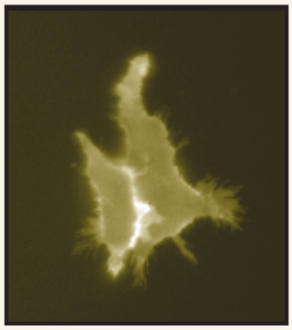
Fretting away at drug targets



Over half of all drug targets are so-called G-protein coupled receptors (GPCR). However, measuring the variety of intracellular events that GPCRs evoke requires sophisticated techniques that do not readily lend themselves to high-throughput screening. Johns Hopkins researchers have therefore created fluorescently labeled GPCRs to throw light on this problem (*Science* 291, 2408–2411, 2001). GPCRs are formed from a complex of α-, β-, and γ-subunits, embedded within the membrane and extending into the cell's interior. When a drug, hormone, or neurotransmitter binds to the receptor, the subunits break apart. To catch these subunits in the act of separation, Chris Janetopoulos and colleagues tagged α- and β-subunits with cyan and yellow fluorescent labels, respectively. The close proximity of the subunits, and thus of the fluorescent labels, results in so-called fluorescence resonance energy transfer (FRET), and the GPCR complex glows yellow. When the subunits dissociate, the FRET signal decays to cyan. Although the concept has been tested using only a bacterium, Janetopoulos says that they are developing the technique for mammalian cells. "I think that the technique could and will be used with other receptor systems." *LF*

Plants get precocious

Pests find the tender young leaves of corn or rice plants tasty, spurning the less-palatable older leaves. By harnessing a gene influencing such age-related characteristics, researchers could have found a way to genetically manipulate crops to express protective traits, while avoiding the controversy surrounding the insertion of foreign genes or the use of pesticides. Tanya Berardini and colleagues at the University of Pennsylvania's Plant Science Institute (Philadelphia, PA) screened *Arabidopsis thaliana* seedlings for genetic mutations that accelerated the production and distribution of trichomes (glandular leaf hairs), which indicate a plant's maturity (*Science* 291, 2405–2407, 2001). The *SQUINT (SQN)* mutations identified generated plants with elliptical leaves—hence the "squinty-eyed" namesake—similar to mature leaves, but the plants flowered and produced seeds as normal. *SQN* encodes a protein related to bovine cyclophilin 40 (CyP40), which regulates specific cell-signaling pathways. Scott Poethig, co-author on the paper, says: "Our working hypothesis is that *cyp40* regulates phase change by affecting the activity of one or more proteins specifically involved in this process. … [However,] CyP40 may only be useful for truncating the expression of the juvenile phase, not prolonging it." The function of CyP40 in plants is currently being investigated. *JJ*

Research briefs were written by Aaron Bouchie, Liz Fletcher, Judy Jamison, and Christopher Morrison.

Mending a broken heart

Various types of cell transplant have been tried—albeit with limited success—to repair the damage to the heart inflicted by a heart attack. However, two studies raise hopes that cells from a patient's bone marrow could be used to rescue injured hearts. In one study, researchers at Columbia University (New York) extracted a specific subpopulation of stem cells from human bone marrow—so-called angioblasts—that give rise to the endothelial cells lining blood vessels. When injected into the tails of immune-deficient rats, the angioblasts migrated to the heart, triggering the growth of new blood vessels in both damaged and undamaged myocardium (*Nat. Med.* 7, 430–436, 2001). There was a 30%–40% inprovement in heart function in rats treated with stem cells. A different tactic was employed in the second study, in which a specific population of multipotent cells was injected directly into ischemic mouse heart (*Nature*, 410, 701–706, 2001). The cells, which were tracked using a green fluorescent protein label, took up residence in the damaged tissue and created not only new blood vessels but also new cardiac muscle. Moreover, there was a measured improvement in heart function in transplant recipients. Although there are many questions still to answer about the viability of this approach—the least being the practicalities of harvesting stem cells from heart attack patients—the researchers say there is "compelling evidence" that the technique could benefit humans. *LF*

Bacterial serial killers

A novel use has been found for the biotechnologist's ubiquitous laboratory tool—the bacteriophage. Bacteriophages naturally infect and kill bacteria, but researchers have now identified a deadly bacteriophage extract that can kill bacteria on contact (*Proc. Natl. Acad. Sci.* 98, 4107–4112, 2001). Researchers from the Rockefeller University (New York) extracted the enzyme, lysin, from bacteriophage specific to group A streptococci—the cause of "strep" throat, rheumatic fever, and also "flesh-eating" infections. When lysin was given orally and nasally to mice infected with group A streptococci, it eradicated the pathogen by punching holes in its cell walls. The surrounding microflora were largely unaffected. Although further studies are needed to ensure that bioactive bacterial cell wall fragments are not released systemically, bacteriophage enzymes could be a novel means of preventing infections by clearing reservoirs of potentially pathogenic bacteria from human mucous membranes. Because the enzyme kills on contact, it avoids the potential risk of antibiotic resistance. Vincent Fischetti, senior author on the paper, says the team will next engineer a single bacteriophage enzyme to target several pathogenic bacteria. *AB*

Skin therapy

In healthy skin, a thin layer of tough keratinized epidermal cells protects the body from dehydration and attack by microorganisms. This protective barrier is built from basal skin cells, which proliferate and migrate upward from the lower (basal) skin layers. Researchers at the University of California at San Diego (CA) School of Medicine have now identified the essential trigger for this process—keratinocyte-differentiating factor, kDIF (*Nature* 410, 710–714, 2001). While studying the role of I-kappa-B kinase (IKK) in inflammation, Michael Karin and colleagues found that a catalytic subunit of the kinase, IKKα, regulated keratinocyte proliferation and differentiation. IKKα-knockout mice developed basal cell carcinomas, caused by the unchecked proliferation of basal skin cells, but at the time it was unclear why. The researchers suspected that a second factor was involved after grafting skin from IKKα-deficient mice onto wild-type controls. Though abnormal at first, IKKα-deficient skin soon acquired a normal appearance, indicating that a soluble factor was diffusing from the host skin. The molecular identity of kDIF is as yet unknown, but its discovery is a potential boon for the treatment of skin cancers and for tissue engineers hoping to create more functional skin grafts. *CM*