Recombinant DNA: Treating Hemophilia

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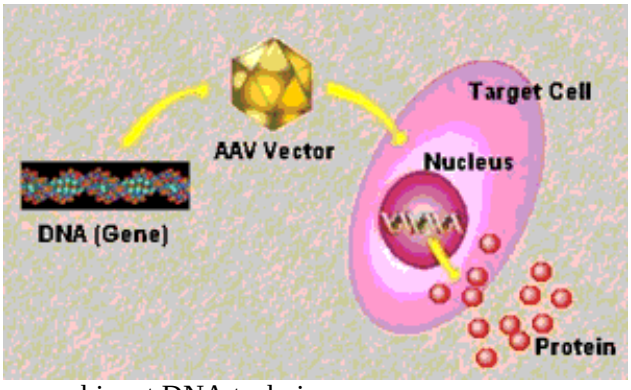
Hemophilia is a genetic disease which impairs or eliminates one's blood clotting ability.
Approximately one in ten thousand males born in the United States have some degree of hemophilia.
For most individuals, blood clotting follows just a few simple steps. First, the broken blood vessel constricts to locally slow the rate of blood flow. Next, platelets in the bloodstream come to the site, and coagulate to form a solid plug over the break. Finally, the thirteen clotting factors sequentially interact to form a fibrin netting over the platelets, holding the solid plug in place. This solid stays there until the wound is healed, finally dissolving back into the bloodstream if an internal bleed, or sloughing off as a scab if external.
If any one factor is missing, or in too small a quantity, the fibrin net cannot form, and the platelet plug will usually become dislodged and the bleed will recur.
Prior to recombinant DNA techniques for producing factor, Hemophilia A (Factor VIII deficiency) and Hemophilia B (Factor IX deficiency) were treated with human factor obtained from donor blood. The purified factor was freeze-dried and infused intravenously in a reconstituted solution. A single treatment would require nearly one hundred thousand blood donations, and multiple purification procedures. The other, exceptionally rare forms of hemophilia were treated with whole plasma transfusions.
With the advent of recombinant DNA technology, factor can be obtained without donor blood. The DNA sequence for human factor production is spliced into the DNA of a virus, to form a viral vector. The virus transfers this genetic material into inert host cells which grow and multiply in a nutritive medium. The host cells are often non-infectious bacteria, bovine cells, or cells from the Chinese hamster ovary. Because of the gene now imbedded in their DNA, the cells produce human factor which diffuses into the medium. The cells are filtered from the medium, and the factor is chemically removed from the medium. After the factor is purified, it is ready to be infused, having never been part of a human system. The recombinant factor behaves exactly as regular human factor, and has nearly identical physical and chemical properties.
The many advantages of recombinant factor include reduced cost, because hundreds of thousands of blood samples needn't be taken. Additionally, the incidence of inhibitors, a form of rejection, is vastly reduced. By far the greatest advantage however is that recombinant DNA is absolutely free of disease. Many people with hemophilia in the late 1970s and early 1980s became infected with HIV, and many more contracted hepatitis and other blood-borne diseases. Though donations have been meticulously screened for disease since the mid-1980s, the risk of infection is still possible.
Despite the many improvements that recombinant factor provides over blood derived factor, there is still one major flaw in its use as a treatment: it is not a permanent treatment or cure. Researchers are currently investigating possibilities that could offer permanent or near permanent clotting abilities. One direction that is being investigated is genetic therapy, which would change the patient's DNA so that their body would produce factor naturally, and on its own. Another area of research that would provide an alternative to intravenous infusions is a mechanical factor pump. This would be especially useful for persistent bleeds, which often require repeated treatments, or for cases of inhibitors, which often need continuous, sustained levels of factor. Also, researchers are analyzing how liver treatments might affect hemophilia. It has been observed that people with hemophilia who have needed and received liver transplants have sometimes had the hemophilia seemingly disappear.
Recombinant factor procedures have helped to focus research attention on genetic aspects, which show promising signs of holding improved treatments and ultimately, may reveal a permanent cure for the disease. Though far from a cure for hemophilia, recombinant DNA techniques for producing human blood clotting factor have provided a major step forward in the treatment of hemophilia and the safety associated the with treatments themselves.

This diagram shows the generalized procedure of



recombinant DNA techniques.