tion rates, except for higher rates of miscarriage, but the risk for the cloned fetus is another matter. In cattle cloning, approximately one out of seven newborns has potentially fatal complications, such as metabolic disorders and abnormal lung development. What's more, cautions Bishop, the long-term consequences of cloning are still not well understood. Safety aside, Anne McLaren, a developmental biologist at the Wellcome/CRC Institute in Cambridge, U.K., doesn't think human reproductive cloning is ready for prime time. Such techniques are "a step too far in assisted reproduction," she says.

One practical barrier might be obtaining enough human oocytes for the transfer procedure, in which an adult cell nucleus is either injected into or fused with an oocyte from which the nucleus has been removed. Even in the most efficient animal cloning labs, fewer than 5% of nuclear transfer attempts result in live births.

Stay tuned, says Zavos, who intends to announce more details on the project at a meeting in March in Rome. **–GRETCHEN VOGEL**

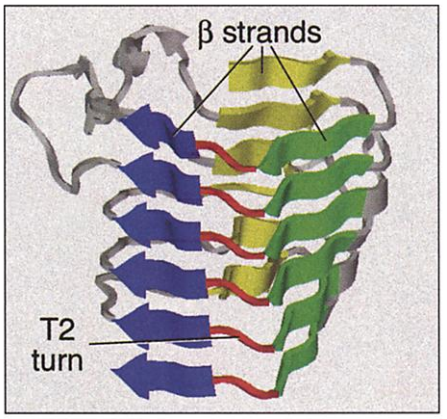
PROTEIN FOLDING

Virtual Molecules Nail Bacteria's Weapon

To understand how proteins work, biologists need to know what shapes they naturally fold into. The straightforward ways of finding out, x-ray crystallography and nuclear magnetic resonance, take as long as a year to reveal a protein's three-dimensional structure. Increasingly reliable mathematical models, however, can now predict parts of the structure much faster. In the latest computer-assisted coup, mathematicians and biologists at the Massachusetts Institute of Technology (MIT) have developed a program that predicts in milliseconds whether a protein folds into a structure called a β helix. To their surprise, they found that a protein with a β helix is like a child with a can of spray paint: It's almost surely up to no good.

"This program found a very interesting subset of proteins—whooping cough virulence factors, *Helicobacter pylori* toxins, ragweed pollen allergens, and so on," says Jonathan King, a biologist on the team who specializes in protein folding. King speculates that the β helix, a long spike, is used for attaching to or penetrating cell membranes. The work is "a tremendous accomplishment," says Peter Kim, a protein biologist who recently moved from MIT to direct Merck Research Laboratories in Rahway, New Jersey. "The bottom line is that a computer scientist has drawn attention to a class of proteins involved in human disease, which are potentially of medical significance."

The first known β helix was reported in 1993 by Frances Jurnak, an x-ray crystallographer who now works at the University of California, Irvine. It turned up in a bacterial protein called pectate lyase, which breaks down the pectin in plants' cell walls. Since then, a handful of other proteins with β helices have been found. One of them is pertactin, made by *Bordetella pertussis*, the bacterium that causes whooping cough. Because it elicits a strong immune response, pertactin has been incorporated into a new vaccine against that disease. But with only 12 known examples out of 12,000 solved proteins in the Protein Data Bank, β helices remained "low on the totem pole for structural biologists," King says.



Do the twist. Parallel β strands wrap up into a β helix.

The MIT group saw things differently. To them, the orderly structure of β helices made them ideal candidates for computational prediction. A β helix is made up of "rungs," consisting of three β strands (flat, uncoiled pieces of protein that stack into sheets with a water-loving side and a water-repelling side). A typical helix contains from 7 to 16 triangular rungs, which twist around gradually to the right. β sheets in general are hard to predict from an amino acid sequence, because residues that are widely separated in the protein's sequence may lie in adjacent rungs. Residues that lie in adjacent β strands usually match, but the residues on the "turns" between strands need not match at all. Because the turns have unpredictable lengths, it is hard for biologists to know where to look for the matching pairs. Fortunately, in the β helix each rung contains an easily recognized landmark: a very short turn, usually only two amino acid residues long, called the T2 turn.

Bonnie Berger, Lenore Cohen, and Phil Bradley in the MIT mathematics department incorporated this information into a computer program called BetaWrap. The program first identifies a likely T2 turn and assigns a score to the adjacent regions based on the probability that they will form β strands. Then it scans farther down the sequence for strands that have a high probability of stacking well onto the two already found. The program computes this probability by analyzing hundreds of known β sheets in the Protein Data Bank, but *not* the 12 known β helices. Tested to see whether it could pick the known β helix–bearing proteins out of a lineup, BetaWrap scored 12 out of 12—a feat no rival program could match.

Next, Berger turned the program loose on the larger SWISS-PROT database, consisting of proteins with unknown structure. BetaWrap found hundreds of β-helix candidates, some of which scored even higher than the known β helices. When Berger showed the list to King, he was astounded to see that the top 100 candidates were all bacterial proteins—even though Berger's team had no way of telling bacterial proteins apart from mouse or human proteins. "That's when he believed us, because we produced these things that made biological sense," Berger says. Berger announced the results at this month's meeting of the American Mathematical Society in New Orleans.

BetaWrap's predictions still must be checked by crystallography, a process that will probably take at least a year. But some researchers already plan to use the program's results as a springboard for new research. "I'm immediately going to run BetaWrap on viral genome sequences," Jurnak says, to see whether bacteria are indeed the only source of β helices. **–DANA MACKENZIE**

Dana Mackenzie is a writer in Santa Cruz, California.

PHILANTHROPY

Gates Gives Booster Shot to AIDS Vaccines

DAVOS, SWITZERLAND—In a huge boost for efforts to develop an AIDS vaccine, Bill Gates announced at the World Economic Forum here on 27 January that the foundation named after himself and his wife, Melinda, will give $100 million to the International AIDS Vaccine Initiative (IAVI). The 5-year grant—the largest single philanthropic donation ever for AIDS research—helps put the New York City–based nonprofit on track to launch clinical trials of three of its most promising AIDS vaccines by 2007.

Unsolicited grant. Gates announcing $100 million to IAVI.

With $21 billion in assets, the Bill and Melinda Gates Foundation gives away hundreds of millions

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