what begot what among the five basic groups of organisms—eubacteria, euryarchaeotes, crenarchaeotes (or eocytes), eukaryotes, and viruses. "Figuring out a way to deal with such controversies gave us a nightmare," says David Maddison, "so we decided that wherever such debates exist, we'd include alternative views." And so the root page holds two competing trees, and will also hold defenses of each version, one authored by University of California (UC), Los Angeles, molecular biologist James Lake and the other by an as-yet-unidentified rival—a public debate that Lake welcomes. "It's absolutely crucial," he says, adding that the TOL "is a wonderful forum for airing this type of important question."

By November 1994, the brothers had planted their prototype on an Arizona computer, and 13 months later announced it as officially germinated.* And while it has shot up since then, the tree is far from being fully leafed out. "There are some gaping holes," says David Maddison. "For instance, mammals have not yet made their appearance," although their pages are being developed.

A user climbing the tree for the first time gets some basic information about the tree and directions for navigating among its branches and leaves. From here, browsers have several choices: They can view sample pages, take express routes to specific organisms, or go to the root page.

From the root, tree-climbers can head into any one of the five major divisions by clicking on its name. For instance, touching "Eukaryotes" takes you to the tree showing the major taxa of protists, plants, fungi, and animals. Browsers can jump from here to the branch for vertebrates, and then with another click leap to one of the tree's more complete pages, that of terrestrial vertebrates. Here, Michel Laurin, a paleontologist at UC Berkeley, discusses his view of this group's origins, along with some alternate phylogenies. Touching the names of particular genera takes users into the tree's twigs; and these, in turn, lead to the individual species, or leaves. The tree even has "lichen"—explanatory pages that grow on a branch or tree. Thus, on David Maddison's page about the beetle *Bembidion litorale* and its relatives, browsers can call up photos of all the species and an explanation of their key identifying marks.

Other researchers quickly recognized the tree's merits, particularly the instant access it provides to the most recent phylogenies. "In my field—the evolution of fungi—year-old phylogenetic data aren't any good, and that's usually what you've got in journals," says John Taylor, a mycologist at Berkeley and a TOL author. He notes that his area is particularly hot since mycologists discovered that nucleic acid sequences are far better at resolving issues of relationships than is morphology, and "this is the best and fastest way to publish this data."

Louisiana State's Blackwell, another tree contributor, adds that "I study insect-dispersed fungi where there is a lot of convergent evolution. It's very important to be able to look somewhere and see that the agents of Dutch elm disease and oak wilt are not related, although they were once thought to be." That kind of knowledge, she adds, has practical as well as theoretical implications: "If you're trying to develop a fungicide for these species, you want to know their evolutionary history." Knowing that two species look alike but don't share a lot of genes makes a great difference when developing such a product, she explains.

For still other researchers, the TOL has allowed them to celebrate the little corner of life that they study—and share it in ways previously unimaginable. "I work on a group of poorly known beetles, the Ptiliidae," says W. Eugene Hall, an entomologist at the University of Arizona, Tucson. Only three other researchers in the world work on these beetles—although Hall suspects more would if they knew how "fascinating" they are. And, in fact, his ptiliid page on the TOL, which is jammed with tidbits about odd variants of traits within one species and the males' giant sperm, has sparked a lot of interest. "I've had requests from all kinds of people," he says, including a scientist in South Africa who needed help identifying a ptiliid he had found in a cave.

This near-instantaneous collegial feedback is a big plus for many TOL users and authors. "The greatest advantage is its rapid publication of ongoing and recent research that's up to date," says Berkeley's Laurin, who notes that shortly after posting his pages he received comments from colleagues in Australia and England that helped him refine his ideas.

The Maddisons, in fact, hope that in time their tree will become an electronic peer-reviewed journal. "Some of the data on catfish and jumping spiders appear here for the first time, so it already is primary literature in that sense," says David Maddison. They plan to enlist a board of editors from among their contributors to work out mechanisms for review. Recognizing that contributors would like to have their pages cited, they are also investigating how this can best be done. Currently, pages that do not bear the "under construction" symbol can be cited, but they have not yet dealt with the tree's dynamic nature and how to archive older versions of phylogenies or discussions about them.

