el will first meet on 6 September. Afterward, "we will take as long as it is necessary to come up with the appropriate recommendations," says Sabloff. Over the next several months, he expects the group to evaluate reorganization plans proposed by Small, Smithsonian scientists, and perhaps even commission members.

Smithsonian paleontologist Brian Huber, a spokesperson for the Senate of Scientists at the beleaguered National Museum of Natural History, is not happy about the wait: "It's going to be a slow process, and we're going to be in limbo for some time." Even so, he says, the delay will be worth it if the panel "will move us in a direction we want to go."

–ELIZABETH PENNISI

GENOMICS

Animals Line Up To Be Sequenced

CHEVY CHASE, MARYLAND—The mouse was a shoe-in. After all, what other organism could better illuminate the human genome? The rat has undisputed standing as a lab staple, and the zebrafish brings a clear vision of development. But, with work on the human genome winding up in 2003, deciphering these other three will only keep the 2000-base-per-second worldwide sequencing capacity busy for so long. So it's high time to add other creatures to the pipeline, sequencers agree. With 1.7 million known species to choose from, however—and almost as many specialists lobbying for their favorites—selecting the next few will not be easy.

The stakes are enormous, researchers agreed at a workshop* here last week designed to set criteria for choosing the next candidates for the sequencing machines. If an organism is picked, its research community is guaranteed to be vibrant and well-funded long into the future. As mammalian geneticist Steven O'Brien of the National Cancer Institute put it, "Species that don't get selected will go away, and species that do get selected will prevail."

At the invitation-only workshop, sponsored by the National Human Genome Research Institute (NHGRI), four dozen researchers touted the research value of sequences from organisms as varied as swine, cats, and sea urchins. Partisans of microorganisms known as protists commandeered the slide projector to woo the crowd with a diagram showing that microorganisms constitute all but a tiny fraction of living things. Primates clearly dominated the discussion—and in this venue, at least, macaques had a home court advantage, as no chimpanzee experts were present.

Meanwhile, meeting organizers urged the group to put horse-trading aside and instead settle on criteria for deciding what to sequence next. With co-chairs David Botstein and Robert Horvitz cracking the whip, the group agreed on two sets. One they called general considerations, such as the ease of obtaining sequence and the factors that will make the sequence useful. These included small genome size, existing technical knowledge, suitability for experiments, and an active and eager research community.

The other was scientific merit—essentially, what questions a particular organism would enable researchers to explore. This was a bit more tricky, because efforts to understand human diseases or probe evolutionary relationships would demand different organisms, the group agreed. To study the evolution of traits, for example, scientists would want to sample groups in each of the major branches of life—say, a mollusk, an earthworm, and a starfish. But to develop new model systems for human neurobiology, a species closely related to humans would be more useful. Still other organisms would help researchers interpret sequence data from humans and model organisms. Although the assembled scientists outlined about 10 questions, they wisely did not attempt to rank them.

The next step in this already-contentious

Contenders. The primate community is arguing over which to sequence first: the macaque *(left)* or the chimp.

CREDITS: (LEFT TO RIGHT) RICHARD T. NOWITZ/PHOTO RESEARCHERS; RENEE LYNN/PHOTO RESEARCHERS

* NHGRI Workshop on Developing Guidelines for Choosing New Genomic Sequencing Targets, 9–10 July.

ScienceScope

Malaria Vaccine Deal An international consortium will spend $1 million to develop a vaccine against India's major cause of malaria. A U.S.-based nonprofit, an Indian research center, and an Indian biotech company this week announced that they will team up to develop a vaccine against the mosquito-borne parasite *Plasmodium vivax*, which causes nearly 65% of India's malaria cases. *P. vivax* is also widespread in other parts of the world, although it is less lethal than *P. falciparum*, the other major malaria parasite.

Under the agreement, the U.S.-based Malaria Vaccine Initiative at the Program for Appropriate Technology in Health will funnel research funds to the International Center for Genetic Engineering and Biotechnology (ICGEB) in New Delhi. Once researchers fine-tune the vaccine, test lots will be manufactured by Bharat Biotech in Hyderabad.

Prior to the deal, "we had no clear way to move this vaccine candidate from the lab to manufacturing and clinical testing," says Virander Chauhan, director of the ICGEB and head of its Malaria Research Group. Human trials are planned for late 2003.

Conflicted at EPA The Environmental Protection Agency (EPA) plans to overhaul how it seeks outside scientific advice in response to a harsh review this week by the General Accounting Office (GAO), Congress's investigative arm. The GAO report, requested by Representative Henry Waxman (D–CA), finds "limitations" in the EPA Science Advisory Board's (SAB's) procedures for reviewing conflicts of interest that "do not adequately ensure independence and balance." The lapses include not requesting sufficient information from panel members, lax record-keeping, and limited public disclosure. SAB staffers apparently failed to notice, for example, that a panelist reviewing an EPA report on whether 1,3-butadiene is a carcinogen had worked on a legal case for a manufacturer, and that others had done industry-funded research on the chemical.

SAB staff director Don Barnes says the report is "useful" rather than "damning" and insists that no panel has been biased by conflicts of interest. But he says the 100-member board is planning to adopt new procedures similar to those followed by the National Academy of Sciences. For example, Barnes's office will now invite the public to suggest panelists and comment on a proposed slate of candidates.

