation and differentiation in many contexts. But the role of HRSpo1 in normal cellular processes is obscure—and it may also operate outside the intestine since it is expressed also in the kidney, prostate, adrenal gland and pancreas. —*CS*

Manipulating mosquitoes

To a parasite, its host's physiology is nothing more than evolutionary putty, to manipulate and control at its whim and for its benefit. A study of malaria transmission shows that we—in our capacity as hosts—have even less control than we might have thought.

Renaud Lacroix *et al.* report that the malaria parasite, *Plasmodium falciparum*, can make infected children particularly attractive to mosquitoes.

Previous work in the area produced conflicting findings, some showing that infection had no effect and others showing increased mosquito attraction. The researchers attributed this ambiguity to a lack of proper controls. So they undertook a rigorous study of 12 groups of three children.

In each group, one child was uninfected, and one was naturally infected with the non-infective stage of the parasite. The third child harbored the transmissible stage and attracted twice as many mosquitoes as the other children—but after drug treatment, mosquitoes showed no preference. The report appears in the 9 August issue of *PLoS Biology* (**3**, e298).—*CS*