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In This Issue

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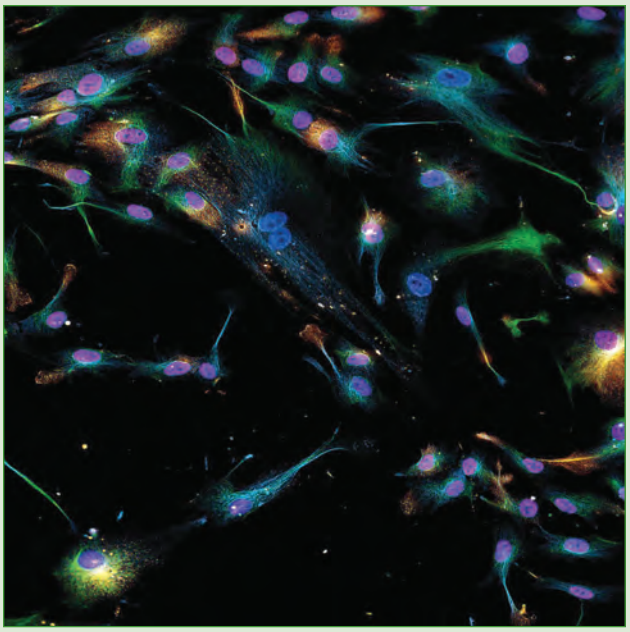
Tracing a virus' path to the brain

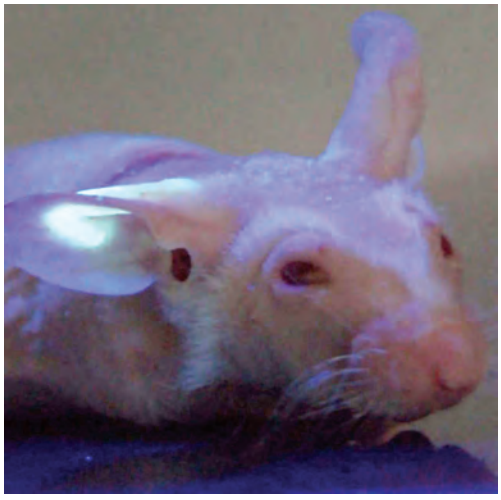


Human olfactory ensheathing cells are a potential path for HHV-6's entry into the brain.

Human herpesvirus-6 (HHV-6) has been tied to neurologic disorders such as multiple sclerosis, encephalitis, and a form of epilepsy, but how the virus gains access to the central nervous system remains a mystery. Erin Harberts et al. (pp. 13734–13739) attempted to trace the virus' route of entry into the brain by examining brain tissue samples from human autopsies. Because the human olfactory system serves as a portal for some viruses, such as influenza and rabies, the authors scoured olfactory tissues for signs of herpesvirus-6 by using a molecular technique that helped identify DNA from the virus. The authors detected HHV-6 DNA throughout the brain in autopsy samples of patients with multiple sclerosis and cancer; viral DNA was found largely in the olfactory bulb, a brain region involved in olfaction. In addition, HHV-6 DNA could be found in nasal mucus samples from healthy people, people suffering a loss of smell, and people with multiple sclerosis, suggesting that the nasal cavity, like saliva, might harbor the virus in healthy and diseased individuals. Further, the authors demonstrated that HHV-6 could successfully infect lab-grown human olfactory ensheathing cells, which help olfactory brain cells grow and establish connections in the brain. The finding suggests that the virus might deploy the ensheathing cells as a bridge across the blood-brain barrier, according to the authors. — P.N.

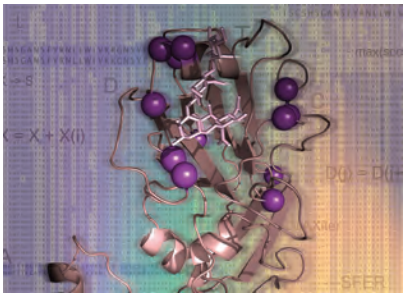
Long-lasting, implantable glucose monitors

Sensors that glow upon detecting glucose can help people with diabetes monitor their blood glucose levels in a minimally invasive manner when implanted under the skin. But most such sensors, whose fluorescent signal can be detected across the skin, fail to stay at the implantation site long enough to enable long-term glucose monitoring. Because replacing such sensors can cause tissue damage to patients, Yun Jung Heo et al. (pp. 13399–13403) immobilized a fluorescent sensor on 1,000 micron-wide hydrogel fibers, thus increasing the sensor's contact with tissue and reducing its mobility. When implanted under the ear skin of mice using a syringe, the authors report, the sensor enabled continuous and accurate blood glucose monitoring for more than 4 months, compared with currently available fluorescent beads that were dislodged after only 1 month. The fibers can be cut to length to achieve a desired amount of fluorescence, and removed from the skin by using a pair of tweezers, obviating the need for invasive surgery. Further, impregnating the sensors with a chemical known as polyethylene glycol (PEG) helped reduce inflammation, often triggered by skin implants. PEG-containing sensors, the authors found, caused less reddening, swelling, and scabbing in the ears of mice than did sensors without PEG. Although the sensors are far from ready for use in people, further technical refinements could help fashion a device for long-term glucose monitoring for people with diabetes, according to the authors. — P.N.