Contributors: Gretchen Vogel, Jeffrey Mervis, Pallava Bagla, Jocelyn Kaiser

process, said NHGRI chief Francis Collins, is to turn these preliminary ideas into formal recommendations. The co-chairs are expected to issue a report in the next few months. Collins recommended that over the next few years, NHGRI solicit white papers, hold additional conferences, and support pilot projects to explore the scientific and political questions underlying the choice. Ultimately, said Collins, the institute will issue a call for investigator-initiated proposals, and the decision will be left to the peer-review process. From the looks of things last week, there will be no shortage of applications.

–JOSH GEWOLB

MICROBIOLOGY

S. pneumoniae Genome Falls to Sequencers

At the height of his power, Genghis Khan and his armies swept from the steppes of Mongolia, capturing two-thirds of the known world. But for sheer ferocity, Khan's forces pale next to those of a tiny microbe called *Streptococcus pneumoniae*. These pathogenic bacteria readily move from the throat to invade the lungs, blood, or brain—every year killing millions of children and elderly people worldwide with pneumonia, bloodstream infections, or meningitis. Now, researchers have uncovered clues to just what makes the organism so savage.

On page 498, a team led by Claire Fraser and Hervé Tettelin of The Institute for Genomic Research (TIGR) in Rockville, Maryland, reports the exact order of the 2.16 million bases that make up the genetic code of a virulent *S. pneumoniae* strain. By examining the sequence and comparing it with those of other strains, the team found that the microbe is particularly well equipped to invade the body's tissues. It also seems adept at shuffling its genes—an ability that may help it evade the immune system. This "thrilling view" of the *S. pneumoniae* genome offers "a [new] glimpse into the lifestyle of the organism," says microbiologist Alexander Tomasz of Rockefeller University in New York City.

It should also provide new targets for better drugs to treat *S. pneumoniae* infections and vaccines to prevent them, both of which are badly needed. The microbe's resistance to penicillin and related antibiotics has skyrocketed worldwide in the last decade, and none of the vaccines on the market can ward off all the dangerous strains.

The TIGR team began the sequencing project in 1996, but progress was slowed by a series of technical problems and a split with the institute's original sponsor, Human Genome Sciences of Rockville, Maryland, that caused a temporary funding drought. Although TIGR made most of the raw sequence data available in 1997, the team took several more years to finish the sequencing and characterize the genes, a process called annotation.

Meanwhile, several companies, including Glaxo Wellcome and SmithKline Beecham (now merged to form GlaxoSmithKline) and Eli Lilly & Co., sequenced most of the genomes of three other *S. pneumoniae* strains. GlaxoSmithKline's Damien McDevitt predicts that "there are at least 10 genomes out there from different companies." So far, however, only two have been made public.

A team led by Jose García-Bustos of GlaxoSmithKline's molecular microbiology division in Tres Cantos, Spain, published the annotated but incomplete genome of a virulent, antibiotic-resistant *S. pneumoniae* strain in the June issue of *Microbial Drug Resistance*. After publishing an incomplete draft of the genome of a widely studied, nonvirulent laboratory strain in 1998, an Eli Lilly team says a more complete version is in press at the *Journal of Bacteriology*.

Comparing multiple genomes is key for stopping *S. pneumoniae*, because 92 different strains infect humans—and researchers would like to protect against all of them. The TIGR team has taken a step in that direction by comparing its strain with both a nonvirulent laboratory strain and a second virulent one. This revealed that about 10% of the genes in the virulent TIGR strain are missing in the other two, pointing to several genes that may be important for infection. (In the June issue of *FEMS Microbiology Letters*, microbiologists Gianni Pozzi and Marco Oggionni of the University of Siena Medical School in Italy, who also used TIGR data, reported similar results.)

Among the potentially important genes are a group that encodes a variety of unusual cell-surface enzymes that the microbe uses to break down the carbohydrates that help hold biological membranes together, thus weakening barriers to invasion and freeing sugars for the bug to eat. Indeed, *S. pneumoniae* appears to have sworn off many amino acids in favor of sugars. If similar carbohydrate-degrading enzymes are found in all the pathogenic strains, they might be good drug targets or vaccine candidates.

But another finding suggests that *S. pneumoniae* may be more capable than most bacteria of undergoing the genetic changes needed to elude such protective agents. Several of the microbe's genes appear to be foreign—possibly acquired from other bacteria. In addition, 5% of the *S. pneumoniae* genome is made up of small genetic elements that can hop to new locations in the chromosome—compared to 3% or less in more typical bacteria. "That's an incredible number," Tomasz says.

In another departure from the norm, almost all of these so-called insertion sequences had hopped between genes rather than into them. Together, the results suggest an "extraordinary capability to take DNA, move it around, shuffle it, and do it without making any mistakes," says infectious-disease specialist Elaine Tuomanen of St. Jude Children's Research Hospital in Memphis, Tennessee.

Despite the bug's craftiness, experts are optimistic that the genome data will help uncover how the microbe activates key genes as it invades the deep tissues of the body. "It will be like having a frozen picture that all of a sudden starts moving," Tomasz says.

–DAN FERBER

Fearsome invader. Squads of sugar-digesting enzymes may help *Streptococcus pneumoniae* bacteria, such as these, eat their way through human tissue.

CREDITS (TOP TO BOTTOM): BARRY GRAY/SPARTANBURG REGION HEALTH CARE SYSTEM, SOUTH CAROLINA; OLIVER MECKES/PHOTO RESEARCHERS