Project number : **LSHG-CT-2005-512036**

Project Acronym : **EVI-GENORET**

Project title: **Functional Genomics of the Retina in Health and Disease**

Instrument: **Integrated Project**

Publishable Final Activity Report

Period covered: **01/04/2005 to 31/03/2009**

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Start date of project: **01/04/2005**

Duration : **4 years**

Project coordinator organisation name: **European Vision Institute EEIG, Rue du Trône, B-1050 Bruxelles;** ***info@europeanvisioninstitute.org***

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1. Project Execution

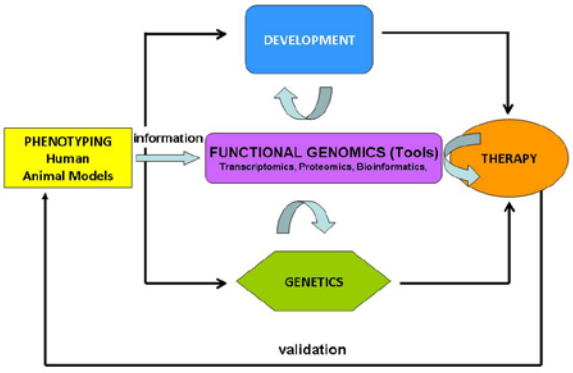
1.1.1 Introduction and Project Summary

Over 15 million people in Europe have impaired vision and 2.7 million people are totally blind. The number of people suffering from serious visual impairment is constantly growing, a phenomenon related (at least in part) to the rapidly aging population. This paradox also reflects the fact that mechanisms underlying the evolution of the retinal disorders towards blindness are yet scarcely understood and therapeutic strategies to stemming or repair retinal damage are insufficient.

Understanding the genetic causes of blindness is critical to reinforce the prevention of vision loss, as the commonest causes of blindness: age-related macular degeneration (AMD), retinitis pigmentosa and numerous rarer inherited blinding diseases are likely associated with mostly unknown genetic and modifying factors. Saving sight through understanding the genetics and cellular mechanisms underlying the retinal development, maintenance and function was the overarching goal of the **EVI-GENORET** project.

The **EVI-GENORET** project is an **Integrated Project** funded by the European Commission in the frame of the Sixth Framework Programme's 'Life sciences, genomics and biotechnology for health' thematic area (**Contract Number LSHG-CT-2005-512036**). The project was started on 01/04/2005 and was concluded on 31/03/2009, for a total duration of four years.

1.1.2 Project Objectives



The **EVI-GENORET** project aimed at building-up understanding of the fundamental molecular and cellular biology of the retina, of its development and the way it is perturbed by genetic mutations, environmental factors and age. For this purpose, a multidisciplinary approach with five interacting components from academic and industrial partners (phenotyping, genotyping, functional gene analysis, development and therapeutic strategies) has been implemented (illustrated in the Figure).

To obtain this aim, the following objectives have been established:

1) To acquire and integrate information on gene function through numerous human, animal and *in vitro* models of retinal degeneration and developmental studies
2) To standardize and analyze this information using databases, bioinformatics, transcriptome, proteome and expression studies
3) To validate the information *via* bioinformatic and functional assays
4) To generate conceptual and biological models of genes, genes networks and pathways relevant to retinal health and diseases

5) To design novel cell-based and genomic-based therapeutic strategies to preventing blindness

Within these objectives and to be able to spanning the research from biology of vision to fight against retinal blindness, an elaboration of accurate clinical and molecular classification of retinal degenerations has been implemented, together with the identification of novel retinal genes and pathways controlling their functions. The ultimate objectives of **EVI-GENORET** was to generate conceptual and biological models of genes, gene networks and pathways relevant to major the functions involved in the retinal health and disease to optimize the quality of science and care in retinal degeneration.

1.1.3 Consortium

In the **EVI-GENORET Consortium,** 21 academic, 2 industrial partners and 1 patient organisation formed 5 interacting components to establish working platforms, share tools and knowledge within and outside the academic community.

