Wood chips

Genome-wide expression analysis in plants has largely been carried out in model organisms whose genomes have been sequenced, such as *Arabidopsis thaliana* (thale cress) and *Oryza sativa* (rice), rather than in perennial, woody plants. To develop tools for studying perennials and processes unique to them, Swedish researchers have created cDNA spotted arrays for *Populus tremula* (aspens and cottonwoods). Starting with data on over 35,000 expressed sequence tags, they constructed arrays of 13,000 cDNAs, which, they determined, encoded 9,000–10,000 unique genes. Carrying out a five-week long, time-series experiment on autumn leaves taken from a single tree growing in the wild, they found that nearly a third of the transcripts were expressed in all samples. However, by classifying the genes according to function, they demonstrate that groups of genes decreased in expression in the course of the experiment (*e.g.*, those involved with the light reaction and with chlorophyll synthesis), whereas others (*e.g.*, those associated with ethylene production) increased. This represents the first expression experiment carried out on a plant growing in nature. The authors also point out that autumn senescence differs from better studied senescence systems, such as drought and mechanical stress, in that leaves respond to photoperiod and temperature. (*Genome Biol.* **5:R4**, Epub Mar 10, 2004) *LD*

Gene therapy is a gas

Multiple bouts of 'silent' ischemia—characterized by lack of blood flow and oxygen to the heart muscle—cause cumulative tissue damage and are common preludes to fatal heart attacks. Unfortunately, ischemia is often asymptomatic, making prevention and treatment difficult. Phillips and colleagues have generated an inducible gene therapy system that turns on upon sensing low oxygen levels specifically in the heart, and turns off once proper blood flow and oxygen levels have been restored. The authors designed a double plasmid system comprising an oxygen-sensing transactivator under the control of a cardiac-specific promoter, and an effector plasmid expressing the inducible protective human gene, heme oxygenase-1. Mice were injected with the therapeutic vectors or control vectors one hour after being subjected to myocardial ischemia. Treated mice showed reduced heart tissue scarring and increased recovery of heart pumping function. Although plasmid expression lasted for only seven days, future experiments aimed at making a viral system have the potential to prolong expression for up to several months. (*Hypertension* **43**, 746–751, 2004) *NC*

Research Notes written by Kathy Aschheim, Nadia Cervoni, Laura DeFrancesco and Gaspar Taroncher-Oldenburg.

Stem cell heartbreak

Hematopoietic stem cells transplanted into ischemic mouse heart do not transdifferentiate into cardiomyocytes and repair injured heart tissue, according to two new studies by Murry *et al.* and Balsam *et al.* The latter paper also finds that the hematopoietic stem cells differentiate only into blood cells. These conclusions contradict the findings of a widely noted 2001 paper by Orlic *et al.*, which proposed that injection of hematopoietic stem cells into infarcted mouse heart leads to substantial tissue regeneration and functional improvement. The reason for the contrary outcomes is not understood, although one suggested explanation is differences in the techniques used to track the fate of the donor cells. Murry *et al.* and Balsam *et al.* used genetic marking with reporter genes, a more accurate method than the fluorescent antibodies in Orlic *et al.* Given that the earlier study has already prompted clinical trials, the new work underscores the need for thorough animal testing of experimental therapies. (*Nature* **428**, 664–668, 2004; *Nature* **428**, 668–673, 2004) *KA*

Human immunity in mice

In what promises to be a boon to the fields of basic and applied immunology, researchers have developed a functional model of the adaptive human immune system in mice. Markus Manz and colleagues describe the reconstitution of a functional human immune system in immunodeficient newborn mice transplanted with $CD34^+$ human cord blood cells. Previously, attempts to generate *in vivo* models of the human immune system by transplanting hematopoietic cells or tissues into immunocompromised mice had only been partially successful because of limited engraftment and functionality. To overcome these problems, Manz's team specifically targeted the mouse liver (which contributes to perinatal hematopoiesis and hematolymphoid system development) in young mice (establishment occurs mostly during the first weeks of life). This approach led to the *de novo* development of B, T and dendritic cells and formation of spleen, thymus and mesenteric lymph nodes. The authors further tested the immune response by challenging the mice with the tetanus toxoid (TT) and with Epstein-Barr virus (EBV). TT elicited the production of anti-TT IgG antibodies as well as memory B cells. EBV triggered a T-cell response capable of keeping viral replication under control. (*Science* **304**, 104–107, 2004) *GTO*

Simulating cystic fibrosis

Mall *et al.* have produced the first mouse model of cystic fibrosis that replicates most features of the human disease. Cystic fibrosis is caused by mutations in the cystic fibrosis transmembrane conductance regulator (*CFTR*) gene, but mice in which this gene has been knocked out do not develop the pulmonary mucus obstruction and bacterial infection characteristic of the disease. CFTR is a Cl^- channel that also regulates the Na^+ channel ENaC. Nonfunctional CFTR has been proposed to initiate disease by increasing the ionic concentration of the protective airway surface liquid (ASL) and thus inactivating antimicrobial peptides, or by reducing ASL volume and inhibiting mucus clearance. To study the consequences of increased Na^+ absorption, Mall *et al.* overexpressed the α, β or γ subunits of ENaC in mouse lower-airway epithelia. The lungs of mice overexpressing the β subunit showed increased Na^+ absorption, lower ASL volume, impaired mucus clearance, inflammation and a reduced capacity to clear bacterial infection, demonstrating a relationship between altered Na^+ transport and the disease phenotype. (*Nat. Med.* **10**, 487–493, 2004) *KA*