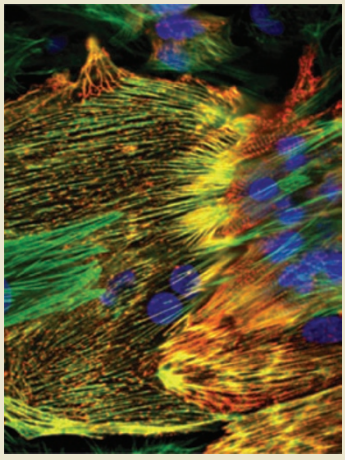
Robots with heart



Feinberg *et al.* show that rat cardiomyocytes can be grown on flexible sheets of polydimethylsiloxane to provide films capable of contracting and flexing with forces comparable to those produced by normal heart muscle. Depending on the shape cut from a sheet, its thickness and how it was patterned by fibronectin, which promotes cell adhesion and directs growth and differentiation of the cells, the authors generate films that fold into predictable three-dimensional forms. These can grip, twist, pump, walk or swim either spontaneously or when prompted by electrical pulses. The impressive range of movements of which the two-dimensional films are capable suggests that they may find applications as robotic devices or in improving insight into the biomechanics of locomotion and muscle contraction. (*Science* **317**, 1366–1370, 2007) *PH*

Genome with a bouquet

A consortium of French and Italian scientists reports a high-quality draft genome sequence for a variety of grapevine (*Vitis vinifera*) related to Pinot Noir. As the fourth sequenced genome of a flowering plant (after *Arabidopsis thaliana*, rice and poplar), the blueprint provides not only insight into the evolution of monocotyledonous and dicotyledonous plants but also clues to the molecular changes associated with domestication of *V. vinifera* over the past eight centuries. Among the >30,000 predicted proteins are an abundance of enzymes responsible for the synthesis of tannins, terpenes and stilbenes that contribute to the aromas and flavors of wine, as well as some of its proposed health benefits. Knowledge of these genes, and of genes conferring resistance to pathogens, may aid targeted breeding programs to modify the aromatic features of existing cultivars or reduce the need for pesticides. (*Nature* published online August 26, doi: 10.1038/nature06148) *PH*

HIV neutralization dissected

Although the protective activities of antibodies against certain viruses have been associated with their crystallizable fragment (Fc) regions, the role of Fc-mediated effector functions in protection against HIV infection has remained unclear. Burton and colleagues dissect the modes of action of b12, an antibody that neutralizes HIV-1 by recognizing a conserved epitope on the CD4-binding site of gp120, to reveal a role for effector functions in protection against the virus. Using a chimeric virus that infects macaques but is still recognized by the human antibody, they show that both b12 and a point mutant compromised in binding complement offer greater protection against vaginal challenge than a variant defective in binding both complement and Fcγ receptors (FcγRs). As all three variants have comparable neutralizing capacities, this suggests that FcγR, but not the complement cascade, contributes to the protective activity of b12. One possible mechanism for FcR involvement in protection is through killing of b12-coated HIV-infected cells by host FcR-bearing effector cells. A role for FcγR function in protection against HIV has implications for vaccine design, as quantifying virus neutralization alone may not fully predict vaccine efficacy. (*Nature* **449**, 101–104, 2007) *PH*

Written by Laura DeFrancesco, Peter Hare & Jan-Willem Theunissen

Antibiotics share mode of action

Although the targets of common antibiotics have been known for years, the mechanism of cell death has not. Now Collins and coworkers have shown that three classes of bacteriocidal antibiotics, regardless of their targets—β-lactams that bind penicillin-binding proteins, aminoglycosides that inhibit ribosome function and quinolones that target DNA gyrases—kill by a common mechanism, hydroxyl radical production. After finding that quinolones kill bacteria by generating reactive oxygen species, the researchers looked to see whether other antibiotics do so as well. Using a fluorescent probe that detects the presence of oxidative hydroxyl radicals, hydroxyphenyl fluorescein, they showed that all three types of antibiotics raise the level of free radicals in bacteria. Using expression arrays, they further show that all three upregulate NADH 1 dehydrogenase with an accompanying increase in the ratio of NAD/NADH, which they believe initiates a chain of reactions that culminates in hydroxyl radical–mediated damage to cellular DNA and lipids. Interestingly, impairing the bacterial error-prone DNA repair (SOS) mechanism, which likely provides a path to resistance to the drugs, potentiates antibiotic killing. These results provide new targets for antibiotic development as well as a strategy for preventing resistance from developing—by pairing SOS inhibitors with antibiotics. (*Cell* **130**, 797–810, 2007) *LD*

Predicting miRNA target access

An important bottleneck in studies of microRNAs (miRNAs)—small endogenous RNAs that regulate gene expression by mediating cleavage or translational repression of mRNA—is accurate prediction of their targets. Gaul, Segal and colleagues optimize computational miRNA target prediction after experimentally demonstrating the importance of target-site accessibility in miRNA-mRNA interactions. The authors use a quantitative luciferase assay that measures miRNA-mediated translational repression in *Drosophila melanogaster* tissue culture cells to study >60 miRNA-mRNA interactions. Forcing miRNA targets that are normally present in open-loop structures into highly paired stem structures substantially reduces miRNA-mediated repression. The authors highlight the importance of target site accessibility by demonstrating that a closed mRNA structure is comparably repressive to single-base mutations, insertions or deletions in the miRNA target sequence itself. To account for target accessibility in miRNA prediction methods, the authors develop a parameter-less, energy-based score $\Delta\Delta G$, which is equal to the difference between the free energy gained by miRNA target binding (ΔG_{duplex}) and the free energy lost by unpairing target-site nucleotides (ΔG_{open}). They further refine this score by including in the component ΔG_{open} the cost of unpairing bases that flank the target. The refined site accessibility model correlates well with the measured degree of repression and its use in a genome-wide target algorithm enables validated targets to be predicted more accurately than with existing methods. (*Nat. Genet.* **39**, 1278–1284, 2007) *JWT*