1 European Vision Institute **EVI** Belgium
2 Prof. Sahel **INSERM** France
3 Prof. Bhattacharya **UCL** UK
4 Prof. Zrenner **UTUB** Germany
5 Prof. Cunha-Vaz **AIBILI** Portugal
6 Dr. Banfi / Prof. Marigo **TIGEM** Italy
7 Dr. Roepmann **UMC** Netherlands
8 Prof. van Veen **ULUND** Sweden
9 Dr. Vescovi **BICOCCA** Italy
10 Prof. Van Heyningen **MRC** UK
11 Dr. Ueffing **GSF** Germany
12 Prof. Gal **UKE** Germany
13 Dr. Grimm **UZH** Switzerland
14 Dr. Scholl / Prof. Holz **UKB** Germany
15 Prof. Humphries **TCD** Ireland
16 Ms. Fasser **RET.INT** Switzerland
17 Dr. Mueller **FZJ** Germany
18 Dr. Tuohy **GENABLE** Ireland
19 Prof. Chakravarty **QUB** UK
20 Dr. Poch **CERBM-GIE** France
21 Dr. Thiam **GENOWAY** France
22 Dr. Ayuso **FJD.UTF** Spain
23 Dr. Kamakari **NKUA** Greece
24 Inserm-Transfert **IT** France

These 24 partners were coming from 12 different European countries: Belgium, France, United Kingdom, Germany, Portugal, Italy, The Netherlands, Sweden, Switzerland, Ireland, Spain and Greece.

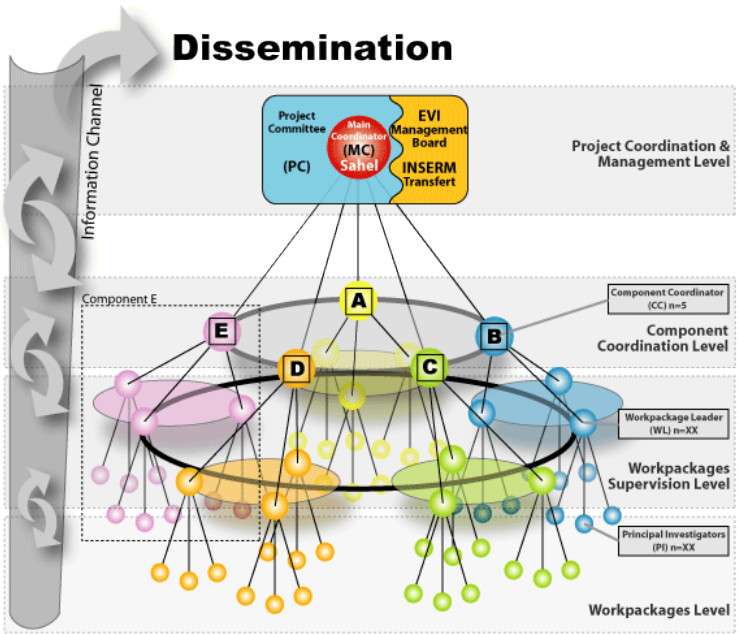
The **scientific coordinator** (Prof. José Sahel, INSERM, UPMC, Institut de la Vision) of the project was responsible for over-seeing the implementation of the work plan. He acted as the primary contact between the consortium and the European Commission.

Because of the size of the consortium and the complexity of the proposal, the project management has been sub-divided in 2 activities, *i.e* scientific management (O. Lorentz, Inserm Transfert) and administrative and financial management (T. Wheeler Schilling, EVI).

Both the scientific and administrative managers worked in close collaboration and supported the Scientific Co-ordinator in maintaining the scientific goals and the administrative structure of the EVI-GENORET.

