the CDMS team says, all appear to be due to neutrons. If so, chances are that the DAMA team is seeing familiar particles, too. Stanford physicist Blas Cabrera says, "With respect to the DAMA results, we're ruling out the signal that they've seen."

Whether or not the DAMA result holds up, Turner says, the search for dark matter may be speeding toward an end. In recent years, researchers have determined that other once-prime suspects, such as neutrinos and brown dwarfs, cannot account for all the missing mass. But WIMPs might, and new experiments scheduled for the next few years will be capable of spotting particles as massive and as weakly interacting as theory says they ought to be. "It's a 70-year detective story," Turner says. "An arrest is imminent."

–ADRIAN CHO

GLOBAL HEALTH

Group Urges Action on Third World Drugs

How can the pharmaceutical industry be enticed to make drugs and vaccines for infectious diseases that sicken or kill billions of people worldwide, yet offer little in the way of economic returns? That conundrum occupied a group of senior policy officials last week at the Global Health Forum, a closed-door meeting hosted by the Institute for Global Health in San Francisco. The 3-day affair, which boasted an "all-star cast" of global health experts, came up with few new ideas, but its message is being heard loud and clear: President Clinton has already signaled his interest in launching an initiative aimed at narrowing the seemingly intractable gap in health between rich and poor countries, and last week a bill was introduced into the U.S. Senate that would incorporate many of the forum's suggestions.

Shot in the arm. Industry needs incentives to develop drugs and vaccines.

CREDITS: (LEFT) WHO; (RIGHT) PAYETTE ASSOCIATES/VENTURI, SCOTT BROWN

Pharmaceutical companies already have the scientific knowledge and tools they need to develop drugs and vaccines for scourges such as malaria, AIDS, and tuberculosis. What's more, such drugs could save millions of lives and spur economic development in poor countries, said the panel, which included representatives from the White House, the U.S. Congress, the World Health Organization, the World Bank, the World Trade Organization, and pharmaceutical giants Glaxo Wellcome and Merck. Yet these diseases attract minimal attention from the pharmaceutical industry because executives don't see a market. And even when effective drugs are available—such as the cocktail of AIDS drugs that has slashed mortality in wealthy countries—they may be too expensive for countries in Africa and Asia.

The solution, according to the panel, lies in a package of incentives that would make it worthwhile for the pharma and biotech industries to step in. One approach is for governments and multilateral organizations to push research and development by subsidizing part of the huge costs, either directly or through tax breaks. Another is to assure companies of a future market—for instance, by establishing "purchase funds" and agreeing to buy certain quantities of a product once it becomes available. The panel also lauded partnerships in which publicly funded scientists work together with industry, such as the recently created Global Alliance for Vaccines and Immunization (GAVI), to speed drug discovery and development.

The Global Health Forum's approach has already found a receptive ear in Washington. In his State of the Union address, President Clinton announced a $50 million U.S. contribution to GAVI, as well as a tax credit of up to $1 billion for companies investing in new vaccines for malaria, AIDS, and TB. A delegation from the Global Health Forum was scheduled to meet with Clinton this week to present their findings and discuss Clinton's proposals, which are "absolutely on the right track," says Richard Feachem, who directs the Institute for Global Health.

Meanwhile, Senator John Kerry (D–MA) introduced an ambitious bill, dubbed the Vaccines for the New Millennium Act, on 24 February. Kerry proposed to "change the death spiral" by making childhood immunization "a major goal of U.S. foreign policy." His bill calls for donations of $150 million to GAVI and $30 million to the International AIDS Vaccine Initiative. It also proposes several tax credits for industry and a purchase fund to buy and distribute vaccines as soon as they are approved. To cover the cost, Kerry is asking Congress to set aside $100 million a year for the next 10 years. The political fate of these plans is uncertain. Even so, Feachem is encouraged by these and other initiatives in the European Union and Japan. Says Feachem, "The global awareness of this challenge is running at a level which we haven't previously seen."

–MARTIN ENSERINK

RESEARCH FACILITIES

Glittering Future for Yale Medical School

The late Bartlett Giamatti, former president of Yale, was fond of saying that "if Yale intends to be the best, it has to be able to afford the best." Its current leaders seem to be taking that aphorism to heart: A month after announcing a planned $500 million upgrade of its science and engineering programs (*Science*, 28 January, p. 579), Yale said last week that it will pour another $500 million into renovations and new construction on its medical school campus over the next 10 years.

Thinking big. Yale's planned six-story lab building (right) is attached to new classroom building.

"The university is in a strong financial position," Yale president Richard C. Levin acknowledges. A 9-year bull market has beefed up Yale's endowment, now $7.2 billion, he says, and "fund-raising efforts have been very well received." He predicts that "invest[ing] simultaneously in science activities on both ends of our campus will be enormously synergistic."

The heart of the expansion is a new six-floor lab building that will increase the medical school's lab space by 25%. Some accompanying growth is also expected in research faculty. Yale is already the fifth-largest recipient of funds from the National Institutes of Health. The medical school will continue to turn out about 100 graduates a year.

"I'm a happy man today hearing this announcement," says Leon Rosenberg, a professor of molecular biology at Princeton University who was Yale medical school

dean for 7 years. "I think it reaffirms the university's goal of maintaining Yale medical school as among the very most research-intensive national institutions."