But that is all part of TOL's future growth, and it does have a lot of growing to do. "How many millions of organisms are there?" asks David Maddison. "We can't even say we've scratched the surface."

–Virginia Morell

* http://phylogeny.arizona.edu/tree/phylogeny.html

GERMAN GENOME PROGRAM

The Right Mix of Form and Function

HEIDELBERG—Last summer, Germany's science minister, Jürgen Rüttgers, made an announcement that many of the country's researchers thought they would never hear: The government would launch a national genome research program, he said, with $130 million by 1999 and more to come later. Convincing the government to take this step took 10 years of lobbying by a few persistent scientists, in a country famous for its fierce public opposition to genetic engineering (*Science*, 16 June 1995, p. 1556). One year and many hard discussions later, with the first projects chosen, the outlines of the enterprise are emerging—although the debate on how to divide up the funds may not be over.

Rüttgers's announcement posed a tough question: How should Germany enter a fast-moving field in which it lags far behind? One camp, which includes some international advisers to the German project, argued that Germany should shoulder its share of high-cost mapping and sequencing efforts already being pursued by other countries. Others, however, felt that Germany had already missed this boat and should instead concentrate on ways to get at the functions of the human genes being uncovered by research and sequencing efforts.

Now, after months of tough deliberations, the program appears to be steering a middle course. The first round of grant proposals was reviewed by the international advisory committee in early March, and the science ministry is now finalizing decisions based on these reviews. Ministry officials say that funds will be split roughly evenly between sequencing, functional studies, and infrastructure development. Although a complete list of projects has not yet been released, committee chair Ernst-Ludwig Winnacker of the University of Munich's Gene Center has provided *Science* with an overview.

The ministry's evenhandedness is unlikely to end the debate over the direction of the program, however. So far they have committed only $50 million, just over one third of the promised total for the first phase, leaving plenty of room for controversy to flare up again. And, although many researchers still have an incomplete picture of the whole program, preliminary reactions are mixed. Some who spoke with *Science* worry that $16 million spread over many functional projects—some potentially very large—

will spread resources too thinly. Herbert Jäckle of the Max Planck Institute for Biophysical Chemistry in Göttingen, for example, says he is happy with his award to search for new genes on the fruit fly X chromosome, but thinks that money should be more focused on a few areas where Germany could make a real impact, "rather than funding many projects where each contributes a little bit to things going on elsewhere." Grantee Rudi Balling of the Center for Environment and Health near Munich is more optimistic, though: "It's a first step. ... Once we [show some results], our hunt for funds will get easier."

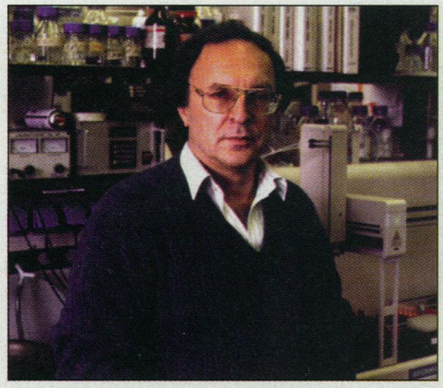
According to Winnacker, a major focus of the functional studies will be large-scale searches for disease genes. The program will, for example, support the building of Germany's first "microsatellite" center, which exploits short repeat sequences present all over the genome to map both simple and complex disease genes (*Science*, 8 March, p. 1352). A joint venture of Jens Reich and Thomas Wienker of the Max Delbrück Center in Berlin and Andre Rech at Humboldt University, the center will take on projects from clinics all around Germany. There is already a waiting list of good proposals, says Reich.

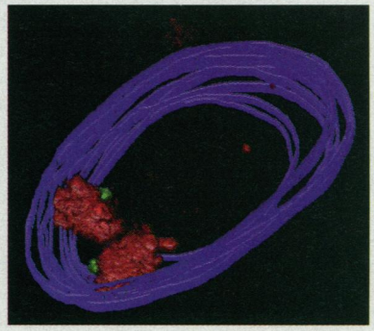
The project will also support an 11-group consortium, based in Munich and coordinated by Balling and Eckhard Wolf at the Gene Center, that will develop strains of mutant mice with specific clinical defects—such as abnormal levels of certain metabolites in the blood—which could help unravel the basis of related human diseases. In a later phase, the consortium hopes to make mutants for studying complex disorders like allergies and hearing impairment.

