Collaborative develops drug that may help hemophilia patients

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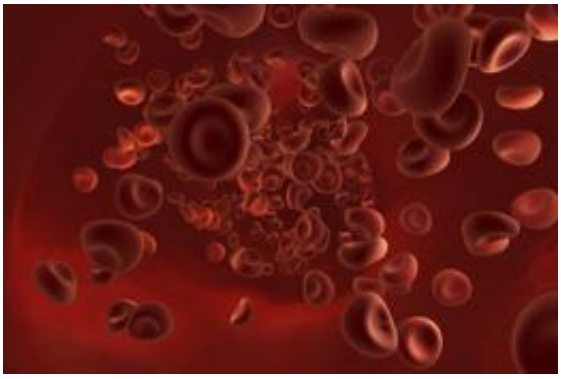

A razor nick in the shower? A fall on a slippery floor? The average person simply calls it bad karma, but for people with hemophilia such episodes can cause prolonged blood loss.

Hemophilia is an inherited bleeding disorder in which a particular protein required for blood to clot is missing or is present at an insufficient level. Currently there is no long-acting hemophilia agent, meaning that patients must either take an injection of the protein in reaction to a bleed, or have intravenous infusions —a method of delivering drugs — two to three times a week to maintain the clotting medication in the bloodstream.

But thanks to collaborative work involving the laboratory of Neil

Simister, an associate professor of molecular biology at Brandeis, and doctors at Children's Hospital and Brigham and Women's Hospital, hemophilia patients may soon have access to long-acting clotting medications that free them from the hassles of frequent infusions and from worries that an internal bleed has gone unnoticed.

Simister's laboratory, as well as labs at the University of Texas and Ohio State University, independently and simultaneously discovered that the receptor FcRn protects antibodies from breaking down in the body. Building on that basic discovery has enabled the formulation of new hemophilia drugs.

One of them, Factor IX Fc fusion protein (rFIXFc), for hemophilia B, is expected to finish Phase III clinical trials by early 2012 then be filed for FDA approval.
The idea behind rFIXFc is genetic engineering of sorts. If you have a therapeutic protein that you want to last a long time in the blood — in this case a clotting factor — you can fuse it to the part of the antibody (called Fc) that will bind to the protective receptor, FcRn.

Since antibodies last a long time in the blood relative to other proteins, this enables the therapeutic protein clotting factor to be protected by FcRn and, as Simister says, enjoy the same protection as an antibody.

Factor IX Fc fusion protein was created by Syntonix Pharmaceuticals, a company formed in 1998 based on breakthrough discoveries from the laboratories of Simister, Dr. Wayne Lencer of Children's Hospital and Dr. Richard S. Blumberg at Brigham and Women's. The labs had been collaborating on the study of FcRn as an antibody transporter in human cells. Biogen Idec bought Syntonix in 2007. It is the first company spun out of Brandeis to be acquired by a large biotech firm.

Approximately one in 5,000 males born in the United States has

hemophilia A, which is caused by mutations in the factor VIII gene. About one in 25,000 males are born with hemophilia B, which is due to mutations in the factor IX gene.

Simister says that many of the problems that occur for people with hemophilia come from internal bleeds that just happen because of the rough and tumble of life. Little bleeds that occur in muscles and joints stop very quickly for those not affected, but people with hemophilia are often unaware — say from a seemingly innocuous fall — and over time will develop muscle and joint damage.

“Because you don’t know that you’ve had a bleed you don’t know to take the clotting factor on demand,” says Simister. “Prophylaxis for people with hemophilia keeps a good protective level of these clotting factors in their blood.”

He adds that people are much more likely to be compliant with preventative therapy, which is now standard of care, if it’s only once a week.

“It’s probably considered one of the most important pipeline products at Biogen,” says Laur Blumberg ’83, one of the Syntonix founders and brother of Richard S. Blumberg, one of the researchers. “It’s contributing billions of market capital to the company.”

In early 2008, Biogen Idec filed an application to begin clinical trials of rFIXFc for the treatment of hemophilia B.

“What’s really exciting is that we’re getting to an ultimate moment for this little company’s [Syntonix's] technology,” says Blumberg. “For biotech companies to make it to Phase III and near registration is very rare.”

Blumberg estimates that they are probably less than 12 months away from getting definitive Phase III results for both hemophilia A and B programs. The next step would be filing for FDA approval.

“A lot of people have to do basic research for some fraction of the discoveries that they make to be useful in some way to people,” says Simister. “To be able to see that progression, from something that was a series of basic discoveries in the lab going through to clinic, is great.”

Provided by Brandeis University