

## Gene Therapy as Molecular Medicine in The 21<sup>st</sup> Century

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Gene therapy is the use of genes as medicines for the purposes of preventing the occurrence of disease or for altering the clinical course of an existing disease. Over the past decade, dramatic progress has been made by many investigators in the field to develop and refine technologies used to deliver genes into various cells and organs in living animals, including humans. In several instances, significant treatment benefits achieved in laboratory animal models of human disease have been observed in recent clinical studies as well. An example is Hemophilia B, which is caused by a deficiency of clotting factor IX in the blood. Normal blood clotting times have been restored for extended durations of time after a single application of the gene in genetically affected mice and dogs. Very encouraging results have also been reported in patients during early phase clinical studies after intramuscular de-livery of a recombinant adeno-associated virus expressing the human factor IX gene. Another example is X-Linked Severe Combined Immunodeficiency Syndrome secondary to a deficiency of the gamma chain of cytokine receptors on T cells. Autologous transplantation of CD34+ cells transduced with a recombinant retroviral vector expressing the normal human gene has resulted in the reconstitution of T cell counts and immune functions in several affected children for up to one year. These achievements resulted from recent technological advancements and will lead not only to extensive applications in the treatment of patients affected with relatively rare inherited disorder such as Phenylketonuria (PKU), but also to the future treatment of complex and acquired disorders such as cardiovascular diseases, cancers, diabetes, obesity, infectious diseases and neurodegenerative disorders that represent the leading causes of mortality and morbidity in developed countries.

The most notable recent accomplishments in these areas include, but are not limited to, the treatment of patients with ischemic limbs by the administration of an angiogenic gene that stimulates blood vessel growth, and the destruction of tumors in patients by the administration of suicide and immunomodulatory genes that specifically destroy cancer cells. While the gene treatments for these complex disease targets are only partially effective at present, future advancements in technologies for the delivery of novel genetic medicines promise to result in much improved clinical benefits for these and other human diseases. It is anticipated that the scientific principles of gene therapy as a new biomedical discipline will be further validated in the coming years and decades. Its future widespread applications in the treatment of various human diseases will have a major impact on the practice of medicine, health and healthcare delivery in this Century.

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