

BIOINFORMATICS AND GENE THERAPY

Bioinformatics has emerged as a multi disciplinary subject that encompasses developments in information and computer technology as applied to biotechnology and biological sciences. Bioinformatics uses computer software tools for database creation, database management, data warehousing, data mining and global communication network, functional genomics, biomolecular structure proteome analysis cell metabolism, biodiversity, down stream processing in chemical engineering, drug designing and vaccine designing are some of the areas in which bioinformatics are an integral component. Functional genomics is a study of genes, resulting proteins and their role while proteomics is the study of total protein expressed by a cell. Bioinformatics involves the creation and development of advanced information and computational technologies for problems in molecular biology. As it deals with methods for storing, retrieving and analyzing and predicting biological data such as nucleic acid (DNA/RNA) and protein sequences, structure, functions, pathway and interaction. The knowledge of multimedia databases and tools to carry out data analysis and modeling of molecules & biological systems on computer workstation as well as in a network environment has become essential for working in medicine in the time to come. Human genome project (HGP) US Department of Energy in association with US National Institute of Health started the project in 1990 by Nobel laureate James Watson. Complete mapping is one of the biggest achievements a heroic task as one set of human DNA contains three billion base pairs and about 10,000

genes. Shotgun sequencing a technique of breaking the DNA into small pieces and sequencing each of them is an important tool in mapping.

It has been announced that the entire human genome has been mapped^{1,2} as a result of human genome project and with continuous genomic and proteomic research soon we will be able to understand their function too. A phenomenal growth has been there in molecular biology and it is estimated that biological data is doubled every six months and this forms the backbone

Some Bioinformatic Websites⁵

- National Center For Biotechnology Information (www.ncbi.nlm.nih.gov)-maintains bioinformatic tools and databases.
- Genbank (www.ncbi.nlm.nih.gov/Genbank)-stores and archives DNA sequences from both large scale genome projects and individual laboratories.
- Unigene (www.ncbi.nlm.nih.gov/Unigene)-gene sequence collection containing data on map location of genes in chromosomes.
- European Bioinformatic Institute (www.ebi.ac.uk)-centre for research and services in bioinformatics; manages data base of biological data.
- BioInform (www.bioinform.com)-global bioinformatics news service.

Table I.

for every research in the field of medicine including therapeutic and vaccine products^{3,4}. Multiple international projects are availa-

ble for providing gene and protein database to whole medical community. Due to diverse nature of emerging data no single website can provide all information most of websites provide information free of charge though some require subscription through credit / cash card or bank account or a regular membership, some websites are listed in table I, the easiest way to identify databases is by database links and searchable indexes provided by one of the major public database. For example, the National Center for biotechnology Information (www.ncbi.nlm.nih.gov) provides the entrez browser, which is an integrated database retrieval system that allows integration of DNA and protein sequences databases. The European Bioinformatics institute archives gene and protein data from genome studies of all organism, whereas Ensemble produces and maintains automatic annotation on eukaryotic genomes. The quality and reliability of databases vary certainly some of them are better known and more established⁵ in one particular field.

GENE THERAPY

The fast growing research and development in molecular biology and its therapeutic role has made it a reality to use gene therapy in diagnostic and treatment purposes, though much work is still required to obtain a routine use in human being. The basic gene therapy use is in delivery and expressing of gene to ameliorate a disease state by DNA recombination technology/somatic gene therapy into somatic cell of the patient. Basic is transferring the gene material across the cell membrane to its nucleus isolating the healthy gene, along with the sequence controlling its expression and by incorporating this gene on vector and delivering it to the target cells⁶. It is also important to ensure continued expressing of therapeutic gene without any loss to target cells due to host immune system There are three ways of gene transfer, *ex vivo* in which patient cells are taken to laboratory and new genes are infused leading to modified

cells. These modified cells are infused back to human being. *Invivo strategy* the genes are transferred through a vector to cell. *In situ strategy* when the vector is infused intravenously or directly to the tissues. It is important to localize and target the correct cell population. This is specifically effective in cochlear disorders / Inner ear diseases as ear is well suited for it being a closed system. Vector can be infiltrated in perilymph of scala vestibuli or scala tympanii through round window or cochleostomy. In animal studies inflammatory response has been found limited to perilymph space and was not observed in spiral ganglion or organ of corti. No galectosidase staining could be detected in vestibule or auditory hair cells of cochlea.

VECTOR

Vectors are carriers used for gene delivery. *Adenovirus*, linear molecule measuring about 35 kb. DNA virus affects mainly on non dividing cells, and is in use in cystic fibrosis. *Adeno associated virus*, again a DNA virus able to integrate in host cell DNA on chromosome 19. The plus point is no known pathogenic effects, while having wide tissues affinity, *Herpes simplex virus* a disabled single copy virus with defective glycoprotein with property to replicate once only hence there is no risk of disease. *Retrovirus* RNA virus replicates through a DNA intermediate and have a distinctive property of affinity to dividing cells hence is very useful in germ line or anti tumor gene therapy. *Liposome vector* a non viral, artificial lipid bilayers which could be incorporated with plasmid carrying the human DNA. Advantage is very weak inflammatory response as it carries human gene of big size and do not replicate hence no risk as of viral gene therapy, *Uncovered plasmids* a weak DNA vector containing human gene without liposome coating, useful for DNA vaccination. The disease of inner ear leading to sensorineural deafness and / or tinnitus due to involvement of hair cell is common and no restorative treatment for hearing impairment

or vertigo is available at present⁷. It becomes necessary at this stage to analyse and identify the particular gene which can regulate and repair the organ as hair cells and vestibular system has got a limited regenerative capability¹.

Gene therapy by altering cytokines can be used for the treatment of middle ear Pathologies like tympanic membrane perforation healing and to check growth of Cholesteatoma. Feline immunodeficiency virus a lentiviral vector carrying gene for green fluorescence protein has been found effective in middle ear⁸. Genes responsible for sensorineural hearing loss has been isolated on chromosome up 16 and adeno associated expression of

genes neurotrophic factor has given promising results^{9,10,11}. A constant upgradation for regular therapy is required as it may be fatal too. Antioxidants usefulness is another important future application in presbycusis¹² ototoxic or hereditary sensorineural deafness. Even the psychosomatic stress can modulate activity dependent gene expression, protein formation, physiological functions and psychological experience which generates molecular messenger, activating immediate early gene, required to synthesize the proteins which transform stem cells into mature well functioning tissues. This forms the basis of hypothesis of mind body healing a concept of Dhyana & Yoga.

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Editor

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