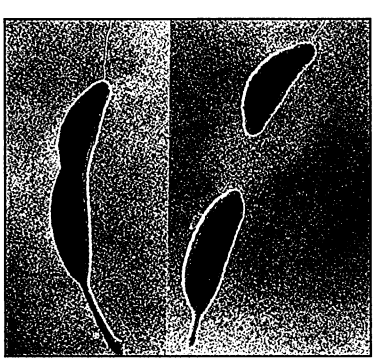
The investment comes at a time when many university medical centers are suffering from rising costs and reduced clinical income, says the Association of American Medical Colleges. But Rosenberg says that because Yale has been so successful in winning research grants, it hasn't needed to rely heavily on clinical income.

–CONSTANCE HOLDEN

MICROBIAL GENOMICS

Culling Genes Early Yields Rich Harvest

CHANTILLY, VIRGINIA—A team of human sequencers using high-powered computers has just finished assembling the entire genetic sequence of the common bacterium *Caulobacter crescentus*. The feat, announced at a meeting* on microbial genomes held here last month, marked another important milestone in the burgeoning business of gene sequencing. But the real news was that even before the sequence was completed, another team had scoured the emerging data and found several hundred new genes involved in the bacterium's cell cycle.



Preview of coming attractions. Microbial genomes are yielding their secrets even before they are complete: *B. anthracis (above), N. meningitidis (right),* and *C. crescentus,* stalked and mobile stages *(below).*

That accomplishment underscored an important take-home message from the meeting: Sequence data don't have to be perfect, or even finished, to be extremely useful. Indeed, another team reported that it has used early sequence data to identify targets for a vaccine against a pathogen that causes meningitis. And researchers studying the microbe that causes anthrax said they will soon start analyzing gene expression even though these genes are still buried in tiny pieces of unconnected sequence data. "It's amazing how fast [the genome data have] been put to use," raves microbial genomicist Siv Andersson of the University of Uppsala, Sweden. "People should be looking at genomes long before they are done," adds Janine Maddock, a microbiologist at the University of Michigan, Ann Arbor.

Take the case of *C. crescentus*, a bacterium that thrives in aquatic environments that lack sufficient nutrients for most other lifeforms. This makes the bug a potential candidate for cleaning up pollution. But microbiologists are fond of it for another reason as well: Because it goes through distinct morphological stages, it is useful for understanding differentiation in prokaryotic organisms (those without a cell nucleus).

Typically, *C. crescentus* has a whiplike appendage called a flagellum that it uses for swimming. But when it's time to reproduce, *C. crescentus* jettisons its flagellum, replacing it with a short stalk that anchors the tiny cell to a nearby surface. The DNA then replicates and the stalked cell divides asymmetrically, pinching off a new, mobile "swarmer" cell. These characteristic "stalked" and "swarmer" stages enable microbiologists to associate genetic changes with distinct stages of the cell cycle.

The Institute for Genomic Research (TIGR) in Rockville, Maryland, has been sequencing the organism's 4-million-base genome, which is about the same size as that of *Escherichia coli*. At the meeting, William Nierman reported that TIGR had just finished putting the pieces of the sequenced genome together. But a team at Stanford University headed by Lucy Shapiro, in cooperation with TIGR, began working with these data about 9 months ago, long before they were assembled—in fact, they were still in 700 separate pieces.

The group scanned the early sequence with gene-finding programs, culling about 3000 tentative genes, team member Michael Laub reported at the meeting. They spotted DNA from each gene onto a glass slide and used this microarray to monitor the RNA transcribed from each gene at 15-minute intervals over *C. crescentus*'s life cycle.

Their initial results indicate that the organism alters the activity of 462 genes—some 400 of which are newly recognized to change—over the course of the cell cycle, says Laub. "They found genes they never would have thought of looking for," notes Andersson. Laub and his colleagues expected to see changes in the expression of the genes that make the flagellum, for instance. But they can't explain why 107 genes related to energy use and metabolism are altered as well. Laub speculates that metabolic requirements change depending on where the organism is in its life cycle. "The array data are leading us in new directions," he notes.

Other microbiologists at the meeting were impressed not just with the Stanford team's data but that they were able to garner them at all with a microarray. Microarrays are still tricky to use, and bacterial RNA is much harder to work with than, say, yeast or human. "This is the first successful microbial cell cycle experiment that's ever been done," says Maddock. Moreover, it demonstrates that microbial RNA can readily be put to use in these global expression studies, adds Frank Rosensweig, an evolutionary biologist at the University of Florida, Gainesville. "I regard this as a real breakthrough paper."

Microarrays aren't the only way to make use of preliminary sequence. For the past 2 years, TIGR researchers have been working with E. Richard Moxon, a microbiologist at the University of Oxford, to sequence a strain of *Neisseria meningitidis*. Early in the sequencing process, Moxon and TIGR's partner, Chiron Corp. of Siena, Italy, began analyzing those DNA fragments to look for proteins that might be new vaccine candidates. Rino Rappuoli and his team at Chiron used computer programs to identify DNA sequences likely to code for proteins found on the surface of the bacterium. The researchers then inserted these genes into bacteria, isolated the proteins produced, and injected the proteins into mice that were later exposed to the pathogen. Rappuoli reported at the meeting that, of some 600 proteins the computer identified, 350 were successfully produced in bacteria, and 25 of those induced a protective immune response in the mice—some strong enough to warrant further investigation.

Other global expression studies will start soon on the anthrax genome. Even though the entire sequence may not be complete un-

CREDITS: J. MADDOCK/UNIVERSITY OF MICHIGAN

* The Fourth Annual Conference on Microbial Genomes, 12 to 15 February.