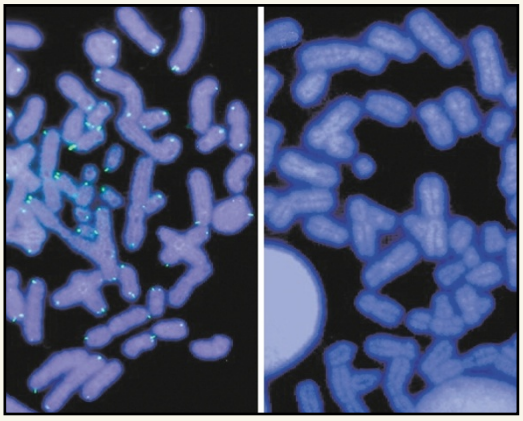
DNA nanocircles



Researchers at Stanford University (Stanford, CA) and the University of California at Santa Barbara have developed a test-tube method for elongating telomeres—the highly repeated sequences at the ends of chromosomes—using a tiny circular DNA template (*Proc. Natl. Acad. Sci. USA*, doi/10.1073/pnas.252396199, 2002). Lead author Eric Kool states that the feat was accomplished by synthesizing 54-nucleotide circular single-stranded DNAs encoding nine uninterrupted human telomeric repeats, which were then incubated with chromosomes from metaphase-stage human kidney cells, fluorescein-labeled nucleoside triphosphates, and DNA polymerase. Ingeniously, chromosome ends present in the mixture could act as primers for the DNA nanocircles, resulting in elongation of telomeres. The authors propose that the nanocircles might offer a means of reversing the shortening of telomeres of cells in primary cultures, which occurs after multiple cell divisions and is linked to cell senescence. As telomerase, the natural enzyme for elongating telomeres, not only increases the likelihood of a primary cell becoming cancerous but also is difficult to reconstitute in pure form, DNA nanocircles may provide an alternative. *AB*

Cytokine traps

Immunex's (Seattle, WA) etanercept (Enbrel) is a soluble version of tumor necrosis factor (TNF)-α receptor that achieved $800 million in sales last year for use in the treatment of rheumatoid arthritis. Repeating the approach with other cytokine targets of potential importance in disease pathogenesis has not proven easy, however, because many cytokines mediate activity through multicomponent, rather than single-component, receptor systems. In this month's *Nature Medicine* (**9**, 47–52; 2003), researchers at Regeneron Pharmaceuticals (Tarrytown, NY) report a generally applicable method for creating high-affinity blockers of cytokines called "cytokine traps" using two formats. In the first, extracellular domains of two different cytokine receptor components are fused to the Fc portion of human IgG; in the second, the same domains are arranged in-line (one on top of the other) and fused to IgG as before. The latter format is much more efficiently expressed in Chinese hamster ovary cells and constitutes the most potent blocker of interleukin (IL)-4 and IL-1 action so far reported, indicating that this could lead to new therapies. *AM*

Research News Briefs written by Kathy Aschheim, Aaron Bouchie, and Andrew Marshall.

Soil microbe sequenced

The genome of *Pseudomonas putida*, a soil bacterium commonly used in bioremediation efforts, has been deciphered and analyzed by an international collaboration of scientists at The Institute for Genomic Research (Rockville, MD; TIGR) and at four research centers in Germany. The genome was published in the December issue of *Environmental Microbiology* (**4**; 2002). Despite technical difficulties in downloading papers from the journal, a preliminary look at the *P. putida* genome reveals a single circular chromosome with nearly 6.2 million DNA base pairs. A homology search analysis by associate investigator Karen Nelson of TIGR and Vitor Martins Dos Santos from the German Research Center for Biotechnology (Braunschweig) found previously unidentified metabolic pathways in *P. putida* KT2440 that allow the organism to transform aromatic compounds, including phenylalkanoates, ferulate, vanillate, and coniferyl and coumaryl alcohols, aldehydes, and acids. TIGR's Ian Paulsen, who studied the correlation of metabolic pathways with membrane transport capability, also notes that *P. putida* has "lots of novel pathways and transport capabilities to break down aromatic and other unusual compounds." *AM*

Plant resurrection

A recent study in the *Proceedings of the National Academy of Sciences* (**99,** 15898–15903; 2002) by Wu and colleagues borrows a clever design from nature to engineer rice plants with higher tolerance to drought, cold, and salt. The approach is inspired by so-called "resurrection plants," a loosely defined group of flowering plants with a remarkable ability to withstand drought. "Drought-stressed resurrection plants look like they are dead and gone forever, then they pop back to life when moisture is available," says first author Ajay Garg. This death-defying talent is due to the presence of high amounts of trehalose, a sugar that stabilizes proteins and cellular structures in the face of desiccation. Previous attempts to produce transgenic plants constitutively expressing trehalose synthetic genes were unsuccessful because the transgenes led to faulty metabolism and stunted plant growth under normal conditions. By placing two *Escherichia coli* trehalose synthetic genes under the control of tissue-specific or stress-inducible promoters, the researchers created transgenic plants with higher resistance to abiotic stresses. *KA*

Bacterial sugar change

Mammalian cell culture is currently the gold standard for the production of biopharmaceuticals because of its capacity to add post-translational modifications to proteins. Now, researchers in Switzerland and the UK report a way of engineering *Escherichia coli* to carry out oligosaccharide modifications similar to mammalian cells, providing a system that is not only applicable to mammalian protein expression, but also robust and relatively low in cost. Exploiting knowledge that the bacterium *Campylobacter jejuni* encodes the pglB protein with high sequence homology to a protein essential in the process of *N*-linked glycosylation (the most frequent eukaryotic protein modification), they introduced pglB into *E. coli,* producing a mutant that is able to glycosylate proteins in a way similar to eukaryotic cells (*Science*, **298**, 1790, 2002). They also reconstituted more of the *C. jejuni* glycosylation machinery (*pglB* and AcrA) into *E. coli*, demonstrating expression of a glycosylated form of AcrA protein. At present, the protein-linked oligosaccharide structure in *E. coli* differs significantly from the eukaryotic modifications; however, it might be possible in the future to generate *E. coli* strains that attach the specific desired glycan to proteins. *AB*