Gene Therapy Concepts

Gurdyal Singh¹, Urmal², Singh, G*

¹ Affy Parenterals, Village Gullarwala, Baddi, HP, India

² Rajindra medical college and hospital, Patiala, India

*Department of Medical Laboratory Sciences, Lovely Professional University, Phagwara, Punjab, India

Abstract

In the last decade, DNA recombinant technology, cell line development and understandings about human metabolic processes improved a lot. On the other hand rising in the high level of sophistications in bio engineering and righteous implications of ‘OMICS’ in gene therapy that solved or improved the cumbersome technical problems of complex process of gene delivery at appropriate place with an accurate precision. As a result may gene therapy will come soon in main stream of treatment as the remedy for genetic diseases and disorders.

Key word: Gene therapy, gene, diseases, bacteria

Introduction

The pharmaceutical biotechnology sector is extensively based upon the application of genetic engineering for the manipulation and production of therapeutic agents. Most of the licensed/patented biopharmaceuticals are proteins and produced in genetically engineered microbes. The terms such as molecular biology, genetic engineering and recombinant DNA (rDNA) technology are used interchangeably and often similar or slightly different concepts to different experts [1]. It is well known fact; gene manipulating therapy impressed scientists, and the common public due to of its power to treat many diseases at gene level. This can be procured only by substitution of bad functioned genes present in the cells negatively affected by the disease. The perception of gene transfer looks simple, but there are unlimited hurdles to be solved before practices are really challenging [2]. Many gene manipulating therapy trials had been done during past decades for hereditary malfunctions, cancer and chronic diseases, but very less apparent clinical roles and individuals experienced harsh effects linked to the viral vectors. Instead of several ambiguities and questions on the future of gene therapy, several top and small scaled pharmaceutical industries have invested millions of dollars in 2014 and 2015, for developing the gene therapies mechanisms to commercialise this most awaited novel way of curing the genetic disorders. The prime focus of this chapter to increase the understanding about genetic engineering and it’s applications in depth, that is continually implemented in pharmaceutical industry worldwide for the advancement of medical treatments in present and for the future.
Application of genetic engineering in gene therapy

Gene therapy is the novel way of treatment that can provide the resistance or may cure the genetic disorder/disease by an addition of the appropriate gene with an intention that added gene’s product will function as a therapeutic agent [3]. By the use of genetic engineering, isolation of well functioning gene from a cell is possible and insertion into the germ cells is also feasible. Different clinical trials on gene therapy have demonstrated excellent remedial effects on patients. Trials also provided the firm evidences that gene therapy can give promising treatment for severely disabling genetic disorders. Behind these advances came in gene therapy as a result of superior vector sequences that facilitate the secure insertion of beneficial genes to precise cells [2].

Gene therapy types

Therapy in Germ cells

Germ cells can be customized with insertion of expressional intact genes that can integrate into their genome. Such an improvement will come in severity of genetic diseases, this kind of gene therapy can hereditary and is passed generation to generation. This advancement should be extremely successful in combating various genetic and hereditary disorders [4].

Therapy in Somatic cells

In this type of gene therapy, genes can be transferred to the somatic cells of patients. The modifications created by this will be limited to the individual host only and cannot be transferred to the next generations.

Methods for insertion of the normal genes

In the majority of gene therapies, a standard gene is transferred to the genomic set to counter an abnormality by a defective gene. One of the great challenges in gene therapy is how to insert the new gene or substitute the present gene into the defective cells. Therefore, gene carrier vehicle, which is known as the vector that can appropriately insert of replace the gene in patient’s cells.

Use of viruses as the vectors

Harmless viruses are considered as the most reliable vectors for the insertion of genes to the target cells. Viruses have the capability to deliver their genes to nucleus of human cells. Researchers have worked to manipulate the viral genes and inserted the required mammalian genes. Some kind of the viruses only can introduce their genes to the host genome, without entering to the cell. Some viruses can penetrate to the cell membrane like protein molecules and reach to the nucleus of the cell. Once the transplanted gene reached and fit at the appropriate place in the genome of the diseased host, then therapeutic protein can produce and cure to genetic disease is possible. Followings are the examples of some viral insertions that can be acted as the vectors for gene therapy.

Use of retrovirus as the vector

Retroviruses were the first viral vectors tried in gene therapy experiments. Viral cDNA can be added to the host genome with the help of viral enzyme called integrase. Such as the host cell become modified genetically that hold a novel gene. After modified host cell division, their genealogy will enclose the original genes. Though retroviruses had been applied in several gene manipulating therapy practical’s [5]. One difficulty in this method is that integrase can put in DNA fragment of retrovirus into any random location in the chromosome of the cell, which can direct to insertion mutations or uncontrolled cell division leading to uncontrolled cell division. This
trouble had recently began to address by using zinc nuclease[6] or using other sequences like β- globin locus organize region to control the location of insertion.[7]

Adenovirus use as the vector for gene therapy
To overcome the problem of inserting genes at incorrect places on host chromosome, molecular biologists have tried adenoviruses in gene therapy. Adenoviruses belong to the type of viruses that contained double stranded DNA that is not integrated into the genome of the host cell. DNA remains free in the nucleoplasm of the cell and the function of this external gene is translated in the same way as any other gene. Adenovirus has potential to transfect a larger range of cells than that of retrovirus. Cells that divide at very slow rate, like lungs cells can also be transformed by adenovirus. But, adenovirus is more liable to be opposed by the host’s defence system and therefore, more concentration of the virus is needed for cure that can incite an adverse inflammatory response. Instead of these disadvantages, these vectors have been promoted to treat the diseases like hepatocellular carcinoma and ovarian cancer. The initial gene therapy invention to treat the cancer of neck and head regions, Gendicine, p53 based adenovirus has been licensed.[8-10]

Ethical considerations regarding gene therapy
- Scientists and lay segment of society have a question on affordability of the expenses concerned in preparation and execution of gene therapy, without disturbing the quality of standard health measures.
- Gene therapy of somatic cells cannot affect the genetic make-up of sperm and egg cells. On the other hand, it promotes prolonged existence and reproductive competence of the patients.
- Resistance to gene therapy has been raised as it changes the basic blueprint of the genome.
- The voice against the therapy has usually included a rational and spiritual argument.

Few bioethics people speak that therapy of genes involve modifying genes or genomes which had been given from birth.

Aspects about the commercialization of gene therapy in near or distant future
Gene therapy is considered as promising and optimistic future for many patients who are suffering from wide varieties of genetic disorders and diseases. During, 2014 and 2015, several top pharmaceutical industries have invested in various gene therapies development. This investment is a gesture of responsible and solid approach towards the advancement of gene therapy for bringing this to mainstream of treatment. The gene therapy commercialisation model considered as different from the conventional one, because of with the big pharma players small biotech companies also in row for developing novel gene therapies and collectively hold 83% of the cell and gene therapy pipeline, the current funding environment is motivating them to produce in-house manufacturing and commercialisation structure. However, it is not likely that small biotechs will be as efficient and effective at launch in comparison to large pharma companies. Unfortunately new sophisticated instrumentations are cost intensive to set up due to stringent product specifications and good manufacturing practice (GMP) guidelines. On the other side, practical implications of extracting genes or replacing with well functioning gene(s) in patient body, needs high level of communication between the physician, hospital and the
manufacturer and will require significant organisation and process management. There is no market for cell and gene therapy. Companies need to be equipped to cover the long way of intricacies. Instead of a number of difficulties, there might be many gene therapies introducing into market and would be available for various genetic diseases.

References