Another model system that got modest support is the zebrafish, a newcomer to national genome programs. Several years ago, Christiane Nüsslein-Volhard's lab at the Max Planck Institute for Developmental Biology in Tübingen isolated hundreds of fish carrying mutations in genes essential for normal development—a potential gold mine of models for human disease and gene function (*Science*, 13 May 1994, p. 904). So far, only a few of these genes have been identified, but Pascal Haffter's group at the same institute has been awarded a genome grant to begin mapping the rest—a first step toward cloning them—although the lack of a dense genetic map in the zebrafish will make this tough going, he says. Neighbors Alexander Crawford and Camila Esguerra will also tackle zebrafish gene function. In collaboration with Hans Lehrach at the Max Planck Institute for Molecular Genetics in Berlin, they will start the huge task of creating a "gene expression atlas" for zebrafish. The idea, says Crawford, is to work out "what genes are expressed in which tissues and cell types ... at different time points during development"—information that could yield vital clues to their roles.

And Svante Pääbo's lab at the University of Munich will look at a real zoo of creatures. By comparing sequences of selected regions in humans to those in species ranging from great apes to platypus and kangaroo, his group hopes to learn more about the evolution of the mammalian genome and possibly the functions of its noncoding regions, he says.

These and other projects will be supported by infrastructure grants, including $13 million awarded last summer for two "resource centers," one run by Lehrach and a smaller unit headed by Annemarie Poustka at Heidelberg's German Cancer Research Center. These centers will help construct and distribute biological materials, such as DNA libraries, and will rely heavily on robotic technologies developed by Lehrach's group to analyze hundreds of thousands of DNA samples in parallel.





Ready to roll. Wilhelm Ansorge's new sequencing machines will be key to Germany's effort to sequence cDNA from chromosomes 21 and X (*right*, in red)

Details of the sequencing portion of Germany's program will not be finalized until year's end. But the ministry has already allocated about $13 million for genomic sequencing, to include portions of chromosomes 21 and X, plus a few other selected regions agreed upon with sequencing labs abroad. And an additional $3.3 million will be spent on sequencing some cDNAs from these regions.

Still to be decided is who will do this work. According to ministry officials, proposals from two consortia requesting $1 per base were considered too expensive, and the groups have been asked to revise their proposals to aim for a total price of 33 cents per base, averaged over 3 years. Germany's smaller operations will have a tough time achieving this price, say several of their scientists, which leaves the main candidates for genomic sequencing the Institute for Molecular Biotechnology in Jena headed by Andre Rosenthal and another run by Helmut Blöcker at the National Research Center for Biotechnology in Braunschweig.

Other savings should come from the new sequencing machines developed by Wilhelm Ansorge's team at the European Molecular Biology Laboratory in Heidelberg, which is slated for a big role in the cDNA sequencing effort. Ansorge's team developed the ALF sequencing machine in the late 1980s, models of which are still being sold by Pharmacia. Their latest in-house version can sequence far longer pieces and handle more samples than other commercially available systems, according to Ansorge.

With the program now taking shape, the next important step is getting pharmaceutical and biotechnology companies to help support it. Minister Rüttgers set industrial participation as a key goal, both to bring in additional funds and to lend credibility to his efforts to strengthen biotechnology in Germany. But so far, getting companies to sign on has been "very difficult," says advisory committee chair Winnacker. Sticking points, according to one industry insider, include industry's reticence to invest in a new German effort rather than in established ventures abroad. There is also the familiar problem of industry wanting access to the data before it is generally released—while academic researchers want the fastest possible release. But he adds that there has been "great progress" on many of these issues, with industry especially interested in the resource centers. Final agreement could come soon, he says—depending on which projects are chosen in this first round.

Once these projects get going, the ministry will begin planning the next round of applications—which could be equally tough. One hard decision will be whether to continue supporting many functional projects or to focus funds on the most promising few. And pressure to invest more heavily in sequencing could grow as other national genome projects move into an all-out assault on the human sequence. Says Wolfgang Frühwald, president of Germany's main research grant agency: "It went well in the first round, but there are signs that this conflict will arise again." Considering the fight to get the program started, however, it's a nice problem for Germany to have.

–Patricia Kahn