An occasional column, in which Caveman and other troglodytes involved in cell science emerge to share their views on various aspects of life-science research. Messages for Caveman and other contributors can be left at **caveman@biologists.com**. Any correspondence may be published in forthcoming issues.

"I'll have a genome with chips, please"

A new era of science has dawned. The completion of DNA sequences of whole genomes of plants, large and small eukaryotes, bacteria and viruses is providing an unprecedented amount of information on the genes that define complex organisms. Together with this veritable tsunami of data come new words (genomics, proteomics, data mining), new types of biologists (bio-informaticians), and the appearance of (biotech) companys that specialize in the development of software to analyze and display genomic information. Perhaps the most measurable change that access to this vast quantity of genomic information is having on the average scientist is the potential to identify genes, and I mean all genes, in a given metabolic, developmental or oncogenic pathway - we are able to examine gene expression on a genome-wide level. The As Ts, Gs and Cs will be presented to us on a computer screen in an easy-to-read format; complex characterization and cross-matching of references are just a few keyboard strokes away. The equipment budget for most labs will provide faster and more powerful computers to store, access and manipulate this information.

What are the potential consequences of having all the genes laid out for us like a book both for the way that we do science and for how others think that we should do science? With proteomics and consensus-sequence alignments, we may be able to identify protein functions (coiled-coil domains for protein-protein interactions, kinase domains, sites for phosphorylation, etc.) and, possibly, a representation of the encoded protein's three-dimensional structure (based on similarities to proteins with the same domain organization). No more fussing around with genetic tests; out with the suppressor screens; gone are probing complex pathways of tissue development; thank goodness we won't have to consider how to purifying protein complexes; two-hybrid analysis begone.

But, as everything is laid out like a book, what need is there for an old-fashioned, bench-trained scientist who develops hypotheses (remember the old catch-phrase, "No Hypothesis, No Science!") and performs 'wet' experiments (purify proteins, run gels, localize mRNA and proteins in tissues and cells). Where is the hypothesis if one scans a genome for a family of proteins and then systematically ablates the function of each of them (knockouts, RNAi) in an organism and hopes for an effect?

Previous Sticky Wickets can be viewed at: www.biologists.com/JCS/caveman/index.html

Genome-wide analyses are also available in a ‘carry-out’ format - the seemingly ubiquitous CHIP. Here, the genome is laid out in a matrix and can be ‘read’ with an automatic analyzer (for a princely sum of money). All you need to do is supply the manipulation (heat shock, a drug, serum) and mRNA, and, ‘hey presto’, presented to you in glorious greens and reds are the ranges of changes in gene expression (up, down, no change) for all the genes in that organism. (This is a minor point, but who chose the colors? With our heightened sense of equal rights for all, what about those who are color-blind? Who is looking after their interests in this emerging area?) But, I digress. These experiments are very easy to perform, assuming that you have access to the CHIPs, a reader and have the money to buy everything ($60,000, or EU25 billion, for a full set of human CHIPs, and that’s before all of the genes have been identified! However, I assume that market forces and competition will increase availability and drive down the prices.) Easy experiments are very attractive to many scientists. I worry that trainees (graduate students and postdocs) will be drawn to these approaches, where again the only skills required are the ability to hit a cell over the head (or add a drug), isolate mRNA (thank goodness for the ubiquitous kit) and then read information off a computer screen. This requires years of training? It will absorb some of the brightest minds?

I worry that the sequencing of genomes and the availability of CHIPs have been proffered, by the Genome Politburo, as an end to hypothesis-driven science. The new era will apparently free us from the shackles of thinking, imagination and interpretation. Are we to become automotomes, reading off the results of another experiment from a CHIP analyzer? This seems to be a job for computers or, perhaps, computerized scientists.

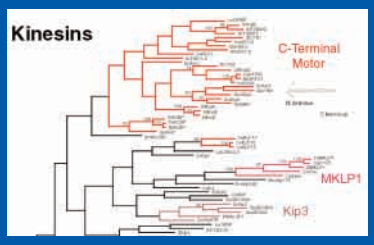
So, am I a Ludite, because I worry about the genome and CHIP revolution? No, I think that the information obtained from the analysis of genomes will be immensely important and lead to new insights into the very complex regulation of genes in a wide variety of experimental and biological conditions. However, I am also an old-fashioned, stick-in-the-mud, wet-bench scientist who enjoys conjuring up hypotheses, designing experiments to test them and interpreting results? I plan to continue to think like this and to train my students to think like this. Personally, I think that, when the dust clears from the genomic blitzkrieg, there will be an even greater need for scientists who can untangle protein networks, define how protein-protein interactions are formed and regulated, and determine protein functions. No doubt someone will write about the new terminology that has arisen to describe this new science - cell biology, physiology, biochemistry and biophysics. I only hope that scientists will who know how to do this be left?

Caveman

Cell Science at a Glance

Our new section – Cell Science at a Glance – is included as a poster in the paper copy of the journal and available in several downloadable formats in the online version, which we encourage readers to download and use as slides. Future contributions to this section will include signalling pathways, phylogenetic trees, multiprotein complexes, useful reagents . . . and much more.

A Myosin Tree (October)



A Kinesin Tree (November)

The Nuclear Pore (December)

We would like to encourage readers to submit ideas for future contributions to this section. Potential Cell Science at a Glance articles should be addressed to the Staff Editor and sent to Journal of Cell Science, 140 Cowley Rd, Cambridge, UK CB4 0DL