tions so distort the structure that it doesn't reflect the natural molecule.

Now, a team of structural biologists at Harvard's Massachusetts General Hospital in Boston has overcome those obstacles to bag one of the most important membrane proteins yet. In work published online this week by *Science* (www.sciencexpress.org), Mass General's M. Amin Arnaout and colleagues have determined, for the first time, the crystal structure of one of the many integrin proteins.

These important denizens of the cell membrane control many cellular activities, including proliferation and migration. For example, the integrin studied by the Arnaout group, which is designated $\alpha V\beta 3$, is believed to play a major role in tumor growth, bone maintenance, and inflammation. What's more, some infamous viruses, including the culprits in AIDS and foot-and-mouth disease, use the integrin as a port of entry into the cells they infect.

Now that they have the structure, researchers should get a better picture of just how the integrin engages in those activities, and that insight may spur the design of new drugs to combat diseases. "It's definitely one of those spectacular results that will change a field," says structural biologist Dan Leahy of Johns Hopkins University School of Medicine.

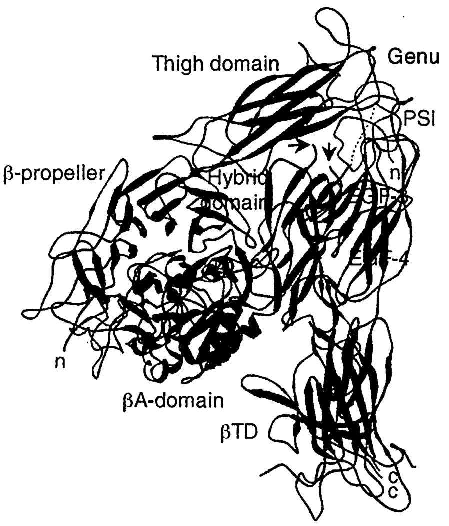
Like all integrins, $\alpha V\beta 3$ includes two distinct protein subunits encoded by two different genes. It's large, containing roughly 2000 amino acids, and flexible—a disadvantage when it comes to producing the highly ordered crystals needed for x-ray crystallography. Indeed, Arnaout had to cajole Jian-Ping Xiong, the paper's first author and a postdoctoral fellow at Mass General at the time, to participate in the project. Xiong feared squandering precious fellowship time on what he viewed as a hopeless task.

Researchers at Merck KGaA in Darmstadt, Germany, provided purified protein for Arnaout's team to crystallize but, says Arnaout, Merck wanted no part in funding a project that seemed so unlikely to bear fruit.

Despite the doubts and frustrations, scientists worldwide have hotly pursued $\alpha V\beta 3$'s structure for years, holding their cards tightly to their chests to avoid alerting the competition to what they were doing. As recently as last February, most scientists attending an integrin conference in Ventura, California, presumed that it would be years before an integrin crystal structure was complete. At the time, Arnaout gave no hint to the contrary.

To make the integrin soluble—a prerequisite to crystallization—scientists at Merck KGaA truncated the tiny segments that anchor it to the cell membrane and allow it to transmit signals into and out of the cell. Once the Merck group provided enough protein, the Arnaout team spent more than 3 years tinkering with conditions before they could produce crystals worthy of study. Their x-ray analysis, conducted at Argonne National Laboratory in Argonne, Illinois, revealed a structure that was partly expected, but it also contained a few bombshells.

The integrin includes 12 distinct regions, or "domains," four in the α protein subunit and eight in the β protein subunit. They are arranged in a molecule with an oval head and two tails.



First look. This ribbon drawing shows the overall structure of the integrin and its various domains.

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Previous work by Arnaout's group and others, including Harvard pathologist Timothy Springer, suggested that some of these domains might exist. Springer's prediction several years ago that part of the protein would be shaped like a propeller has held true. A couple of domains, though, are new.

A hybrid domain combines portions of known structures, and a domain tacked onto the end of one tail is folded in a novel pattern. But perhaps the biggest surprise was the finding that the two tails, which appeared to extend stiffly from the head section in earlier electron micrograph images, are folded sharply in on themselves. The researchers don't yet know whether that bending occurs naturally; it could be an artifact of the preparation or of crystallization procedures.

Most intriguing, though, the shape might help cell biologists understand how the integrin transmits its signals. The Mass General group argues that it has crystallized the protein in its "on" structure, but left unanswered is how that differs from the inactive form and how the protein might pass signals to the cell with which it's connected.

Pharmaceutical companies, meanwhile, are expected to use the $\alpha V\beta 3$ structure to guide the development of new drugs aimed at the protein. Compounds that block the

ScienceScope

More Censure for Hopkins Johns Hopkins University's process for reviewing studies of human subjects is "grossly inadequate," and "it is critical that the culture of the institution change." That stark assessment comes from an outside panel tasked with probing the death of a volunteer in an asthma study last spring.

The conclusions of the five-member panel—led by Samuel Hellman, dean emeritus of the University of Chicago's medical school—are similar to those of an internal review and the federal Office for Human Research Protections, which found problems with informed consent procedures and university oversight (*Science*, 27 July, p. 587). In its 8 August report, the panel also found "possible subtle coercion" of staff to volunteer for studies. But Hellman is "optimistic" that Hopkins can correct course in light of many reforms now under way.

Want to Be a Millionaire? Maybe money can't buy happiness. But the Howard Hughes Medical Institute (HHMI) is hoping that it can buy a better science education for thousands of U.S. undergraduates. The Bethesda, Maryland–based philanthropy last week announced plans to give $1 million over 4 years to each of 20 faculty selected from 84 top research universities.

"It's a grand experiment," says molecular biologist Edward Cox, who runs a Hughes-funded summer research program for undergraduates at Princeton University. Cox says that the challenge for Hughes is "finding people with the right blend of an active research program and high-quality teaching skills." The first grants will be awarded in August 2002.

Cluck, cluck China, the United Kingdom, and other nations say the chicken should be the next vertebrate fed to the genome sequencers. Researchers attending the 10th International Strategy Meeting on Human Genome Sequencing last week in Hangzhou, China, agreed that sequencing the chicken could not only help agriculture, but also "medicine, [as it] helps us to understand humans [and] developmental embryology," said sequencing guru Eric Lander of the Whitehead Institute for Biomedical Research in Cambridge, Massachusetts. The Beijing Genomics Institute may take the lead on the project, but poultry genome planners must still decide on which chicken variety to work on and how to raise the $35 million needed to start. Lander says those decisions could come within 6 months.

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