MEDICAL INNOVATION: RECOMBINANT FACTOR VIII (PHARMACEUTICAL: BIOLOGICALS)

Physician: Gordon Vehar, William Wood, Richard Lawn, Daniel Capon et. al.
Industry: Genentech, Genetics Institute

Situation

A treatment leads to a deadly disease

Hemophilia refers to a group of largely hereditary bleeding disorders in which it takes a long time for blood to clot. When the human body bleeds, it launches a series of reactions that help blood clot, involving special proteins called coagulation "factors." When one or more of these clotting factors are missing, there is usually a higher chance of bleeding. The disease most often affects men; approximately one in 5,000 males born in the United States has hemophilia.

Hemophilia A is the most common type of the disease, and is known as Factor VIII deficiency, or classic hemophilia. Hemophiliacs are treated by replacing the missing clotting factor, Factor VIII in the case of those with type A. A quarter century ago, Factor VIII was only available from donated blood plasma, and its transfer into the blood stream of a patient with hemophilia often led to the transmission of diseases such as HIV-AIDS and hepatitis B and C.

Physician-Industry Collaboration

A new disease sparks a new urgency in searching for an alternative

A number of genetic scientists had a different idea. They imagined using new research into the human genome to discover a way to make Factor VIII without using donated blood -- something that could save the hundreds of thousands of hemophiliacs around the world from becoming infected with a crippling or even life-threatening disease.

In the early 1980s, a small group of scientists in the San Francisco Bay Area teamed up with the young biotechnology company Genentech with this aim, motivated by the added urgency of the recent discovery of a deadly new disease called HIV-AIDS that could be transmitted through contaminated blood plasma. Another Boston-based group of scientists at Genetics Institute (GI) worked in parallel toward the same goal.

But isolating the genetic structure of Factor VIII was a monumental task -- the protein contained in Factor VIII was enormous and complicated, and very fragile to study in the lab. Combined with its especially low abundance in plasma, it seemed an unlikely candidate for cloning success. However, backed by the resources of both companies, the Genetech team led by Gordon Vehar, Bill Wood and Dick Lawn finally struck gold in early 1984 and produced the first genetically engineered clotting factor for bleeding in hemophiliacs. A short time later, the team from GI led by Daniel Capon made the same breakthrough.

The FDA approved the technology for so-called "recombinant" Factor VIII for GI in 1992, and for Genentech a year later. Both companies eventually agreed to cross-license its production worldwide.

Innovation Benefits

Transmission of diseases virtually eliminated

The discovery has been a godsend for hemophiliacs. Recombinant Factor VIII has all but replaced the use of human-derived Factor VIII, and the transmission of diseases such as HIV-AIDS and hepatitis has been virtually eliminated. Worldwide demand for recombinant Factor VIII has been so strong that companies producing it have had to dramatically scale-up production to meet demand. It has even been recommended for use in other therapies, including as a preventive agent against developing joint ailments in some patients.

Patient Benefits

"It was a roll of the dice"

As told by CSL Behring, Jens B. in childhood frequently experienced bruises and bleeding in his joints and in his mouth following visits to the dentist. An examination by his doctor revealed he had hemophilia A, or classic hemophilia.

Since early childhood, Jens has been treating his condition with Factor VIII replacement therapy, but always faced the threat of infection from each infusion. "It was a roll of the dice -- I never knew when I might catch a deadly disease, all just from treating a condition I was born with."

After the discovery of recombinant Factor VIII, he immediately switched to using the new product that was identical to his usual treatment derived from human plasma. Currently, he manages his disease by self-infusing recombinant Factor VIII three times a week.

When not at work, Jens remains active. He enjoys spending time with his family, fishing and playing games on his computer.

"By managing my condition I can lead a normal life; I just have to make sure I make time for my infusions and be careful not to get injured," Jens said. "But at least I don't have to worry ever again about the safety of my therapy."