general-purpose distributed computing grid across the Internet. The project, called FightAIDS@Home (http://www.fightaidsathome.org), runs the AutoDock software to perform flexible dockings of candidate inhibitors against wild type and mutant HIV proteases. This massively distributed computing approach is facilitating large-scale, coevolutionary drug design at the atomic level of detail. At the time of writing, the system had reached ~2 teraBytes of RAM and ~23 teraBytes of disk space.

Functionality from fuzziness

Jacquelyn Fetrow presented a proprietary technology of GeneFormatics, Inc. (San Diego, CA, USA) that was capable of predicting the functionality of a protein structure. A 'fingerprint' is built up for proteins of known function, using sets of distances between key residues in the active site, giving a so-called 'fuzzy functional form' (FFF). New proteins with unknown function but known structure are then compared with all the known FFFs to find any possible matches. The great advantage of this approach over more traditional sequence alignment-based methods is that the FFF accounts for 3D information. Fetrow presented results in which the method identified a previously unknown redox regulatory site on a serine–threonine phosphatase.

The meeting presented a lively array of investigators who are tackling the problems of novel therapeutics discovery from many different angles. It demonstrated that computers are more relevant than ever to structure-based lead discovery, virtual screening and drug design, and will be a key part of the drug design cycle for a long time to come.

Garrett M. Morris
The Scripps Research Institute, Dept Molecular Biology, MB-5, 10550 N. Torrey Pines Road, La Jolla, CA 92037-1000, USA.
e-mail: garrett@scripps.edu

Is too much risk assessment risky?

James K.M. Brown

The Environmental Implications of Genetically Modified Plants with Fungal Disease Resistance Conference was held at Roskilde, Denmark, 9–11 November 2000, and was organized by Rikke Bagger Jørgensen, Hanne Østergård and Lisa Munk.

It is often claimed that more effective, durable and environmentally friendly control of fungal diseases will be one of the main benefits of the genetic manipulation of crops. The genetic modification of commercially useful plant varieties to render them resistant to fungi has, however, been slower to appear than resistance to herbicides or insects. Perhaps for this reason, comparatively little consideration has been given to risks that might be associated with fungal resistance in genetically modified (GM) plants. This recent meeting was an early step towards addressing this issue.

Do fungi matter?

A significant public concern about GM crops is their impact on the natural environment. In scientific terms, this concerns both population genetics and ecology. First, there is concern about whether resistance transgenes or resistant genotypes will spread into natural populations of the crop species or its wild relatives. Second, there is the issue of whether GM plants will replace wild species in the natural flora. Understanding the highly complex interactions between plants, pathogens, pests, predators and symbionts in natural ecosystems is a challenging scientific problem but participants at the conference had widely divergent opinions about the implications of these interactions for risk assessment. Broadly speaking, one view was that ecological complexity must be thoroughly understood for risks to be managed, whereas another view was that the very complexity of these interactions is so great that populations are likely to be buffered against the relatively minor, additional disturbance imposed by transgenes, over and above the enormous effects of agriculture itself. Current regulations require intensive study of both actual and potential risks, and so tend to support the first point of view.

The perceived hazards of fungal resistance include, damage to mycorrhizae and other beneficial microorganisms, increased persistence and spread of volunteer plants, and gene flow from crops to related wild plants (Jeremy Sweet, NIAB, Cambridge, UK). A key issue is how to define appropriate regulations, given that complex interactions in population biology are poorly understood.

What regulates populations?

Research by Bitty Roy (Federal Institute of Technology, Zürich, Switzerland) relates to the spread of both transgenic varieties and transgenes themselves. Several companies wish to engineer apomixis (i.e. production of asexual seeds) into crops to fix desirable, heterotic genotypes, and Roy is investigating the dispersal of apomictic genotypes of wild *Arabis* species. The Red Queen hypothesis suggests that asexual populations should be more heavily diseased than sexual populations[1] but, at least in the short term, apomictic populations might suffer lower levels of disease. The potential risks, therefore, are either that natural ecosystems might be invaded by apomictic, disease-resistant crops or that apomixis transgenes will spread into wild relatives of crops[2]. However, if it is thought that disease resistance might substantially increase the risk of undesirable spread of genes involved with apomixis, one must ask why modern, disease-resistant cultivars of selfing crops, such as wheat and barley, have not become major weeds. Clearly, having a genotype fixed for good disease resistance is not sufficient in itself to cause a plant to become a pest.

Part of the answer to this conundrum might lie in the extent to which pathogenic microorganisms regulate

http://tibtech.trends.com 0167-7799/01/$ – see front matter PII: S0167-7799(00)01570-5