might carry fewer side effects, Voorhees says. "There's nothing else like it" for getting compounds into cells, he states. In fact, the new transporter group has proven so successful that the Stanford team has created a company called CellGate to commercialize the technology.

The new peptide is far from the first molecule researchers have tried to use as a chemical pass card. Researchers have long known that positively charged, or cationic, peptides and synthetic polymers make decent access keys. But progress toward a universal key has been mixed. Recently, help has come from a surprising source: the AIDS virus. In the early 1980s, researchers discovered that a protein fragment called Tat helps HIV viral proteins enter cells and initiate synthesis of RNA. And researchers at the Massachusetts Institute of Technology and elsewhere went on to show that linking HIV Tat to drugs can boost their uptake as well.

Unfortunately, HIV Tat is so complex and hard to synthesize that it is too expensive for widespread use, Wender notes. So he and his colleagues set out to find a cheaper, more effective alternative. They started by looking carefully at HIV Tat. Like other cell entry tags, HIV Tat is made up of cationic subunits—in this case six arginine amino acids, two lysines, and a glutamine. That structure initially seemed to confirm the conventional wisdom that a tag's positive charge is what gets it inside cells, says Jonathan Rothbard, head of research at CellGate. But when the researchers looked further, that turned out not to be the case. By testing a variety of cationic peptide chains, the Stanford-CellGate team found that peptides composed entirely of arginines were orders of magnitude more effective at infiltrating cells than counterparts made from leucines or glutamines. "So it's not just a cation story," Wender says.

To find out why, Wender's team synthesized short amino acid chains made from ornithine, an amino acid that differs from arginine in just one respect: It harbors a nitrogen in place of an oxygen, a change that does away with arginine's ability to form weak hydrogen bonds with its neighbors. To their surprise, the researchers found that the ornithine chains were virtually useless at shuffling drug cargo into cells, suggesting that arginine's ability to form hydrogen bonds is the key. And as it turns out, that hydrogen-bonding capability is a talent leucines and glutamines don't share.

Just what the peptides bond to and how polyarginine wends its way into cells are still mysteries. But whatever the mechanism turns out to be, it is clearly effective. At the ACS meeting, Wender reported that his team has used polyarginine tags to spirit drugs such as cyclosporin and Taxol into cells, and they are working to extend the method to other compounds. Apparently the new tags and their cargo don't just diffuse across cell membranes, Wender says; rather, it looks as if cells actively pump them inside.

In one sense, in fact, the peptide may be too effective. "It works with every cell type we've looked at," Rothbard says. That could make it difficult to target drugs only to particular cells such as cancerous ones. For that reason, Wender says that he and his colleagues are initially focusing on linking their tag to drugs that can be applied locally, such as topical creams to treat skin diseases. Still, even if that's as far as they get—and that seems doubtful—a new access key for getting drugs into skin cells could make a profound difference for patients suffering from psoriasis and other chronic skin conditions.

–ROBERT F. SERVICE

TV CRITIQUE

Dinosaur Docudrama Blends Fact, Fantasy

Amid the majestic sequoias of what could be a state park in Northern California, the silence is broken by an unearthly, guttural bellow. An enormous beast plods across the television screen. She kicks out a shallow nest and begins to lay her eggs. Each white egg, the size of a soccer ball, slides gently down an ovipositor and comes to rest in the ground. Then, as a velvet-voiced narrator intones about the dangers that await the young hatchlings-to-be, the giant scrapes soil over the clutch and abandons her brood to their fate.

On the move. A herd of 4.5-ton iguanodons kicks up surf in the Cretaceous.

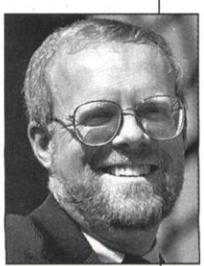
It looks and sounds just like a wildlife documentary—so much so that, if you watch long enough, you almost forget that the animals it shows have been extinct for more than 65 million years. But this is *Walking With Dinosaurs*, a sometimes stunning dino-extravaganza that uses computer animation and detailed puppets to resurrect the creatures

CREDITS: (TOP TO BOTTOM) STANFORD UNIVERSITY; BBC/DISCOVERY CHANNEL

ScienceScope

New Blood Following its history of finding new leadership within, Stanford University this week tapped Provost John L. Hennessy (below) to take over as president beginning 1 September. Hennessy, who succeeds Gerhard Casper, is expected to place the university in a strong position to reel in donations from supporters who have struck it rich in neighboring Silicon Valley.

