Plant-made proteins on the double


Ya-Chun Chang

Plants could provide a cost-effective platform for producing protein therapeutics, but so far, researchers have been unable to produce large quantities of complex hetero-oligomeric proteins, like antibodies, in plants. Recent work by Giritch *et al.* using a transient expression system offers a possible solution. These researchers got coexpression of both heavy and light chains of human IgG in tobacco (*Nicotiana benthamiana*; see image) by transfecting plants with two different viruses, each carrying a separate antibody chain. Whereas using a single viral vector (tobacco mosaic virus, TMV) led to coexpression in only 5% of the plant cells, transfection with the two different vectors (TMV and potato virus X) raised the level to 85%. The authors go on to show that plants cotransfected with the two vectors can produce ten times more (0.5 g/kg of leaf) correctly assembled antibody molecules that retain antigen specificity than conventional (*Agrobacterium tumefaciens*) expression systems. Why the two-virus system works so well is unclear, but the authors speculate that different viruses require different cellular constituents for their replication and thus do not compete for cellular processes and resources. The transiently expressed dual-vector system has the advantage of producing high titers of antibody in a few days. *(Proc. Natl. Acad. Sci. USA*, **40**, 14701–14706, 2006) *LD*

Antibacterial discovery gets a shove

A novel mechanism has been elucidated for certain types of lantibiotic, a class of small peptide antibiotics, which may open up opportunities for novel antibacterial discovery. Many lantibiotics (e.g., nisin) exert their bactericidal effect by 'punching' holes into bacterial cell walls through interaction with lipid II, a key component in cell wall formation. But some lantibiotics, such as mutacin, gallidermin and epidermin, appear to mediate their antibacterial activity through another mechanism. With a series of simple and elegant experiments, Breukink and colleagues have now unveiled the mechanism by which these lantibiotics exert their bactericidal powers. Rather than punching holes into cell walls, these peptides 'shove' lipid II away from sites of active cell wall formation, thereby effectively stopping cell proliferation. The authors show that this mechanism essentially involves sequestration of lipid II from its natural location along cell division sites, the septa, to a random and patchy distribution throughout the cell wall. This second mechanism provides researchers with a novel strategy for antibiotic development. (*Science* **313**, 1636–1637, 2006) *GTO*

Cataloging mutations in breast and colorectal cancers

Sjöblom *et al.* report a first attempt to systematically identify the full complement of somatic mutations associated with breast and colon cancers. They set about this task by sequencing 120,839 nonredundant exons from 14,661 different transcripts in 11 breast and 11 colorectal tumors, and 2 normal samples. After removal of silent and germline mutations, nucleotide changes also present in the normal-cell controls, known polymorphisms and unconfirmed changes upon resequencing, the authors obtained a list of 1,307 somatic mutations in 1,149 genes. To assess the mutation spectrum and frequency in these 1,149 genes, they then sequenced them in 24 additional breast or colorectal tumors and identified 365 additional somatic mutations in 236 genes. A bias toward C:G to T:A transitions at CpG sites in colorectal cancers indicates that the mutagenesis mechanisms differ between the two tumor types. By calculating the probability that the number of mutations in each gene that was mutated in both sequencing rounds was higher than that expected from background mutagenesis, the authors identified a total of 189 candidate genes (an average of 11 such genes per tumor tested) that were mutated at a significant frequency in the two cancers. Even though the number of somatic mutations associated with the two cancers was much larger than previously thought, the authors conclude that similar mutation cataloging efforts in other tumor types, as proposed by the Cancer Genome Atlas Project, should be both feasible and affordable. (*Sciencexpress*, published online 7 September 2006, doi:10.1126/science.1133427) *JWT*

Research Highlights written by Kathy Aschheim, Laura DeFrancesco, Peter Hare, Gaspar Taroncher-Oldenburg & Jan-Willem Theunissen

A new path to human ES cells

To sidestep ethical and political obstacles to research on human embryonic stem (ES) cells, Lanza and colleagues are developing a derivation method that would avoid the destruction of embryos. Their approach piggybacks on a technique that is sometimes used in fertility clinics to evaluate *in vitro*–fertilized embryos. In preimplantation genetic diagnosis, a single cell is detached from an 8-cell embryo and analyzed for genetic abnormalities; if all is well, the remaining 7-cell embryo is capable of normal development and can be implanted in the uterus. Lanza and colleagues propose to expand the biopsied cell so that it can be used both to test for genetic disease and to create ES cell lines genetically matched to the donor. Following an earlier study on mouse embryos (Chung *et al.*, *Nature* **439**, 216–219, 2006), they now report proof of principle that single blastomeres removed from human embryos at the 8- to 10-cell stage can generate ES cell lines. The efficiency is still low, as 91 blastomeres from 16 embryos gave rise to only two lines. Although none of the embryos described in the paper were allowed to continue development, the authors suggest that the method could be used without embryo destruction in the context of preimplantation genetic diagnosis. (*Nature*, advance online publication 23 August 2006, doi:10.1038/nature05142) *KA*

Nanoparticles deliver inside and out

Most traditional nonviral delivery systems, such as liposomes, are limited to delivering one type of drug. But a system that would allow codelivery of nucleic acid together with an accompanying hydrophobic small molecule could offer the possibility of improved uptake of the former and/or synergistic therapeutic effects. Yang and colleagues now describe amphiphilic polymers that self-assemble to form particles with a hydrophobic core, ideal for encapsulating most drugs, and a cationic shell that can be coated with nucleic acid. Cationic core-shell nanoparticles loaded with both the hydrophobic chemotherapeutic paclitaxel (Xyotax) and either a plasmid encoding interleukin-12 or siRNA directed against the anti-apoptotic protein Bcl-2 suppressed the growth of mouse mammary carcinoma 4T1 cells more effectively than naked particles encapsulating the drug or empty shells coated with the DNA or siRNA. Although the toxicity of the nanoparticles needs more thorough evaluation, and modification of their isotropic surfaces for targeted delivery will likely be challenging, these nanoparticles are easier to fabricate and size than liposomes. (*Nat. Mater.*, advance online publication 24 September 2006, doi:10.1038/nmat1737) *PH*