EDITORIAL

Gene Therapy on the Move

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Gene therapy was conceived about 30 years ago when symptoms of sickle-cell anemia came to light for the first time. This blood disease occurs in one out of every 500 black Americans, which stems from a tiny mutation in one of the genes for human hemoglobin.

Molecular biology can now enter a cell and fix broken genes, which cause a variety of illness. This is done, not by knife or scissors but by a virus. Normally viruses are vehicle for their own genes. These tiny creatures are little more than genetic material wrapped within a shell that allows the virus to travel from one cell to the next. They penetrate a cell, then order the cells genetic machinery into making thousands of virus copies. Mulligan, in 1979, used the tools of recombinant DNA technology to splice a rabbit gene into a monkey virus. Mulligan had pulled out the genes that allow the virus to replicate and put in their place the gene for hemoglobin, the molecule in red blood cells of rabbit and man - that carries oxygen. Mulligan believed that the genetically modified virus upon entering a cell would no longer tell it to make more virus particles but it would just order hemoglobin proteins. Mulligan collected his viruses, all with the rabbit hemoglobin gene and dumped a soupy solution of those viruses into a dish of cells cultured from a monkey kidney. Kidney cells have no role in oxygen transport, and so they normally make no hemoglobin. These kidney cells, however, after invasion by viruses transformed miraculously, and began to produce chains of hemoglobin protein. The production of these proteins, ushered in a revolutionary new vision of therapy for human genetic disease. Mulligan's experiments of gene - transfer showed that one could transform viruses into molecular ambulances capable of shuttling beneficial gene into defective cells. there was a great break through in biological research. This opened a new era of medical research by which physician could research by which physician could reach down into the molecular foundation of a disease and tackle a disease by correcting its cause.

By engineering viruses that can transplant human hemoglobin gene into developing blood cells in a mouse, producing cells with perfectly functioning hemoglobin, gene therapy has come close to reality. A team at the National Cancer Institute has now used a virus to transfer a tracer genome into immune cells taken from cancer patient and injected it back into the patient and used the gene to trace the cells progress in the body.

For laymen who consider virus an agent of disease, using them to perform gene therapy sounds like a science fiction. Soon however this will become a fancy medical procedure which doctors will use to treat sick patients. Take a normal copy of a human hemoglobin gene and stick this gene into blood - forming cells of the bone marrow. This cell, which is called as stem cell, produces all the cells in the blood. In the sickle-cell patients, stem cells with a transplanted normal gene would make red blood cells packed with normal hemoglobin protein thus curing anemia. Genetic defects involving this molecule creates the most common inherited diseases and therefore, hemoglobin has attracted a great attention.

The hemoglobin molecule constitutes two types of protein chain, curled side by side which are referred to as alpha and beta. Each is encoded by a separate gene. However, most of the hemoglobin related diseases are caused solely by mutations in the gene for beta globin. Beta-thalassemia, a type of nutrition caused disease, is commonly found in people of Mediterranean descent. In this case, red blood cells simply do not make enough beta-globin protein both knob - like protuberance and a hole into which a knob from an adjacent chain become stuck. Chains of the mutant molecules can become glued together forming long fibers that wrap normally circular red blood cells into a crescent or sickle shape. The malformed cells are too rigid to pass through narrow blood capillaries. They form a cellular logjam.