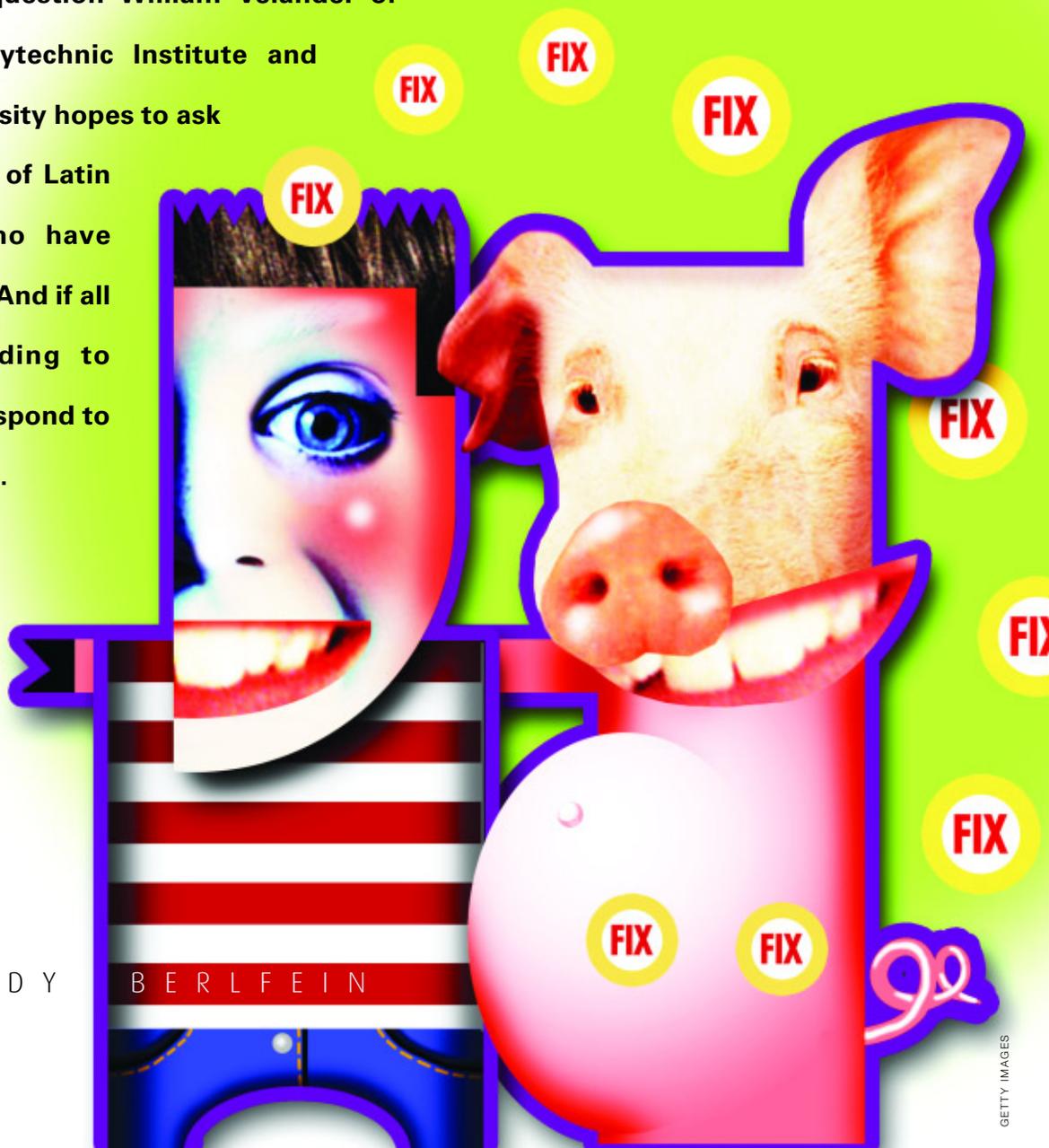


# TRANSGENIC PIGS— A FACTORY FOR FACTOR PRODUCTION

“Do you prefer your factor by intravenous infusion or sipped slowly from a glass of chocolate milk?”

That’s the question William Velander of Virginia Polytechnic Institute and State University hopes to ask the children of Latin America who have hemophilia. And if all goes according to plan, he’ll respond to their desires.



BY JUDY BERLFEIN

For 17 years, Velander and his colleagues have been developing methods of producing large quantities of factor. The key, Velander repeats several times in an interview, is abundance. If we have enough factor, he believes, we can provide it to all who need it at an affordable price. Using today's methods of generating recombinant factor, quantity remains an issue. But if Velander's methods are proven sound, scarcity will no longer be a stumbling block.

What's the trick? With nearly two decades of research on the project, Velander has successfully inserted the gene for factor IX (FIX) into developing pig embryos. When these pigs mature, the female pigs are able to synthesize large quantities of FIX in the mammary glands. According to Velander, each liter of milk produced by the pigs contains up to a million units of activity, far exceeding the levels found in today's recombinant preparations. These animals have become an efficient factory for FIX. "Factor purified from the milk of 10 to 20 animals could provide hemophilia B treatment for all of Latin America," Velander asserts. Velander does not envision children drinking milk straight from the animal. Once purified, the protein could be reconstituted for an intravenous infusion, similar to the approach used with today's recombinant factor. However, another possibility exists that Velander and Oral Alpan of the National Institute of Allergy and Infectious Diseases have begun to study. It may be feasible to mix purified factor with pasteurized cow's milk or any other

desired drink and provide it as an oral treatment.

Independent teams of researchers in Japan and the Netherlands demonstrated two decades ago that factor could be given orally. The large protein successfully nav-

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igated the harsh conditions of the gut and made it safely to the bloodstream. Velander says the experiments weren't pursued further because the protein was not available in sufficient quantity to study. "But now abundance is no longer an issue,"

he states. With nearly unlimited FIX available from his pigs, Velander and colleagues plan to complete the work initiated by the Japanese and Dutch scientists.

At first glance, many are skeptical about the possibility of oral administration. It sounds a bit too simple. Velander notes that proteins won't routinely pass through the gut, especially if they're taken on an empty stomach. When food is absent, the high acid content of the stomach and enzymes designed to destroy proteins in the intestine will quickly break proteins down into constituent parts. However, if the preparation is taken after a full meal and inhibitors are used to discourage enzyme activity, the odds of pushing intact protein into the circulation improve. Milk, he comments, provides a useful vehicle for carrying factor, as it contains casein, a natural inhibitor of enzymes aimed at proteins. Other foods, such as soy, also have natural inhibitors, and could be a favorable addition to the factor mixture.

Velander still has several hurdles to cross. He has completed preliminary experiments in healthy dogs, feeding them milk from his pigs and achieving measurable FIX levels in the blood stream. The next step is to purify the factor and administer it intravenously to hemophilic dogs to determine if it is effective in correcting the bleeding disorder. All of this requires funding. Agreements are in the works with the ministry of health of the Brazilian government to provide that support. The ministry would administer the experiments in animals and conduct the ultimate trials in humans. If therapy is successful, they would then market it throughout Brazil and other Latin American countries.

Velander dreams big. But the mantra of all research applies to his plans as well. Perseverance, time and good luck will determine if his dreams come to fruition. 🍀