Expression map reaches new heights

Genome-wide expression profiles in most organisms, including humans, show patterns of expression that, in addition to being determined by bits of information embedded in the sequence *per se*, also correlate in intriguing ways with physical characteristics of the genome such as base composition and gene density. Using a sequence-based version of the human transcriptome, a genome-wide template of all genes for which the existence of transcripts has been confirmed, van Kampen and colleagues have determined a high-resolution 'expression map' of over 25,000 genes. Integrated, chromosome-wide analysis of a library of 120 expression libraries derived from a variety of tissues and physiological conditions established the existence of 30 domains containing highly expressed genes. These 'ridges' happen to coincide with previously identified integration hot spots for viral DNA and could thus be of potential use for the design of better targeted and thus more efficient gene therapies. In addition, such a precise expression map could also prove invaluable as a tool for the identification of genes whose expression is tied to their chromosomal context in diseases such as certain forms of cancer. (*Genome Res.* **13**, 1998–2004, 2003) *GTO*

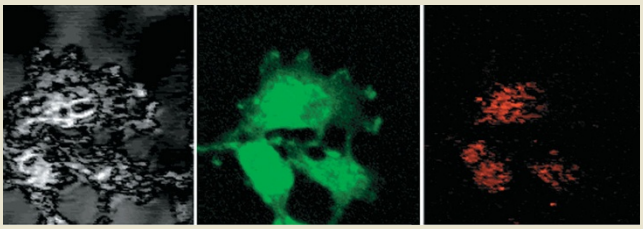
The importance of being connected

Using evolutionary conservation as a metric, recent work by Wuchty *et al.* suggests that structural motifs (topologically distinct interaction patterns occurring in cellular networks) reflect important biological functions. The group studied 678 *Saccharomyces cerevisiae* proteins with homologs in five species and found that proteins participating in interaction networks were more highly conserved than noninteracting proteins and that the larger the degree of connectivity within the network, the greater the degree of conservation. Proteins engaged in some 5-node networks were conserved at a rate several 1,000-fold higher than five proteins chosen at random, whereas those in interacting pairs, showed only a 3-fold difference. Wuchty *et al.* also analyzed the distribution of 11 structural motifs in different functional classes of proteins and found that some classes had many motifs (*e.g.*, transcription uses all 11 motifs) whereas others had few or none. This represents the first attempt to tie structure, function and network topology together and shows that interacting motifs tend to occur together in genomes, extending the idea of evolutionary conservation to topological features. (*Nat. Genet.* **35**, 176–179, 2003) *LD*

AAV-5 target revealed

Researchers have identified platelet-derived growth factor receptor (PDGFR-α) as a receptor for adeno-associated virus type 5 (AAV-5), an important step in optimizing targeting of AAV-5 gene therapies. AAV shows promise as a gene therapy vector because it is naturally defective for replication and is considered nonpathogenic. It can infect both dividing and nondividing cells, transfer genes to a variety of different cell types and mediate long-term gene expression. Although most preclinical studies and early clinical trials have employed AAV-2, AAV-5 can more efficiently infect cells in the central nervous system, eye, muscle and lung, and elicits a lower level of neutralizing antibodies in seropositive individuals. To identify proteins involved in AAV-5 transduction, Chiorini and coworkers correlated gene expression profiles in AAV-5 permissive and nonpermissive cells using cDNA microarrays. They observed a significant correlation between the pattern of AAV-5 transduction and the level of PDGFR-α expression. Treatment with an inhibitor of PDGFR-α expression altered virus binding and transduction. Moreover, coprecipitation experiments revealed a direct interaction between AAV-5 and PDGFR-α. (*Nat. Med.* **9**, 1306–1312, 2003) *MS*

PICturing single molecules



Scientists have extended a technique known as photothermal interference contrast (PIC) to cellular samples, imaging individual membrane proteins labeled with gold nanoparticles. Lounis and colleagues transfected Cos7 cells with cDNA encoding a glutamate receptor tagged with myc at the extracellular N terminus. The cells were fixed and stained with anti-myc-Alexa568 antibodies and anti-IgG secondary antibodies conjugated to 10-nm gold particles, and labeled receptors were imaged at the single-molecule level. Existing optical methods for visualizing metal particles have so far been limited to much larger particles. PIC imaging of metal nanoparticles has several advantages over fluorescence microscopy for single-molecule detection: unlike fluorescent labels, the metal particles are not subject to photobleaching and blinking, and there is no background autofluorescence. The high sensitivity of the method suggests that it will be useful for detecting low-abundance proteins. (*Proc. Natl. Acad. Sci. USA* **100**, 11350–11355, 2003) *KA*

Bacterial RNA buildup

Metabolic instability of mRNA provides organisms with a way to respond quickly to changes in their environment, and much research has centered on understanding the degradosome, the mRNA-protein complex involved in mRNA turnover. Now, Georgiou and coworkers report a novel mechanism for regulating RNA levels in *Escherichia coli* that provides insight into the process and might provide an avenue for antibiotic design. Georgiou and his team were looking to enhance bacterial production of disulfide bond–containing proteins (*e.g.*, human tissue plasminogen activator), which require elevated levels of bacterial disulfide isomerases (DsbC). They discovered a protein called regulator of ribonuclease activity A, RraA, that inhibits RNAse E. Overexpression of RraA leads to the accumulation of RNAse E–targeted transcripts, such as DsbC. This protein, RraA uses a previously unknown mechanism to inhibit RNAse that is not substrate dependent. In addition, overexpressing RraA alters transcription globally, leading to an increase in the abundance of over 2,000 transcripts, and ultimately killing bacteria. The authors believe that this activity, which occurs widely in nature, might one day lead to new approaches to antibiotic design. (*Cell* **114**, 623–634, 2003) *LD*

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