In This Issue

Mitogenomes reveal variegated origin for native North Americans

A consensus view holds that modern Native Americans descended from a few original founders, who crossed Beringia carrying a gene pool derived from Asian groups living in northeast Siberia prior to the Last Glacial Maximum. Researchers disagree, however, on whether the migration occurred in a single wave 15,000–18,000 years ago or as multiple streams. In light of recent work that points to at least three separate population movements, Alessandro Achilli et al. (pp. 14308–14313) conducted a detailed evaluation of Native American genetic diversity using information stored in the entire mitochondrial genome, or mitogenome. The authors focused on two haplogroups known as A2a and B2a, genetic markers found almost exclusively in Siberia, Alaska, and surrounding regions, and in Native Americans from the American Southwest, and determined that even three waves of migration is likely a simplistic estimate. Instead, the authors suggest, although the original founders left the greatest mark, the genetic makeup of North American Natives was subsequently reshaped by multiple new streams of gene flow and local population dynamics. According to the authors, a detailed migration model that traces Native American lineage across Asia, northern North America, and Canada might help uncover the origin of native North Americans. — T.J.

Northwest coast totem pole.

To resist antibiotics, pathogen "eavesdrops" on commensal's communication

Researchers have suspected that human intestinal pathogens interact with resident commensal bacteria to sustain infections, but the precise molecular nature of the interaction remains unclear. Nicole Vega et al. (pp. 14420–14425) tested whether *Salmonella typhimurium*, a bacterium that causes gastroenteritis and sepsis in humans, can exploit the signaling mechanisms used by *Escherichia coli*, a human commensal, to establish a persistent infection. Because *E. coli* produces indole, a signaling molecule that allows the bacteria to tolerate antibiotics, the authors tested whether *S. typhimurium* can increase its antibiotic tolerance in response to indole, which the pathogen does not synthesize. The authors report that the pathogen increased by threefold its resistance to two main clinical antibiotics—carbenicillin and ciprofloxacin—in response to indole added to cultures. Similarly, *S. typhimurium* increased its tolerance to ciprofloxacin when cultured together with wild-type *E. coli* but not *E. coli* incapable of producing indole. Further, the authors found that indole signaling triggers the expression of genes in the oxidative stress and phage shock response pathways in both bacteria, suggesting a potential mechanism for indole-mediated antibiotic tolerance. In addition, the authors demonstrated that indole increased the tolerance of *S. typhimurium* to ciprofloxacin in the intestine of the round worm *Caenorhabditis elegans*, an established model for the analysis of antibiotic efficacy. According to the authors, indole can serve as an interspecies signal that allows pathogens to benefit from commensals' signaling ability to enhance antibiotic tolerance in host intestines. — P.N.

3D technique helps visualize retinal, subretinal microvasculature

Angiography imaging, currently a clinical option of choice for viewing disease-related microvascular changes in the human retina, consists of photographing an intravenously injected fluorescent dye flowing through the retinal vasculature. While providing some capillary detail, this approach does not adequately reveal microvascular structures such as the choriocapillaris that lie deep within the eye beneath the retina. To address the shortcoming, Dae Yu Kim et al. (pp. 14354–14359) devised a noninvasive 3D microvascular imaging technique called phase-variance optical coherence tomography (pvOCT), which can help identify vasculature without fluorescent

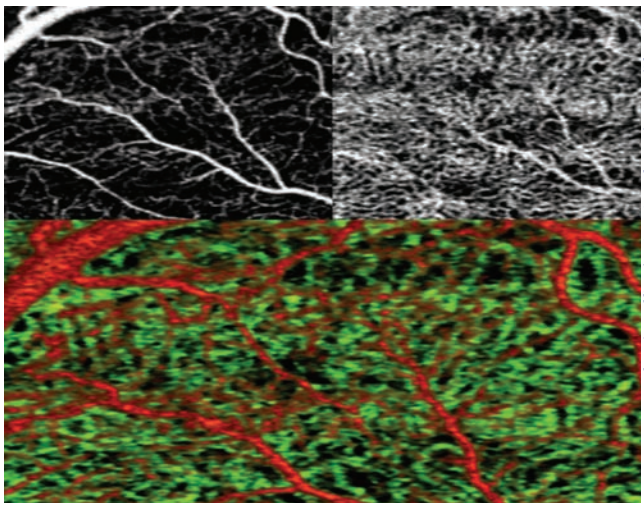


Image courtesy of Seth Ruffins (University of Southern California, Los Angeles) and Dae Yu Kim.

In vivo image of capillary networks in the retina (*Top Left* and red) and choroid (*Top Right* and green).

dyes through the analysis of data acquired with OCT systems. In addition to generating capillary perfusion maps of the retina, the authors report, pvOCT imaging has 3D capabilities that allow the identification of vasculature in different layers of the retina and choroid. To demonstrate the potential of pvOCT, the authors imaged and compared the anterior layers of choroidal vasculature in a healthy eye with eyes afflicted by geographic atrophy associated with age-related macular degeneration, a potentially debilitating eye disease. The authors also present findings showing that pvOCT can reveal details about crucial microvascular structures currently obscured from view when other techniques are used. According to the authors, pvOCT can aid the treatment of retinal diseases such as age-related macular degeneration. — T.J.