1.1.4 Research Design and Methods

a. Research design



In order to cover all aspects of the scientific programme and to cope with the complexity of coordinating such a large number of teams, the consortium has been subdivided into the following coordinated components with corresponding component leaders:

Components

- A Phenotyping / *CC: Zrenner*
- B Development / *CC: Van Heyningen*
- C Genetics / *CC: Bhattacharya*
- D Therapy/ *CC: Moss*
- E Functional genomics / *CC: Ueffing*

Nineteen Work Packages (WP) have been established and distributed as follows in the corresponding component, each WP having a specific scientific objective and work plan:

A Phenotyping

WP1: Phenotyping, tissue and DNA collection in patients with age-related macular disease (AMD)
WP2: Phenotyping of Monogenic Retinal Dystrophies (MRD)
WP3: Assessment of retinal function and morphology and evaluation of therapeutic strategies in animal models of retinal degeneration

B Development

WP4: Expression of key developmental regulators in retina and stem cells
WP5: Derivation and characterization of stem cells with therapeutic potential
WP6 : Functional studies of eye development pathways in model systems

C Genetics

WP7: Genetic mapping and gene identification of a novel monogenic retinal dystrophy
WP8: Role of retinal pigment epithelium (RPE)-expressed genes in monogenic and complex retinal disorders, including age-related macular degeneration

D Therapy

WP10: Functional genomics of the host retinal response to cell and tissue based therapies
WP11: Therapeutics using agents derived from functional genomics
WP9: Strategies for controlling gene expression

E Functional Genomics

WP12: Transcriptional regulation in healthy and degenerating retinal tissue
WP13: Proteomic analysis of retinal tissue
WP14: Identification of genes of interest in order to design models
WP15: Functional analysis and functional assays

The following WPs were mostly involved in transversal activities like management and quality assurance of the project:

WP16 Development of methods and standard operation procedures (SOPs) for handling and processing biological materials and data, quality assessment
WP17 Management and dissemination
WP18 Establishment of an internal ethics review board
WP19 Training activities

The 5 components, superordinated over the respective Workpackages have been responsible for the following workflows, described here below:

A Phenotyping

Translation knowledge of pathological conditions into clues for disease mechanisms, gene identification and therapeutic strategies, by in depth analysis and establishment of standards for phenotyping these conditions, thereby allowing improved genotyping**.**

B Development

Identification of molecular and cellular differentiation pathways involved in normal and disease-associated retinal development, using model organisms.

C Genetics

Identification and functional analysis of disease-associated genes in humans using positional cloning, linkage analysis, – i.e. experimental genetic approaches and *in silico* analysis with model system validation.

D Therapy

Through new strategies for controlling gene expression, analysis of host response to therapy and identification of novel preventive therapeutic mechanisms.

E Functional Genomics

Establishment of standardized protocols, utilization of bioinformatic and laboratory methods for analysis of gene regulation and transcriptome complexity, assessments of the retinal proteome and protein interactions.

The integration of the workflows has been enforced by periodic consortium and component meetings and by the establishment of a comprehensive and integrated database (s. for further details in 4. Project Website and Logo) where all information on models, diseases, phenotypes, functions, pathways has been implemented by the contributing groups and related to individual genes as well as networks of genes. Continuous quality assessment was a key element to the validation of the database. For the whole consortium was possible during the 48 months to follow the development of the project and its outcomes.

Here below, illustrated are the respective leaders of the 5 components

b. Methods

A wide variety of research methods have been employed to achieve the objectives planned. These include transcriptome, proteomics, protein-interactome analyses, functional cellular and biochemical assays, bioinformatics and model organisms to analyze patterns of gene expression and gene function in retinal development, normal function and degeneration. Some of the most important methods and techniques are listed below:

* *In vivo* methods for the assessment of retinal function and morphology, including native scanning laser ophthalmoscopy (SLO), fundus autofluorescence analysis, angiography, advanced Ganzfeld-electroretinography (ERG), double and bright flash ERG and multifocal ERG.

