

SB-0905-BERLIN-GENORET-SAHEL

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EVI-Genoret (LSHG-CT-2005-521036)- integrating European vision research

By Stefanie Petrou Binder MD

In Berlin

Researchers from across Europe are collaborating in a new project designed to hasten the application of genetic and genomic research to eye diseases that are presently difficult or impossible to treat. Sponsored by the **European Commission and coordinated by the** European Vision Institute, the EVI-Genoret programme is bringing together partners from industry and academia to conduct research for the prevention and treatment of diseases that affect the retina, such as AMD and inherited retinal degeneration. This Integrated Project is financed (10 Million Euros) by the EU for a 4 years period.

“The number of people suffering from serious visual impairment is actually growing. We are approaching this problem by combining research that begins with the basic biology of vision and spans to include sophisticated investigations in the identification of novel retinal genes and pathways and their context dependent function in normal and degenerating tissue,” EVI-Genoret scientific coordinator José Sahel MD, Institut de la Vision, Hôpital St-Antoine, Paris, France said during a symposium dedicated to EVI-Genoret at the Joint Meeting of the European Society of Ophthalmology and the German Ophthalmology Society (SOE/DOG).

EVI-Genoret’s ultimate goal is to improve the understanding of the fundamental molecular and cellular biology of the retina, its development, and the way it is altered by genetic mutation, environmental factors and age. Its first step therefore is to obtain and integrate the information on gene function from the available human, animal and in vitro models of retinal development and degeneration, and standardize and analyze the data through database and expression studies.

Once the researchers validate the information through functional assays and models, they can use their better and broader understanding to facilitate the design of genomic-based therapy and propose function models.

EVI-Genoret researchers believe that the mechanisms for understanding retinal degeneration are genetic, bearing in mind, however, that the physiological representation of gene mutations is context dependent. Interrelationships between affected and non-affected genetic loci, as well as interactions within functional protein networks determine the risk and penetrance of disease. It is therefore the interplay between different genes and proteins networks that create regulatory networks determining the molecular nature of blindness.

Dr Sahel explained that EVI-Genoret addressed the systematic analysis of gene regulatory and protein networks by studying regulatory mechanisms that guide transcription, large-scale chip-based transcriptome analysis, proteomics, protein-interactome analyses, functional cellular and biochemical assays, and data integration through bioinformatics and model organisms. These are the keys to help analyse patterns of gene expression and gene function in retinal development, normal function and degeneration, and for the ultimate identification and validation of novel therapeutic targets.

Genetic linkage studies and positional cloning/candidate gene approaches have led to the identification of a large number of genes for degenerative retinopathies. According to EVI-Genoret member Shomi Bhattacharya PhD, such work offers important clues to the biological and biochemical functioning of certain cells. But a great deal of work still remains both in relation to the identification of novel genetic loci/genes for hereditary retinopathies as well as the characterisation of novel retinal genes.

Dr Bhattacharya noted that research addressing a variety of photoreceptor and retinal pigment epithelial (RPE) cell diseases as seen in patients with retinitis pigmentosa and macular dystrophies, including age related macular degeneration, was on EVI-Genoret's agenda. This includes identifying genes expressed specifically in RPE (implicated in both monogenic and genetically complex retinal dystrophies, including AMD), and identifying proteins that interact with RPE-expressed gene products and components of RPE signalling pathways, which may point towards new candidate disease genes.

He noted that related research efforts targeted identifying new candidate genes for AMD by identifying the proteins specifically interacting with the

CIQTNF5 short-chain collagen and its proposed RPE signalling pathway, as well as identifying the molecular basis of age-related sub-RPE deposit formation resulting from mutation in the *CIQTNF5* gene in late-onset retinal degeneration (L-ORD) and investigating its relationship to sub-RPE deposits in AMD.

The therapeutic component of the EVI-GenoRet consortium dedicates its research to investigating new therapeutic strategies, such as the efficiency and feasibility of gene silencing and gene replacement strategies, by means of therapeutic DNA delivery to the retina via electrotransfer or by the use of viral carriers. With this approach, researchers hope to be able to cure or slow down the progression of degenerative retinal disease.

They also aim to improve cell or tissue transplantation by analyzing host responses to subretinal grafting and enhance neuroprotection of retinal tissue by the identification of new endogenous factors counteracting photoreceptor cell death and by testing such factors in various models of retinal degeneration.

EVI-Genoret scientific deputy coordinator Eberhart Zrenner MD, University Eye Hospital Tübingen, Germany, explained that the EVI is legally constituted under European law as a European Economic Interest Grouping, with a defined aim of safeguarding the procedures for high-quality vision research throughout Europe and worldwide.

The objectives of the EVI include improving coherence and coordination and reducing fragmentation of European vision research within the EC by facilitating and coordinating basic and clinical research activities, and providing organisational resources and funding on demand for detailed and high quality research. With the help of an appointed core group of European academic vision researchers and expertise from public institutions and private enterprises, the unified management and decision-making structure provides advice and guidance in vision research on a supranational level.

EVI members have access to a high-qualified European research infrastructure through the high level of integration and coordination with allied national and international research and patient organisations involved in the area of vision research. The researchers believe that their research will lead to sight-saving treatments, reduce visual impairment and blindness, and improve the quality of life for people of all ages.

For more information on EVI-Genoret visit www.evi-genoret.org.

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