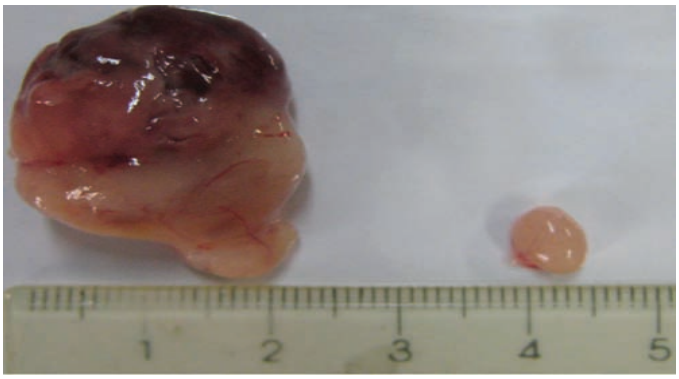
Technique helps fabricate inexpensive gas sensors on paper

With electrical properties that enable sensitive response to changes in the chemical environment, carbon nanotube (CNT) materials seem ideal for building simple, low-cost sensors to detect harmful gases and volatile organic compounds (VOCs). However, the poor solubility of CNTs in most solvents poses challenges to typical fabrication, a process by which the constituent materials are dispersed in a liquid, chemically functionalized to impart selectivity, and then deposited on electrodes. Katherine Mirica et al. (pp. E3265–E3270) developed a two-step, solvent-free procedure that can help fabricate selective gas sensors on paper in less than 15 minutes from commercially available materials. Using a solvent-free, mechanical mixing technique and compression, the first step generates solid composites from CNTs or graphite that are specially designed to interact with a specific class of gases. The second step deposits these conductive building blocks onto the surface of paper via mechanical abrasion, resulting in a type of sensor known as a chemiresistor, which detects chemical vapors in air. Furthermore, by using parallel fabrication to create multiple chemiresistors from diverse composites, the procedure can be expanded to rapidly generate cross-reactive arrays capable of sensing and differentiating gases and VOCs at concentrations of just a few parts-per-million, according to the authors. — T.J.

Array of selective carbon nanotube-based gas sensors on paper.

Reducing the tumor risk associated with stem cell-based therapies

Human pluripotent stem cells (hPSCs) hold great promise for use in regenerative therapies and personalized treatments due to their capacity for self-renewal and ability to differentiate into any cell type. But hPSC-based therapies carry a risk of tumor formation due to undifferentiated cells that remain in the cell mixture after most of the hPSCs have differentiated. Mi-Ok Lee et al. (pp. E3281–E3290) sought to identify small molecules that selectively eradicate residual undifferentiate hPSCs but spared differentiated cells. The authors analyzed the expression profiles of apoptosis-related genes in differentiated and undifferentiated hESCs, reasoning that hESC-specific antiapoptotic factors could represent promising targets for selectively eliminating undifferentiated cells. Two genes encoding the antiapoptotic proteins Bcl10 and survivin were more highly expressed in hESCs than in differentiated cells and chemical inhibitors of either protein selectively induced apoptosis in hPSCs. Furthermore, survivin inhibitors selectively eliminated undifferentiated hPSCs from a partially differentiated population of hESCs, and prevented tumor formation following transplantation of hESC-derived cells in mice. The findings suggest that small molecule inhibitors of key antiapoptotic factors in hPSCs may represent a promising strategy for preventing tumor formation following transplantation of hPSC-derived cells, according to the authors. — N.Z.



Tumors formed in mouse testes injected with hESCs treated without (NT) or with a survivin inhibitor.

Odor response is dynamic and produces an afterimage

Odorant receptor neurons encode information about the identity and concentration of each odorant they detect and communicate this information to mitral/tufted (M/T) cells of the olfactory bulb. To determine whether the mammalian olfactory code alters its representation of a stimulus over time, Michael Patterson et al. (pp. E3340–E3349) studied the firing patterns of M/T cells in mice. As was previously observed, M/T cells responded to odorants in a series of electrical spikes that coincided with the breathing cycle. However, the authors found that the response of many M/T cells evolved between breaths. The greatest change occurred between the first and second breaths, with shifts occurring in the phase and/or intensity of the response and some cells switching between excitation and inhibition. Following dissipation of the odor, 30% of M/T cells had a postodor response, or olfactory afterimage, that could differ from their response before or during odor presentation. The observed change in M/T cell firing following the first breath, coupled with the observation that odor discrimination is most accurate during the first breath, may indicate an adaptation of the olfactory system to permit new odors to be detected in the background of a known odor, while the afterimage may represent a form of short-term memory, according to the authors. — C.B.