Mouse with a glowing glucose sensor implanted in its right ear.

Amino acid determinants of swine flu emergence

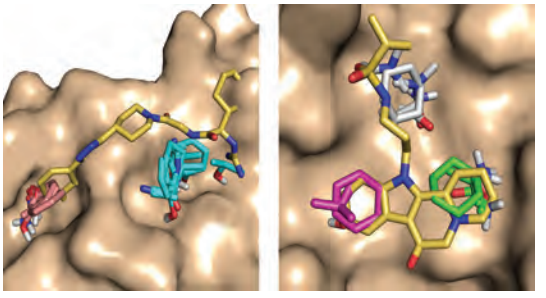


Pandemic swine influenza.

Mutations in a swine influenza virus allowed it to emerge in humans, leading to the swine flu" pandemic of 2009. But it remains unclear what molecular factors permitted the virus to cross the species barrier and avoid human immune recognition. Daphna Meroz et al. (pp. 13522–13527) used a computational approach to look for amino acid signatures that distinguish the pandemic strain from a typical seasonal human flu strain and from other swine strains. The authors focused on alterations in the hemagglutinin protein, which allows the virus to bind and enter host cells. Compared with typical seasonal flu viruses, the pandemic strain showed different amino acid residues around sites that the human immune system uses to recognize the virus—changes that likely allowed this strain to escape immune recognition. Most differences in the sequences of the pandemic strain and normal swine flu viruses were found near receptor-binding sites, suggesting that these mutations may have influenced how well the pandemic virus binds to human cells. The researchers also experimentally altered two amino acids in a swine strain to make it more similar to the pandemic strain. These changes affected binding to red blood cells and made the virus more virulent in mice, according to the authors. — M.L.P.

Protein binding "hot spots" may reveal targets for drug discovery

Protein–protein interactions are considered ripe targets for drug discovery because they have been implicated in disease pathways on so many levels. To find drugs capable of disrupting protein–protein interactions, Dima Kozakov et al. (pp. 13528–13533) used computational solvent mapping, which explores the surface of proteins using small probe molecules to identify sites on proteins where drugs might act. Using a four-step algorithm, the authors found that sites capable of binding drug-sized ligands are made up of a cluster of binding "hot spots," distinguishable by a concave topology combined with a pattern of hydrophobic and polar functionality. The drug binding sites consist of a main hot spot that binds at least 16 probe clusters when mapped with 16 different types of probe molecules, and one or two additional hot spots nearby. This particular set of characteristics suggests hot spots tend to bind drug-like organic compounds that possess some polar functionality attached to a largely hydrophobic scaffold. The results suggest that researchers can detect druggable sites at protein–protein interfaces based solely on the structure of the unliganded protein, thereby streamlining the drug discovery process, the researchers suggest. — B.A.



Protein hot spots in druggable (IL-2, *Left*) and undruggable (Zip A, *Right*) targets.

Molecular clock for eukaryotic evolution

The majority of eukaryotes—organisms with a relatively complex cellular structure and membrane-enclosed compartments—are taxonomically grouped into more than 70, mostly microbial, lineages. But the time period during which eukaryotes diversified into their myriad present-day forms remains shrouded in mystery. Laura Parfrey et al. (pp. 13624–13629) used fossil evidence and molecular data to estimate the timing of early eukaryotic evolution. The authors report that the last common ancestor of eukaryotes likely lived between 1,866 and 1,679 Ma, a finding largely consistent with fossil data but contradicting a hypothesis that eukaryotes evolved only 850 Ma. Further, the authors suggest that the earliest eukaryotic fossils reported in paleontological literature likely belonged to groups that went extinct before the emergence of present-day forms, a likelihood supported by the authors' reckoning that the major groups of extant eukaryotes diverged around 1,200 Ma. By the authors' estimate, the diversification of eukaryotes coincided with the onset of great changes in the chemical composition of the world's oceans—particularly in their iron, sulfur, and oxygen contents—that set the stage for the evolution of their diverse forms. According to the authors, the molecular clock analysis and fossil evidence together suggest that the eukaryotic evolutionary tree has long stems that support varied branches. — P.N.