Hennessy, a professor of electrical engineering and computer science, is also a Silicon Valley entrepreneur; he founded MIPS Technologies, which specializes in microprocessors. He was also instrumental last year in securing a $150 million donation from Netscape founder Jim Clark, who worked down the hall from Hennessy when both were Stanford professors. As president, Hennessy's early priorities are expected to include expanding interdisciplinary research and ensuring affordable housing for faculty and students.



Initial reaction to the pick was glowing. "I'm thrilled," says Richard Zare, a Stanford chemistry professor and former chair of the National Science Board. Hennessy's experience in academia and high-tech, Zare says, made him "the obvious natural choice."

Too Cautious? In what many view as a victory for science, a U.S. court last week slammed the Environmental Protection Agency (EPA) for proposing tighter guidelines for safe drinking water than its scientists thought necessary.

The case is the first test of draft risk guidelines that use molecular data to assess whether low doses of a substance can cause cancer. After reviewing studies suggesting that tiny doses of chloroform—a carcinogenic byproduct of chlorinating water—are harmless, EPA scientists in 1998 proposed increasing the goal for maximum tap-water levels from 0 to 300 parts per billion. But under pressure from environmentalists, the agency nixed the change. The Chlorine Chemistry Council sued, claiming EPA had violated a law that requires it to base decisions on the best science.

On 31 March, a federal judge agreed, finding that EPA "openly overrode" the scientific evidence. Toxicologist Jay Goodman of Michigan State University in East Lansing says the ruling should be "a wake-up call to EPA," which now plans to reevaluate its stance.

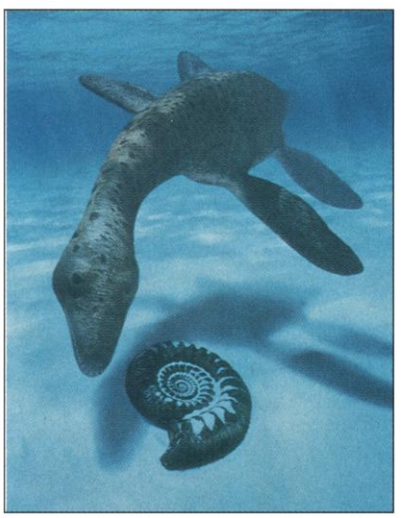
Contributors: Andrew Lawler, Eliot Marshall, Adrian Cho, David Malakoff, Robert F. Service, Jocelyn Kaiser

and place them in real landscapes. When the $10 million program aired in the United Kingdom last fall, 17 million people—almost a third of the population—tuned in to the six weekly installments, making it the BBC's most watched science program ever and one of its top 20 programs of all time. It also stirred up a controversy.

Some researchers were unstinting in their praise: "This is going to stand out as one of the best dinosaur shows ever done and certainly the most novel one," says Tom Holtz, a vertebrate paleontologist at the University of Maryland, College Park, who consulted with the BBC on the project. But others cringed at the way it blurred fact and fiction. Most of the egg-laying sequence, for example, is a screenwriter's fantasy: There is no scientific evidence that the giant dinosaur *Diplodocus* had an ovipositor or abandoned its young. "Some of the arguments were just so far-fetched, so ridiculous," says Norman MacLeod, an invertebrate paleontologist at the Natural History Museum in London. "I was embarrassed for the profession." The British media debated whether docudrama was a suitable way to convey science to the public. Would TV viewers be stimulated, misled, or just confused? On 16 April millions more will get the chance to make up their own minds as the Discovery Channel airs a revised 3-hour version of the show in North and South America.

The idea of making a wildlife program about dinosaurs was the brainchild of BBC producer and former zoologist Tim Haines. "We used natural history grammar, and we had [the dinosaurs] doing the range of things you expect a living animal to do," Haines says. To prepare for the show, the BBC team consulted with more than 100 experts on the Mesozoic era, then combed the globe for exotic landscapes in which to film models and puppets. Triassic scenes were shot in New Caledonia, the Jurassic episode in redwood forests of Northern California, and Cretaceous dramas in Chilean lava fields. Meanwhile, animators and scientists hashed out details of dinosaur physiology and locomotion. For information, such as crest displays and camouflage, that couldn't be gleaned from bones alone, they drew analogies from birds and other living animals. It took 2 years to animate the computer figures, paste them into the landscape footage, and add shadows.