* To investigate the visual acuity in photopic and scotopic conditions, behavioral technique (optomotor response) was implemented.

* Spectral-domain optical coherence tomography (OCT) was adapted for its use in small animal models. Moreover, a multielectrode array to record ganglion cells acting as biosensors of the retinal cell activity was used.

* Different transgenic mouse models for retinal diseases have been generated and analyzed successfully (PRPF31, RdCVF, IMPDH1 knock out animals).

* Stem cell biology methods for isolation and differentiation of suitable cell types for transplantation have been used in chick and mouse.

* Gene identification and gene mapping has been done through a combination of approaches involving functional genomics, candidate gene analysis and positional cloning.

* Concerning elaboration of therapeutic strategies, the sophisticated RNA interference (RNAi) technology was used.

1.2.1 Project Results and Achievements

1.2.2 Component A: Phenotyping

A key achievement of this component was the development and implementation of a pan-European central phenotype-genotype patient database available to all EVI-GENORET partners. Retinobase is a Java-script based comprehensive relational database specifically dedicated to retinal transcriptomics data for age-related macular disease (AMD) and monogenic retinal dystrophy (MRD). The phenotyping database was an integral part of the consortium database. A routine search and a tool to upload electronic data from electrophysiological and perimetry data were implemented. Customized interfaces for pre-existing databases in Bonn, Madrid and Belfast were developed. Data sets of thousands of

patients were collected. Training sessions for the usage of the database were provided. Furthermore, a special paper bound case report form (CRF) was developed serving as common basis to report on patients and setting standards for best practice counseling.

Moreover, standard operating procedures (SOPs) have been developed to bring up clinical examinational routines to a high and well comparable level. Distinct major achievements have been obtained, notably:

i) identification and characterization of target genes through the analysis of distinct transcriptomics experiments,
ii) creation of a unifying gene identity card relating very diverse information concerning retinal target genes or
iii) design of Retchip, the retinal-specific low-throughput micro-array.

EVI-GENORET is the first European project to build a database fostering integrated research on hereditary and age related retinal diseases. Retinobase now enables the European scientific community working on the retina to integrate their data towards comprehensive meta-analysis.

This bioinformatics tool was successfully used to publish the analysis of two mouse models of inherited retinal degenerations, the rd1 and the Nxnl1-/- mouse. It is also used for analyzing the Prff31 knock-in mouse and even more importantly, the retinal detachment using human surgical specimens. By giving easy access and display to the distinct treatments and results, Retinobase allows the biologist to visualize and understand the limits and inconsistencies inherent to the high throughput analysis and facilitate the introduction of the biological expertise and knowledge in the analysis. All in all different transgenic mouse models for retinal diseases have been generated and analyzed successfully (PRPF31, RdCVF, IMPDH1 knock out animals).

1.2.3 Component B: Development

Molecular insight into disease is a major step towards developing better management and therapy. The most common retinal anomalies are, however, poorly understood at this level. Component B focused on matters of eye development and provided significant proofs about the role of genes implicated in both developmental and postnatal (or even later in life) control. This was done mainly in model systems (mouse and chick) but also in human eye malformations with retinal anomalies as part of the phenotype. Various contractors with diverse but complementary skills combined their efforts in the field of stem cell biology and the isolation and differentiation of suitable cell types for transplantation. The work on stem cells was carried out in chick and mouse. The areas explored included definition of suitable starting cell types from different sources and culture conditions for generation of cells that may be useful for transplantation in the retina. In chick, the generation of retinal precursor cells under the influence of CNTF (Ciliary NeuroTrophic Factor) was explored. Cell types were analyzed by marker immunohistochemical and RNA-level expression studies. Final testing of a few mouse precursor cell samples was studied by retinal injection.

