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In This Issue

APPLIED BIOLOGICAL SCIENCES

Tear down these walls for fruit ripening

Disassembly of the cell wall is a major part of the ripening process in fruit and causes a dramatic increase in its susceptibility to pathogens. Dario Cantu *et al.* report that two proteins active in cell wall disassembly are also responsible for increasing the fruit's susceptibility to fungal infection. The authors studied three tomato lines that had reduced expression of the polygalacturonase gene, the expansin gene, or both. When both genes were suppressed, ripe tomatoes were much less susceptible to infection by *Botrytis cinerea*, the cause of gray mold. The suppression of only one gene was not sufficient to limit the infection. The authors say that the two gene products work together to promote fruit softening. They suggest that suppressing the two genes reduces infection by changing the structure of the cell wall polysaccharide substrates or their accessibility, preventing *B. cinerea*'s virulence enzymes from breaching the cell wall. The authors suggest that managing cell wall metabolism could be a useful strategy for preventing pathogen damage to fruit during storage, handling, and distribution. — P.D.

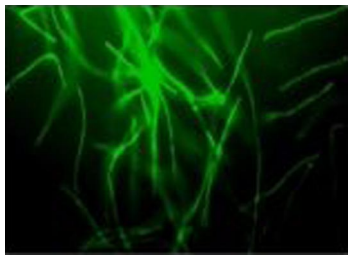
Botrytis cinerea growing on ripe tomato fruit.

"The intersection between cell wall disassembly, ripening, and fruit susceptibility to Botrytis cinerea*" by D. Cantu, A. R. Vicente, L. C. Greve, F. M. Dewey, A. B. Bennett, J. M. Labavitch, and A. L. T. Powell* (see pages 859–864)

MICROBIOLOGY

NO way out for anthrax?

Nitric oxide (NO), a chemical "weapon" produced by phagocytic cells of the immune system (macrophages), is part of the first wave of defense against invading pathogens such as *Bacillus anthracis*, the anthrax bacterium. With the aid of an intracellular fluorescent sensor for the chemical, however, Konstantin Shatalin *et al.* have found that NO may actually help the bacterium evade the immune system and protect it from attack. The authors show that the survival of the anthrax bacterium *in vivo* depends on its ability to produce its own NO. Anthrax bacteria deficient in the enzyme that generates NO, called bNOS, had low survival when grown inside macrophages and lost their ability to cause illness in mice. The authors determined that bacterial resistance depends on rapid NO-stimulated activation of the antioxidant system that protects germinating spores from the immune cells. Given the importance of NO in protecting these bacteria from immune attack, Shatalin *et al.* suggest that bNOS is an attractive candidate for antimicrobial therapies. — M.M.



Fluorescent image of bacteria treated with NO-detecting probe.

"Bacillus anthracis*-derived nitric oxide is essential for pathogen virulence and survival in macrophages" by Konstantin Shatalin, Ivan Gusarov, Ekaterina Avetissova, Yelena Shatalina, Lindsey E. McQuade, Stephen J. Lippard, and Evgeny Nudler* (see pages 1009–1013)

NEUROSCIENCE

Sleep loss leads to insulin resistance

Slow-wave sleep (SWS), characterized by delta EEG oscillations in the brain, comprises the deepest stages of non-REM sleep. Because SWS onset coincides with hormonal changes that affect glucose metabolism, Esra Tasali *et al.* hypothesized that SWS deprivation might affect blood sugar control. The researchers found that SWS suppression caused healthy adult volunteers to develop insulin resistance, a trait linked with weight gain and type 2 diabetes. The authors first established a baseline for normal sleep in nine subjects. Then, on the next three nights, they monitored subjects' EEGs for delta waves and, upon detecting the waves, roused the subjects to lighter sleep with loud noise. The subjects' total nightly sleep

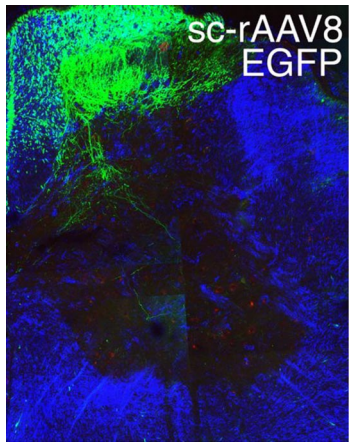
time remained unchanged. In the morning, the researchers injected the subjects with a glucose bolus and measured their systemic response. Using a model of insulin response, Tasali *et al.* inferred that eight of the nine volunteers had become less sensitive to insulin, without a compensating increase in insulin secretion. The authors suggest that the reduced sleep quality that occurs in older and obese individuals may increase their risk for type 2 diabetes. — K.M.

"Slow-wave sleep and the risk of type 2 diabetes in humans" by Esra Tasali, Rachel Leproult, David A. Ehrmann, and Eve Van Cauter (see pages 1044–1049)

NEUROSCIENCE

Targeting chronic pain

Chronic pain is a vexing condition affecting >50 million Americans. Most currently used painkillers, including opiates such as morphine, are typically administered systemically and often come with unwanted side effects. In an effort to find a more effective treatment, Benjamin Storek *et al.* developed a gene therapy technique that simulates the pain-killing effect of opiate drugs. The authors designed a viral vector to carry the prepro-β-endorphin gene into primary sensory neurons and selectively activate the opiate receptors. The agents were delivered directly to the spinal fluid of rats by lumbar puncture, or spinal tap. With only a single injection, the rats remained symptom-free of chronic pain for >3 months. The authors found that the prepro-β-endorphin gene was targeted selectively to nerve cells at the "pain gate" and that its activity was long-lived. Another therapeutic gene, interleukin-10, was also effective when similarly administered in small doses directly at the spine. Storek *et al.* suggest that the improvement in symptoms and the narrow range of targeting, together, indicate that gene therapy via lumbar puncture could be an effective method for treating persistent pain while avoiding the side effects associated with drug treatment. — T.D.



Axons entering the spinal cord were EGFP-positive.

"Sensory neuron targeting by self-complementary AAV8 via lumbar puncture for chronic pain" by Benjamin Storek, Matthias Reinhardt, Cheng Wang, William G. M. Janssen, Nina M. Harder, Michaela S. Banck, John H. Morrison, and Andreas S. Beutler (see pages 1055–1060)