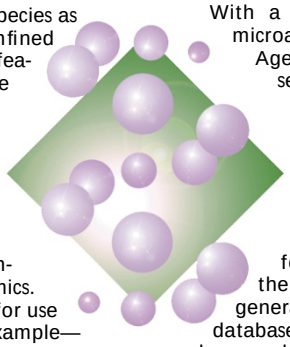
TOUCHING**base**

A virtual ark

The notion of preserving the DNA of endangered species as a hedge against their extinction has long been confined to the realm of science fiction. Whereas it is still not feasible to use such a strategy as a means to conserve entire species, a new collaboration between the Zoological Society of San Diego and Molecular Dynamics (a division of Amersham Pharmacia Biotech) offers a practical step in this direction. The organizations plan to analyse mitochondrial reference sequences from the Zoological Society's 'Frozen Zoo™', a collection of over 3,200 cell lines from 355 species, using the high-throughput sequencing facility of Molecular Dynamics. Results will be made freely available to researchers for use in a variety of studies—phylogenetic studies, for example—and applications such as determining the best breeding pairs for conservation efforts. According to Michel Milinkovitch, of the Free University of Brussels, the initiative is somewhat limited but still a good start. "We want to know [the sequence information] quickly…for many of these species, there may not be much more time." But Milinkovitch cautions that utility may be limited by the characterization of mitochondrial sequences from small numbers of individuals within a particular species. "If there are only 20 animals left, there isn't much genetic diversity to conserve. But for a sound management program with thousands of individuals, it could be quite useful."

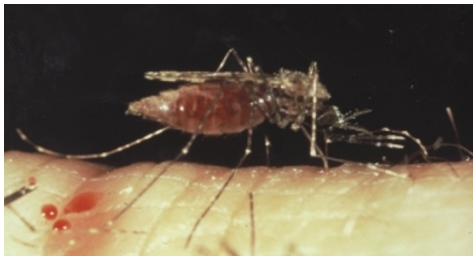


Microarraying the mini-mouse

With a view to enabling comparison between spotted microarray data, researchers at the National Institute of Ageing have distributed a mouse cDNA clone set representing over 15,000 genes to ten academic centres in Canada, the United States, Europe and Japan (see http://lgsun.grc.nia.nih.gov/ for details). These centres will redistribute the clone set to at least eight other groups—on a 'first come, first serve' basis for a nominal sum that covers the cost of materials, handling and shipping (roughly US $200–4,000; some centres may charge for shipping only). Constraints on usage are minimal: the clones are distributed on the condition that data generated through their use be deposited in a public database and that the array nomenclature of individual clones and their order within the set be kept intact. The cDNAs, isolated and characterized by Minoru Ko (of the NIA), are derived from microdissected pre-implantation and peri-implantation embryos. 'Pre-implantation' cDNAs, which comprise approximately half of the set, are derived from unfertilized and fertilized ova, embryos of the 2-, 4-, 8- and 16-cell stage, and blastocysts. Those from peri-implantation tissues are derived from embryos of 7.5 gestational days and tissues excised from the embryonic genital ridge and mesonephros of females of 12.5 gestational days. cDNAs from newborn ovary are also included Approximately 80% are reckoned to be new cDNAs (that is, genes that are not yet named) and approximately two-thirds are not available from commercial sources. Ko and colleagues are presently working on an expanded set of 30,000 cDNAs which they hope to complete in the autumn.

The mosquito as…anti-malarial agent?

Malaria remains among the most devastating infectious diseases worldwide, killing nearly one million people each year. Only recently have genomics efforts been directed at combating the disease, and these have focused largely on mapping and sequencing the genome of the causal agent, *Plasmodium falciparum*, in an attempt to understand the biology of the organism and design therapeutic approaches to prevent infection of mammalian cells. But *P. falciparum* has a complex two-stage life cycle, only one part of which is spent in the mammalian host—the other takes place in the salivary glands of the mosquito *Anopheles gambiae*—and disruption of either part of the cycle could conceivably block transmission of the disease. The mosquito's own immune system is capable of substantially reducing the level of *P. falciparum* infection even in 'susceptible' strains, and the parasite is completely destroyed in resistant ones. These findings have fuelled the hope that knowledge of the mosquito's defence against infection may lead to an effective strategy to reduce transmission to humans. George Dimopoulos (of the European Molecular Biology Laboratory) and colleagues now report the findings of a pilot study to characterize gene expression in the mosquito immune system (*Proc. Natl Acad. Sci. USA* **97**, 6619–6624; 2000). Using a 'responsive' *Anopheles* cell line, they have characterized more than 3,000 ESTs representing possibly 2,300 individual genes—more than four times the number previously known. From this pool, 38 clones have significant homology with factors implicated in immune responses, and 19 could be induced by bacterial challenge—indicating potential involvement in the response against the parasite.



Robert Gwadz, NIH

The basis of complexity

Some would have it that the biological complexity of multicellular eukaryotes is due to an evolution of genetic pathways and the way in which they interact—which may (or may not) be proportional to gene number. Others posit that a greater flexibility in modulating protein expression or splice variants is the main source of complexity. Supporting the case of those in the 'splicing' camp is a paper published by Dietmar Schmucker and colleagues in a recent issue of *Cell* (vol. **101**, 671–684; 2000), which announces a gene whose potential for alternative splicing is little short of mindblowing. The gene encodes a *Drosophila melanogaster* homologue of the Down syndrome cell adhesion molecule (*Dscam*), which maps to a region of chromosome 21 implicated in neurological phenotypes of the eponymous disorder. *Dscam* is an immunoglobulin-like molecule; as such, one expects a degree of alternative splicing. On analysing the genomic sequence, Schmucker *et al.* discovered that the spliceosome is faced with a wealth of choice when it comes to exons 4, 6 and 9, for which there are 4, 48 and 33 alternatives, respectively. The authors went on to sample 50 cDNAs; of these, 49 were unique, their individuality defined by different combinations of alternative exons. If each exon that slots into any one position is capable of independent splicing with respect to all exons variably spliced into other slots, *Dscam* could generate over 38,000 variants. For those in the 'gene-number' camp, however, there is also good news! According to the in-flight magazine of Iberia Airlines, PE Celera Genomics has sequenced the 460,000 chromosomes that make up the human genome. And we thought 150,000 *genes* was pushing it…

> ***Ah romance. Particles smaller than pollen binding receptors. And when they flow both ways …***
>
> *—Joni Mitchell, Madison Square Garden, March, 2000*