Molecular Genetics of Eye Diseases

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Formation of the human eye involves complex and interactive processes of molecular and cellular development of the neural and surface ectoderm. These biological developments are essentially all governed by genes. Monogenic eye diseases are often caused by the loss of normal function of genes, due to sequence aberrations or hypermethylation. Most of the common eye diseases, however, are multifactorial in etiology and attributed to a multiple and interactive genetic and environmental factors. Age-related macular degeneration has been reported to be associated with *APOE* genotype and mutations in the *ABCR* and *ARMDI* genes. Age, smoking, intake of saturated fats and exposure to sunlight are risk factors. More than 20 chromosomal loci and 8 candidate genes have been identified for retinitis pigmentosa, which is variable in phenotypic expression. Multiple genetic determinants and secondary factors are also known to be associated with most forms of cataract and glaucoma. Myopia occurs in many ocular and metabolic disorders. Recent genome-side searches have revealed two possible loci on chromosomes 12q and 18p. We are in the process of establishing a database for gene mutations of common eye diseases in Chinese. A wide spectrum of novel and previously reported gene aberrations has been obtained.

Gene Therapy

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Gene therapy is the introduction of functioning genes into a cell to correct an inborn error or dysfunctional gene or to add new function to a cell. The addition of gene has the potential to cure monogenic defect such as hemophilia B, familial hyper-cholesterolemia. Trials are carried out in potentially lethal genetic defective disease. Less well defined genetic diseases such as diabetes mellitus, cancers may also benefited from gene therapy. In cancer treatment, gene therapy not only confined to gene replacement, but involves strategies such as immunotherapy, chemotherapy sensitization and anti-oncogenic therapy.

Techniques consisted of first cloning the gene, select cell target and gene transfer. Gene can be transferred by physiochemical methods such as liposomes, naked plasmid DNA and gene gun or viral vectors such as adenovirus and retrovirus.

Potential problems of gene therapy include choice of gene to be transferred, how to enhance the delivery of the gene (transfer efficiency) into targeted cells (transfer specificity), how to control the expression of inserted gene, how to lower the immune response of host to vectors if viral vector is used.

Our in-vitro study using p53 expressing adenovirus transfer to cervical cancer cell lines showed inhibition of growth as well as apoptosis. Clinical trials in other centres showed encouraging results in advanced cancer treatment such as in carcinoma of lung. To conclude, though there is a potential for gene therapy, it is not ready for clinical practise yet.