



Pharm Animals

By Vadim Liberman

Rick Friedman/WPN

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Take a good look at the person pictured above. Yes, you read that correctly. Granted, it *looks* like a cow. In fact, it *is* a cow. *And* a person. What you see here is actually part human, part bovine. And one day, this creature may save your life.

The biotech industry continues to push the envelope—in this case, genetically engineering animals for medical purposes. At Sioux Falls, S.D.-based Hematech, scientists are cloning cows to develop human antibodies to treat a wide range of diseases and infections. At GTC Biotherapeutics, in Framingham, Mass., researchers are breeding goats with a human gene that allows the animals to produce a human protein to help prevent blood clotting. Meanwhile,

at Burlingame, Calif.-based Origen Therapeutics, experimenters are inserting human DNA into chickens so the birds can lay eggs rich in human anti-cancer proteins.

Every pharmaceutical company is busily searching for breakthrough drugs to ameliorate tomorrow's toughest and most resistant maladies, from the flu to cancer to anthrax exposure. You've seen images of neat rows of petri dishes in sterile labs, with white-gloved scientists peering into microscopes and monitoring scanners. Biotech firms that specialize in transgenic engineering, which involves the combination of genes from different species, are no exception. But their work involves special complications—a polite way of referring to barnyard chores—

soundings

with an especially high set of hurdles to clear.

For starters, the development process is tedious and lengthy. At Hematech, creating human antibodies in cows begins by extracting a skin cell from a cow and placing it into a petri dish, where researchers remove some of the cow's own genes to make room for human DNA. But before mixing the two, scientists inject artificial human DNA into a mouse cell inside a different petri dish. After numerous chromosome modifications, the new DNA is mixed into a chicken cell, which is then mixed into a hamster cell. Only then is the final DNA mixed into the dish containing the cow cell for still more genetic work. "The reason for using all these animal cells is because each has properties enabling you to do specific types of work on the cell that you couldn't simply do in the original human cell," explains James Robl, Hematech's president and chief scientific officer. Thus, what you're *really* seeing in the photo is a mouse/chicken/hamster/cow/human. (But since it looks like a cow, walks like a cow . . . might as well call it a cow.)

With the final DNA now genetically modified to produce human antibodies,

it is artificially inseminated into a surrogate cow. Once the cloned calf is born, it gets immunized with a vaccine that sparks the cow to create human antibodies. Finally, the cow is hooked up to a machine, as pictured on the previous page, which extracts blood plasma, from which scientists remove the antibodies for eventual health benefits.

Using animals to make antibodies is nothing new. Doctors have for years injected humans with a cow's inherent antibodies to act against disease. So why the need to reverse the needle? "Because there's less risk involved," Robl explains. "The problem is that our immune system can recognize that some of the cow's antibody is foreign to us, so our bodies will work to get rid of it quickly—sometimes too quickly for it to have had time to work effectively. And if you try and use the antibody again, the body may even fight against it, which can cause harmful health effects." Human antibodies taken from the cows pose less potential for complications. (If you're wondering why the cow's own body doesn't similarly react negatively to foreign human antibodies, Robl explains that since the cow was born with human genes, its body doesn't consider them to be foreign.)

Trying to convince a squeamish public that Dr. Moreau isn't working to transform animals—and even people—into freakish hybrids presents another obstacle. "There are a lot of people who don't fully understand transgenics," says Tom Newberry, GTC's vice president of corporate communications. "So it makes sense for them to naturally feel apprehensive about what we're doing."

What GTC and other firms are doing, says Newberry, is, arguably, *safer* than traditional medical methods. Robl points to flu shots as an example. The flu vaccine contains a weakened flu virus that induces the body to produce antibodies that will fight the virus should the body again be exposed to it. Injecting people with antibodies from the start, Robl explains, avoids the step of having to infect people with the virus, which is especially hopeful news to the elderly, the very young, and others who respond poorly to vaccines.

Still feel you'd rather take medicine derived from your fellow man rather than a goat? You'd better reconsider, suggests Newberry, who points out that "we know everything—literally *everything*, right down to the genetic makeup—about our goats, which are kept in a tightly controlled and monitored environment." The Red Cross, by contrast, has faced \$21 million in fines since 2003 for the way it collects and processes blood.

