GENETIC RESEARCH

The Asia-Pacific Society of
Eye Genetics

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The APSEG was established in February 2001 with a view to engage, advance and further research, education, academic exchanges of knowledge and skill transfer in eye genetics. One of its goals is the promotion and spread of knowledge of eye genetics and related issues among the public through lectures, exhibitions, classes and conference, as well as the promotion of collaboration and interaction among schools, universities and charitable organizations.

Genetic eye diseases can be congenital, hereditary, or acquired. Some have monogenic etiology, while others are oligogenic or multi-factorial. The latter are attributed to multiple and interactive genetic and environmental factors. Most of them are heterogeneous in genotype and complex in mechanisms. The advent of advanced technologies in molecular biology and the near completion of the Human Genome Project have led to the identification of many loci for genetic diseases. Mutations in a gene may cause over-expression, under-expression, or dysfunction of the corresponding protein product. Studies on gene variants causative of disease have lead to understanding of the disease etiology. There are ethnic variations in the occurrence of disease causative mutations and phenotypic expressions in certain disease entities. Our studies of Chinese patients with genetic eye diseases have revealed novel mutations that shed light on the functions and properties of the respective genes. Both similarities and differences in the patterns of sequence alterations and phenotype-genotype associations have been found between Chinese and other ethnic groups, even in other oriental populations. Our results exemplify the need for establishment of ethnic specific eye disease databases that contain both clinical and genetic information for identification of genetic markers with diagnostic, prognostic or pharmacological values.
Asia-Pacific Society of Eye Genetics (APSEG)

Such developments form the backdrop of the formation of the APSEG, which was established in February 2001 with a view to engage, advance and further research, education, academic exchanges of knowledge, and skill transfer in eye genetics. Among its members, exchange of information and ideas in relation to various aspects of eye genetics should facilitate the publication and communication of information with members of other bodies on all matters of relevance to eye genetics. The society has as one of its goals the promotion and spread of knowledge of eye genetics and related issues among the public through lectures, exhibitions, classes, and conference, as well as the promotion of collaboration and interaction among schools, universities and charitable organizations in the Asia-Pacific region involved in research and the study of eye genetics.

The inaugural symposium of APSEG was held in Hong Kong on 1 February 2001 and the second symposium in Singapore on 30 September 2001 in conjunction with the First Singapore Eye Research Institute International Meeting. More than a dozen renowned speakers from various regions of the Asia-Pacific area delivered informative talks on recent advances in genetic eye diseases, in both clinical and basic perspectives. Over 300 ophthalmologists and laboratory scientists attended the more recent meeting. The next two symposia are planned for April 2002 in Sydney and June 2002 in Shantou, China. We are also in the process of establishing an APSEG web site and a retinoblastoma database.

We hope that the APSEG will provide a good platform on which all interested parties can build and extend the frontiers of eye genetics in the Asia-Pacific region and beyond.

REFERENCES


* Dennis S.C. Lam is the president of the Asia-Pacific Society of Eye Genetics.
Searching for Genes that are Responsible for Eye Disease

Roger Beuerman
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The causes of becoming ill are many and at least superficially. Some general reasons for becoming ill can however be recognized. A common cause is infection by a bacterium or a virus and we are all familiar with types of illness associated with infection. Another cause of illness is that genes within the cells of the body may start to malfunction. Such genetic malfunction may be the result of genetic inheritance or may be acquired. Factors important in this regard include diet, aging, and the environment, all of which may tip the scale of genetic activity from normal to abnormal function.

Genes are numerous and complicated and finding those that are malfunctioning is difficult. New technology however allows us to identify which genes are functioning normally and which abnormally. This technique is DNA array technology, which allows us to search for those genes involved in specific diseases. The identification of such causative genes is a necessary first step on the road to developing more specific and effective treatments.

Many eye diseases fall into the category where malfunctioning genes play a significant role. These include diabetes and diabetic eye disease and a common cause of blindness in the elderly, age-related macular degeneration.

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Gene directed activities are important and one important activity is the production of proteins that form most of our body tissues and are involved in enzymic and other crucial activities. Each gene produces its own specific protein as its gene product. An example of a common protein is collagen, a biological polymer that is an important constituent of skin, the cornea, and the sclera in the eye and in many other tissues including scar tissue formed in response to injury. Collagen is synthesized continuously over our life span and has been used cosmetically by women to make their skin look younger.

One of the reasons why it is difficult to determine which genes are malfunctioning is that there are so many. Within the nucleus of each cell there are many thousands of genes, perhaps 40,000 or more. Together with other cellular machinery they specify what types of biomaterials each cell will manufacture. Thus genes direct how we function overall. Proteins make up much of each cell and individual cells may make as many as 100,000 proteins, some of which are exported out of the cells, such as the keratin proteins for hair and fingernails.
Genes determine which proteins are manufactured in each cell and how much protein is made. Genes may be up-regulated or down-regulated, producing too much or too little protein. An example is the condition of keloid scar where following an injury or an operation a grossly excessive amount of scar tissue is formed. Knowledge of what genes are responsible for this overproduction might enable the development of medicines capable of turning off the genes and so eliminating their malfunction.

One disorder that may have a basis in local genetic malfunction is pterygium. This is a growth that originates in the white of the eye (conjunctiva) and grows onto the normally clear cornea (Figure 1). Eventually vision in the affected eye may become severely abnormal. In Singapore, some seven percent of those over the age of 40 have pterygium and worldwide there may be 30–50 million affected persons. In pterygium, the cells in the conjunctiva near the corneal margin have malfunctioning genes that allow these cells to grow abnormally over the clear cornea.

In SERI, we are examining the genes in the diseased tissue to determine which are malfunctioning and also what is the nature of the malfunction, as a first step in the development of rational medical therapy. The eventual aim is to avoid surgery that is currently the only available remedy and after which many patients have recurrence of the trouble. Pterygium is a good condition to study by DNA array technology, as it fits well the necessary conditions for the use of this methodology. In our study of pterygium, we require only a pinhead of tissue to examine the activity of over 9000 human genes. Currently we cannot investigate the rest of the 40,000 genes as at present their exact location and function is unknown.

The genes in the tissue to be studied are labeled with a material, the brightness of which can be measured and compared with normal tissue. In pterygium, one gene that is overactive is involved in the over-production of collagen (Figure 2). The next aim is to identify medical treatment that will stop this unwanted collagen production. Gene array and related procedures are complex and SERI has been fortunate to have skilled assistance from a group at the National Cancer Center (NCC) led by Dr. Patrick Tan and also valuable advice given by Prof. Soo Kee Chee, director of the NCC.

The preliminary results of our study have been presented at the leading international meeting on eye research, the Association for Research in Vision and Ophthalmology. Our future aims include the identification of genes involved in diabetic eye disease and in age-related macular degeneration.

We have just formed the Singapore Pterygium Study. This will be an all-out effort on the implicated genes using DNA array, tear biomarkers, inflammatory mediators and programmed cell death and involve multiple hospitals and surgeons. We will collect about 30 samples per year for these molecular biological studies.
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