# Plants Help Prevent Inhibitors and Allergic Reactions

Great Lakes Hemophilia Foundation
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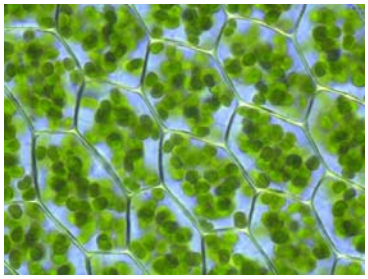

Using genetically modified plants, researchers from two Florida universities are developing a technique that could help prevent treatment-related complications such as inhibitors, an immune reaction that neutralizes infused factor, and anaphylaxis, severe allergic reactions, in people with hemophilia B. The lead authors of the study were Dheeraj Verma, PhD, Department of Molecular Biology and Microbiology, College of Medicine, at the University of Central Florida (UCF) in Orlando and Babak Moghimi, MD, Department of Pediatrics, College of Medicine, at the University of Florida (UF) in Gainesville.

Inhibitors result in approximately 25% of patients with hemophilia A and up to 4% of patients with hemophilia B. Clinicians often use immune tolerance (IT) induction to eliminate an inhibitor. By administering daily doses of factor over time, the body begins to tolerate the therapy. The process is similar to desensitization therapy used to treat food and environmental allergies. The technique is less effective in individuals with hemophilia B than in those with hemophilia A. In addition, because of the large amounts of factor used, IT becomes very expensive. The approach being developed by Verma, Moghimi and colleagues could be more cost effective.

The researchers used a so-called “gene gun” to insert the genetic material that manufactures factor IX (FIX) into chloroplasts, the energy production centers of plants. They then fed the modified plants to mice with hemophilia B for a prolonged time period. Insulated from digestive acids and enzymes by durable plant cell walls, the FIX protein traveled through the stomach and into the small intestines. Once inside the small intestines, bacteria then broke down the cell walls and released the protein, which induced tolerance by the immune system.

“We have made them develop tolerance, and removed the allergic part of this treatment,” said coauthor Henry Daniell, PhD, a Pegasus professor and University Board of Trustees Chair in the College of Medicine at the UCF.

Later the mice were infused with factor product, which triggered little to no inhibitor responses and no anaphylactic events. “I think this is a milestone — nobody has previously achieved such levels of robust immune tolerance by any means using a noninvasive procedure,” explained Thierry Vandendriessche, PhD, an associate professor of medicine at the University of Leuven in Belgium,

who was not involved in the study. He is president of the European Society of Gene Cell Therapy.

Investigators will conduct follow-up studies to test the approach in mice with hemophilia A and then carry out trials in humans using lettuce to produce the therapeutic proteins.

“We’re hoping that our research will, in the future, result in better and more cost-effective therapies,” said study co-author Roland Herzog, PhD, an associate professor of pediatrics, molecular genetics and microbiology in the UF College of Medicine and a member of the UF Genetics Institute. Herzog received the National Hemophilia Foundation’s Career Development Award in 2000.

The study, “Oral Delivery of Bioencapsulated Coagulation Factor IX Prevents Inhibitor Formation and Fatal Anaphylaxis in Hemophilia B Mice,” was published in the April 2010 issue of the *Proceedings of the National Academy of Sciences*.