Of which there's a limited supply. You can extract only so many proteins and antibodies from the nation's blood banks, whereas each of GTC's sixteen thousand goats can produce as much antithrombin (a human protein used to treat a rare blood disorder) as ninety thousand blood donations. "It makes practical sense to use animals," Newberry says. "Eventually, if we can increase the supply of drugs well beyond what we now get from only human blood, prices for medicine may go down." For example, take hemophiliacs, who require a special protein to stop bleeding. At \$1,000 a milligram, the protein is expensive, so an increase in supply can lower demand. But Newberry also points to the importance of supply

But Have You Ever Run a Pizza Parlor?

By Joseph L. Bower

Several years back, I was talking with the founding CEO of a great computer company. Discussing the talents of his executive group, he said, a little wistfully, "I wish just *one* of them had made money running a pizza parlor."

I know what he meant. These were very talented individuals, of course, but they were all completely absorbed by the process of managing a highly successful company. In their early years, they were wonderful sales managers, marketers, engineers, and financiers. Now they were executives, brilliantly running their function or business—but not building the company. They'd become "suits." The CEO wanted people who knew how to make money the way the owner of a pizza parlor would—making customers happy every day, pizza by pizza.

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for supply's sake. Because there's a very limited amount of the available protein, it is currently used only to *stop* hemorrhaging. By having goats produce the human protein, hemophiliacs could receive it in order to *prevent* bleeding and avoid suffering from pinpoint bleeds that cause joint damage.

Yet despite the potential for human benefits, there's also apprehension about the welfare of the animals used in such experimentation. Groups such as People

for the Ethical Treatment of Animals claim that most of the animals are born with birth defects or euthanized if the correct genes were not successfully transplanted. It's an accusation that Newberry denies, insisting that GTC's experiments do not result in any defective goats—which, he adds, live much as they would naturally. Still, given that Hematech confines many of its cows indoors their entire lives, the issue of animal well-being in the biotech industry

is certainly ripe for further examination and debate.

Meanwhile, science continues to go where no cow or goat has gone before. So far, GTC's ATryn (antithrombin alfa) is the only transgenically produced drug to come on the market, and only in Europe. In the coming years, companies will begin extensive clinical trials, and it may not be too long before our cows and goats don't just give us milk but give us life.

So You Want to Strangle Your Boss ...

By John Hollon

I've had great bosses and terrible bosses, smart bosses and dumb bosses. I've also had bosses who were thoughtful managers, bosses who were purposely forgetful, and bosses who were over-the-top political. There were ones I would run through a wall for, but also ones I would run away from if I saw them walking down the street. One was a model leader, a special guy I learned a lot from, while another was a thuggish bully who had no quantifiable skills except the ability to glower and intimidate. I learned a lot from him too.

But through it all, the good and the bad, the smart and the dumb, the special and the crazy, I've never seriously been tempted to take matters into my own hands and throttle my boss. I've been tempted many times, but never, ever, did I seriously think about strangling any of them—even though I had some pretty good motivation to do so.

That's why I was amused to see someone go over the edge and actually do it, as Houston Astros pitcher Shawn Chacon did when he tried to strangle Astros general manager Ed Wade. I'm not in favor of violence to settle a dispute, but

a *Houston Chronicle* story hit the issue square on the head when it asked, "Did Chacon just live out everybody's favorite fantasy? Do worker bees everywhere secretly dream of whupping up on the boss?"

"People are laughing because it is a common fantasy," family therapist Tim Louis told the *Chronicle*.



"They think, 'Wouldn't it be wonderful to react in rage against an authority figure like a boss?'" . . . Louis said there's nothing wrong with the occasional malevolent

thought. But psychiatric treatment is called for when a person obsesses over a boss, makes a plan for how they might hurt him or fear they might actually do it."

It's unclear what Ed Wade said or did to set off Shawn Chacon, but Chacon was under a lot of stress because he had been pitching poorly, had just been demoted to the bullpen, and probably saw his major-league career slipping away. His attack on Wade, of course, only accelerated the process—he was released by the team after this incident.

But lest you think this is a one-sided situation, Wade is known to have a temper, and he reportedly threw a chair against a wall, shattering it, when he was with the Philadelphia Phillies. There's some thinking that Wade is not blameless in this encounter, given his temper and past behavior.

Here's my take: Violence has no place in the workplace, and no matter what Ed Wade said or did, Shawn Chacon was wrong to take matters into his own hands, so to speak. That's a sure way to lose your job in any universe. Thumping on the bad boss may be a workforce fantasy for many, but like most fantasies, it is one best left unfulfilled.

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