EDITORIAL

Gene Therapy – How Feasible and Where Do We Stand ?

Akbar Mohsin Mohammad, MD, FAAP*

Approximately one percent of infants throughout the world are born with a serious genetic defect which is usually manifestated during childhood. There is no known effective therapy for most of the 4000 inherited disorders[1].

This gloomy picture for genetic disorders has motivated scientists to search for illusive cures. One of the first successful techniques was reported in the US in September 1990 when R Michael Blaese and colleagues at the National Institute of Health (NIH) undertook the first federally approved clinical trial of gene therapy for a rare genetic disease that manifested in the form of severe combined immuno-deficiency (SCID). They introduced the gene for the enzyme adenosine deaminase (ADA). The initial results were very encouraging despite the fact that the technique NIH used required repeated treatment throughout life, and it is not a complete cure. The ultimate hope is that the transferred genes will cure the basic defects rather than merely alleviate the resulting damage[2].

Diseases expressed in the bone marrow cells are good candidates for gene therapy due to tissue accessibility. For single defects, for example,in sickle cell anaemia, bone marrow transplantation from a matched donor may effect a cure through a single course of treatment. But gene therapy may however cure hereditary diseases by transferring single genes rather than the whole genome[2]. Other possibilities besides sickle cell anaemia include thalassaemia and combined immuno-deficiency disease due to ADA deficiency. This form of gene therapy calls for patients to donate their own bone marrow and receive it back after the gene defect is corrected. The best chance of success has been reported when the genetic damage is restricted to a single organ or tissue rather than involving multiple sites.

Cystic Fibrosis and Gene Therapy

Although cystic fibrosis (CF) is a hereditary disease with multiple organ involvement, American and French scientists have described results which indicate that important progress has been made in gene therapy in laboratory rats. A modified cold virus containing the gene when sprayed in the lungs of these rats started producing a normal version of the human CF gene product. No animal model of CF has been developed so far. However, these results suggest that if the virus containing the normal gene were to be put into the lungs of CF patients then the CF defect would be reversed. Investigations are being attempted in monkeys before human trials can be initiated. The first clinical tests may begin within two years if all goes well with the animal investigations, with a possibility of routine clinical treatment within five to ten years[3].

Ethical Concerns

Genes can be transferred either into germ cells (sperm, eggs or early embryos) or somatic cells (those not destined to become sperms or eggs). Germ cell therapy is not an option for gene manipulation in the near

* Consultant and Chairman
Paediatrics Department
BDF Hospital
Associate Professor
College of Medicine and Medical Sciences
Arabian Gulf University
State of Bahrain

future because the new genes would be passed from generation to generation; that raises profound ethical concerns. The somatic cell therapy is a less troubling concern because it would affect only the treated patient[1].

It appears that somatic gene therapy for any autosomal recessive disorder, where the target tissue is accessible and the mutuated gene has been isolated and its function understood, is on the agenda in the next decade[4].

Now that targeting accessible tissues for gene therapy has become more feasible and public approval both from within and outside the scientific circles is potentially attainable, it is hoped that the problems of less accessible tissues will soon be solved to permit a wider application of this promising technology.

REFERENCES

1. Verma IM. Gene Therapy. Sci Am 1990;263:34-41.

2. Mange AP, Mange EJ. Genetics: Human Aspects. 2nd ed. Sanderland, Mass:Sinauer Associates Inc, 1990:516.

3. Scott M. An important step towards Gene Therapy of CF. CF News 1992:(Feb-Mar)8-9.

4. Williamson R, Caplen N, Hart S, Sheils C, Kamath S, Coutelle C. Prospects for human somatic Gene Therapy. [Abstract] In: Proceedings of Symposium on Blood Genetic disorders pathophysiology and management. Riyadh, 1992:38.