Sorghum sequenced

Sorghum bicolor is an important staple for humans and livestock in northern Africa and is increasingly cultivated as a biofuel crop in arid parts of North America and Asia, where farmers like the advantages associated with its hardiness and C_4 photosynthetic pathway. Nonetheless, improvements in sorghum yield have lagged behind those of other agronomically important grains. Assembly of the ~760-Mb genetic blueprint of sorghum, using a modified shotgun approach that takes into account the highly repetitive nature of many large eukaryotic genomes, is especially noteworthy as it is the first genome of a tropical grass. The high conservation of grass gene order (synteny) should facilitate improvement of its close relatives, the bioethanol crops sugarcane and *Miscanthus*. Until now, the only cereal genome has been that of rice, a temperate species with C_3 photosynthesis. Knowing the genetic complement of a C_4 plant could thus accelerate realization of the long-sought goal of improving the photosynthetic efficiency of C_3 species. Although the sorghum genome is ~75% larger than the rice genome, the numbers of genes and sizes of gene families are similar in the two species, with a remarkable >98% concordance in intron position and phase. Most of the extra DNA in the sorghum genome is heterochromatin and largely comprises long terminal repeat retrotransposons. (*Nature* **457**, 551–556, 2009) *PH*

Profiling the common cold

Ninety-nine strains of human rhinovirus, the etiological agent of the common cold, have thus far been identified. To better our understanding of the differences among these strains at the genome level, Palmenberg *et al.* report the sequencing and analysis of all known human rhinovirus genomes. The investigators then use this sequence information to build a phylogenetic tree for the rhinovirus genus, incorporating the handful of previously sequenced rhinovirus genomes and including a recently identified virus species as well as ten clinical isolates from rhinovirus-infected people. Using a protocol optimized to sequence the noncoding ends of the viral genome, and taking into account the potential three-dimensional structure of the virus's single-stranded RNA genome, the researchers identify a noncoding region of the genome that varies even among isolates of the same rhinoviral strain and that is analogous to regions in other viral genomes that determine pathogenic potential. The group's analyses also reveal that surprisingly extensive genetic recombination has occurred throughout rhinovirus evolutionary history. This genetic variation may underlie the recent poor performance in clinical trials of antirhinoviral therapies and suggests that the pursuit of clade-specific treatments may prove fruitful. (*Science* published online, doi:10.1126/science.1165557, 12 February 2009) *CM*

Silencing host and pathogen

Although most antiviral therapies have until recently targeted viral proteins, emphasis is shifting to target host proteins associated with viral replication. Wu *et al.* now combine the two approaches by designing a small interfering (si)RNA-based strategy that targets the expression of both a herpes simplex virus type 2 (HSV-2) protein and a host protein in mice. To achieve this, the investigators apply topically, to the epithelium of the vagina, two siRNAs: one that knocks down nectin-1, a cellular receptor for the viral envelope glycoprotein D; the other that inhibits UL29, a viral DNA binding protein. The siRNAs are conjugated to cholesterol to enhance the uptake by the epithelial cells and protected from cervicovaginal RNases by 3′ phosphorothioate modifications. The onset of the protection is extremely fast, and even treatment 3 and 6 hours after exposure to the virus protects 80% of the mice. The protective effect is long-lasting, with mice resistant for up to a week from an otherwise lethal viral challenge. The early onset effects are mainly due to the direct targeting of the viral mRNA, whereas prolonged protection requires the efficient downregulation of the cellular receptor. The approach may prove useful not only for HSV-2 treatment but also for other sexually transmitted viruses, such as HIV. (*Cell Host Microbe* **5**, 84–94, 2009) *ME*

Written by Laura DeFrancesco, Markus Elsner, Peter Hare & Craig Mak

Reversing brain drain

Brain-derived neurotrophic factor (BDNF) is found throughout the entorhinal cortex and hippocampus where memory and learning are established. The loss of BDNF from those regions in Alzheimer's disease led Tuszynski and colleagues to question whether providing BDNF could reverse or ameliorate symptoms of the disease. Their findings in several animal models of neurodegeneration suggest that it can. In a transgenic mouse model, J20, that expresses human amyloid precursor protein, injecting a lentivirus constitutively expressing BDNF into the entorhinal cortices resulted in improvements in tests of spatial memory compared with control lentivirus– or sham-injected mice. Additionally, more normal expression of 55% of genes whose expression is altered by amyloid plaques was restored, as were synaptic markers in the cortex and hippocampus. Similar improvements in test performance as well as gene expression were obtained with cognitively impaired aging rats. BDNF also prevented cell death both *in vitro* (primary entorhinal neurons exposed to toxic Ab1-2 protein) and *in vivo* (injury-induced neuron loss in rats). Finally, in perhaps the best animal model of neurodegeneration, aging monkeys, BDNF injections improved visual-spatial discrimination a month after treatment. Although delivery into human patients would be challenging, the authors suggest that their results warrant consideration in the clinic. (*Nat. Med.* advance online publication, doi:10.1038/nm.1912, 8 February 2009) *LD*

Nanoscale MRI microscopy

Magnetic resonance imaging (MRI) is widely used in medicine and physiology. Its utility for microscopy and structural biology, however, has been limited by its comparatively low resolution. Degen *et al.* now present a new MRI technique that improves the maximal spatial resolution to <10 nm. Their approach is based on sensitive force measurements between a 200-nm-diameter magnetic tip and the sample. The force is generated by triggering nuclear magnetic resonance in the sample by a radio frequency–modulated magnetic field and is proportional to the density of ^1H in the observation volume. Spatial resolution is achieved by moving the probe tip in a three-dimensional pattern at a distances of 24–62 nm from the surface of the sample. A three-dimensional picture is generated by computer reconstruction of the hydrogen atom densities. Degen *et al.* imaged dried tobacco mosaic virus particles at 0.3 K. In the future, this technique could be used to obtain high-resolution images of any biological cryosample using common MRI contrast techniques. (*Proc. Natl. Acad. Sci. USA* **106**, 1313–1317, 2009) *ME*