The effect can be breathtaking. In one amazing shot, the camera looks up at a *Diplodocus* walking overhead; the dinosaur's neck takes seconds to pass over, then huge wattles on its fleshy belly fill the screen. Elsewhere, you get a helicopter's-eye view of a herd of sauropods migrating across Utah, watch an ichthyosaur giving birth underwater, and hide in the bushes as *Tyrannosaurus rex* saliva splashes the camera lens. "True, it's fantasy," says Ken Carpenter of the Denver Museum of Natural History, a show consultant. "But in this case I think it's good, because it shows dinosaurs as living, breathing creatures, not as skeletons that stand stiffly in a museum."



Splash. Marine reptiles such as this plesiosaur get serious screen time.

The show has its rough spots. Not all of the animated creatures are equally convincing, and despite the expert assistance, some avoidable errors crept in. The most oftencited blooper is a scene in which *Postosuchus*, an ancestor of the dinosaurs, marks its territory with gushing streams of urine. As living reptiles and birds don't urinate, it's a good bet their ancient cousin *Postosuchus* didn't, either. MacLeod says that one camp of paleontologists "was outraged at the program because of all of the factual errors and artistic license."

Other complaints concerned the seamless way the BBC production blended science and speculation. "I'd like to see a lot more perhapses and maybes in there," says Karen Chin, a postdoc at Stanford University, who advised the show while a visiting scientist at the U.S. Geological Survey. MacLeod takes a harder line. "*Walking With Dinosaurs* is a work of fiction; it's a work of creative fantasy," he says. "It's not a work of science; it's not a documentary."

But Holtz argues that anything in paleontology—other than drawing the bones in the ground—involves some degree of speculation. And in portraying extinct animals on television, Haines says, guesswork is unavoidable. "You're trying all the time to communicate big pictures based on as much evidence as you can muster," he says. "But in the end, if you want an animal to actually just walk across the screen, you've got to start speculating."

Some of the imagination perished in the trans-Atlantic passage. To make room for commercials, the Discovery Channel cut about 20% of the footage, including scenes deemed too gory for Sunday evening viewers. Discovery's producers also rescripted sections that their reviewers considered inaccurate or misleading. In addition, they deliberately ruptured the wildlife-documentary illusion by inserting sound bites from interviews with paleontologists. (For viewers who want more detail, the hourlong program "The Making of *Walking With Dinosaurs*," set to air on 17 April, gives a lighthearted but informative look at the science and special effects behind the program.)

But all these caveats could be superfluous: Haines believes that the suspension of disbelief won't last long and that nagging doubts can motivate viewers to think scientifically. "When they ask 'How do they know that?' they are asking a scientific question," he says. There may be a less epistemological payoff, too. "The great value to scientists is getting people to think of these as animals living in an ecosystem," says Jim Kirkland, state paleontologist for the Utah Geological Survey, who reviewed the script for Discovery. "We need people to see our vision. It's a wonderful way to bring this home to the public."

–ANDREW WATSON AND ERIK STOKSTAD

Andrew Watson writes from Norwich, U.K.

WALKING'S WINNERS AND LOSERS

Pterosaurs. They fly like aces, but it's the ground-walking that really wows. Insulating fuzz on wings is accurate.

Diplodocus. Herds look so heavy you can almost feel the ground shake. First time animated with frill on spine.

Marine reptiles. Cousteau would have loved graceful ichthyosaurs and plesiosaurs. Realistic birth scene.

Cynodonts. Squat mammal ancestors sport convincing fur and behaviors. Bonus points for not calling them "mammal-like reptiles."

Postosuchus. Producers kept scene of the predator urinating—even though its closest relatives all excrete urea, not urine.

Brachiosaurus. Lighter build makes them better than Spielberg's. But they look stiffer than Al Gore.

Late Cretaceous. Too bleak. North American tyrannosaurs inhabited lush swamps and coasts. Cheer up, guys!

Coatimundi. Cameo by this modern American mammal is totally out of place; its ancestors were never in Antarctica or Australia.

CREDIT: BBC/DISCOVERY CHANNEL