as many as half the megaYAC clones on the 21 map either fall short of their reported length, contain misplaced STS markers, or have deletions of unknown length. "If you look at the distribution of every clone versus the STSs, they were wrong on many, many points," he says. "I hope this isn't the case with every other chromosome."

Gingrich places most of the blame for the problems in the chromosome 21 map on hurried mapping techniques that didn't compensate for known deficiencies in the megaYAC technology. But, adds Evans, "it's obvious from what they published on 21 that there are some really unanticipated problems. It represents a very low resolution map with a lot of mistakes." As a result, he says, "you've got to do it all again and correct all the errors."

That's not the same as starting from scratch, of course. "It's somewhat easier [the second time] because you're basing it on some [known] structure," says Mary Kay McCormick of the Los Alamos National Laboratory's human genome center. But that doesn't mean it will be easy, either. "There was a lot of grumbling at the Santa Fe meeting by people who had tried to construct maps using [megaYACs] as a starting point," she says. "They're not going to be able to construct the physical maps that they had hoped."

This sort of criticism infuriates Cohen. He points out that the *Nature* paper is full of caveats and discussion of problems with the megaYAC libraries and his team's mapping technique. And he has no time for what he describes as after-the-fact nit-picking. "There is no map today that does not need to be refined," he says. "Of course, with this one, the more you study it, the more errors you will find." But that, he says, is the way of science: breakthroughs, followed by refinements.

The search for solutions

No one is suggesting that YACs do not have their place in the genome project. Instead, the problems have forced researchers to find ways to improve the technology. Evans' group, among others, is developing YACs from a hybrid pool of human and nonhuman DNA. That may reduce chimerism, because the yeast is less likely to splice together genetic material of unrelated species. Lander's group is creating special recombination-deficient strains of yeast that may cause fewer deletions. "I'm convinced that by the end of the year, we'll have a good host strain that will solve most of the problems with YACs," says Caltech's Mel Simon. But it is late in the game to be fixing the basic tools, he points out.

The sobering of the enthusiasm for YACs has also spurred a search for YAC alternatives (see sidebar on page 1686). As Collins puts it, the emerging deficiencies of YACs "say that we have not yet discovered the perfect vector for building whole genome maps." But he also emphasizes that the years spent assembling the maps to date were not wasted. "Next year, when some terrific new vector comes along that doesn't have problems with deletions and chimeras, we'll be ready" for high-resolution mapping and sequencing. Just because some 5% of the genome is YAC-unfriendly, he says, "I don't think we should hold off [mapping] the 95%" of the genome that YACs can handle. And the University of Washington's Maynard Olson, who invented YACs in 1987, says he is "more impressed with the megaYACs than with the grumbling about them."

"As the megaYACs trickle down," warns Lander, "there may be people who don't know what they're getting into." Yet just as megaYACs weren't the Second Coming, neither are they the genome Apocalypse. "My view is that this is still a new technology with lots of promise," says David Botstein, chairman of genetics at Stanford. "Like all new technologies, it's going to have drawbacks." If you know what they can and can't do, he says, you won't get burned. Perhaps the best lesson from the megaYAC's troubled U.S. introduction is the oldest: Caveat emptor.

–Christopher Anderson

SPACE PROGRAM

NASA Puts the Squeeze on the Station

Space Station Freedom is beginning its latest painful metamorphosis—by some counts, the third in less than a decade. Under orders from the Clinton Administration to come up with a drastically scaled-back plan by 1 June, National Aeronautics and Space Administration (NASA) planners have begun putting agency administrator Daniel Goldin's "smaller, faster, cheaper" slogan to its toughest test yet. How they will go about it is still far from clear, but last week a few outlines of their plan began to emerge.

Administration officials will not reveal how drastic a cut they are seeking in the cost of the station, but Goldin announced at a meeting of the American Astronautical Society in Crystal City on 10 March that the revised plan may halve the station's current $30 billion development cost and $100 billion, 30-year operating cost. To do so, says space station deputy director Marty Kress, the "redesign team," headed by NASA assistant deputy administrator and Massachusetts Institute of Technology aeronautics professor Joseph Shea, may retreat from the original goal of a full-time manned station to a partially manned, or "man-tended" project. Additional savings might come, said Goldin, from a reduction in the station's planned lifespan from 30 years to 10 or 15 years.

The retrenching should make it possible to build the station with only half of the 17 to 20 shuttle flights planned earlier, Goldin told the Astronautical Society. He also noted that NASA planners are considering the use of other types of rockets to assemble the station, rather than relying only on the shuttle. All of which should make the station cheaper—and also quicker to build, Goldin noted, helping NASA keep promises made before the redesign to get it off the ground by 1997.

So far, he and other NASA officials aren't talking about what sacrifices, if any, the scaled-back station will entail. In a publicly circulated letter to NASA officials Goldin stated, vaguely, that the redesigned station will still "satisfy high-priority research goals in materials and life sciences." But those priorities are still being sorted out, judging by the contradictions in NASA statements last week. In the letter, Goldin said one of the goals of the redesign is to "support long-duration research (but not necessarily permanently manned)." But at a press conference he stressed that NASA is still aiming toward a permanently manned station. "I believe we will have a permanent human presence," he said.

One reason for the ambiguity may be the pressure to keep the project fully manned that is coming from a variety of sources: collaborators in Japan, Europe, and Canada, and members of Congress whose districts are benefiting from space station contracts. Another reason for sticking to the earlier goal is to protect the $8.5 billion NASA has already poured into the current station plans. Contractors and NASA centers have already designed the station's power system, notes NASA's Kress. How much of that work will survive the redesign is not clear, he adds. "That becomes the issue for all of us."

The new slimmed-down design will stand or fall on an even more basic issue, however: Is it still too big for Congress to swallow?

–Faye Flam

NASA

Last year's model. The space station that was.