Clear methodological progress have been done, implementing protocols for detection of specific gene products by RNA *in situ* hybridization of immunohistochemistry on whole-mount explants, tissue sections or *in vitro* cultures of retinal tissue. Expertise and practical training in this matter have been provided to the members of the project. Characterization the

RNA and/or protein expression patterns of several genes implicated as major determinants of eye development, both at prenatal and postnatal stages have been done, specifically focused on Pax6 and Sox2; the retinoic acid receptors (Rara,b,g), the orphan receptor Rorb, and the retinol dehydrogenase Rdh10; several transcription factors including Vax1 and 2. These experiments have been complemented by analyses in specific mutants (e.g. 20b: Rara, Rorb knockout mutants; Raldh1/3compound mutants; 6b: Vax2 mutants).

As retinoic acid is a key regulator of development eye and Vitamin A deficiency is a well known cause of retinal damage, special component of the developmental studies explored the role of retinoic acid handling enzymes (Aldh1a1, Aldh1a2, Aldh1a3 and Cyp26a1) during development in mouse knockout models generated by within the consortium. A non viral approach was developed through an effective ex vivo transfection of rodent embryonic and post natal retinal explants by electroporation. Using this technique, we were able to successfully modify the fate of retinal progenitors by either ectopic expression of specific genes or by silencing gene expression using a plasmid able to transcribe short hairpin RNA (shRNA).

Molecular characterization of adult ciliary body derived retinal stem cells (RSC), sub-ventricular zone derived neural stem cells (NSC) and retinal progenitors have been accomplished. We believe that this is a fundamental task for the evaluation of stem cell potentials as cell source for therapeutic strategies of the degenerating retina.

1.2.4 Component C: Genetics

Specifically, the component objectives were as follows:

- ✓ Mutational analysis of novel functional candidates in our cohort of RD patients.
- ✓ Genetic testing of known adRP loci in new dominant RP families.
- ✓ Potential mapping of new loci for retinal dystrophies including autosomal dominant and autosomal recessive retinitis pigmentosa and Leber congenital amaurosis.
- ✓ Potential identification of new genes for retinal degeneration.
- ✓ Functional characterization of novel RP and LCA genes.
- ✓ High throughput mutation screening including construction and validation of diagnostic microarray DNA chips. All these objectives have been fulfilled by the partners involved in the Genetics Component.

Component C, including WP7 and WP8, had the overall responsibility for the genetic mapping, identification and characterization of novel genes for autosomal dominant and autosomal recessive retinal degeneration (RD). In parallel component C partners have also collected DNA samples from clinically well-characterized patients to establish large RD panels for mutation screening. Important novel RD genes have been identified in this component, and future candidates will yield from the continuing ciliopathy-associated network dissection. A novel Joubert syndrome-associated protein (CC2D2A) has been identified in collaboration with WP13. Given the extensive phenotypic overlap of the clinical features of the ciliopathies, most ciliopathy genes are also candidate RD genes and need to be incorporated in future gene hunting approaches.

Moreover due to the availability of a known rhodopsin mutation chip, the partners of component C reached a consensus that a different chip with the potential to detect mutations in known genes in Leber Congenital Amaurosis (LCA) patients is extremely relevant. This is also based on the fact that preliminary gene therapy trails may involve the LCA patients with RPE65 gene mutations and other gene mutations (such as RDH12) associated with LCA may become subsequent targets for clinical trials.

The constructed chip can provide a simple and inexpensive means of identifying the region of the sequence of interest where a mutation resides. Direct sequencing of the specific identified DNA region would be employed subsequently, in order to characterize the mutation. The method was characterized by significant advantages, such as being straightforward to use and efficient in identifying novel mutations, without the requirement of state-of-the-art detection/analysis software. Furthermore, the method was/is cost-effective, especially when applied in multi-exon genes, as sequencing of the entire coding region is unnecessary. Experimental approaches that directly addressed retinal function have picked out genes that were very good candidates for retinal diseases. The genetic loci and the genes responsible for retinal degeneration we have identified so far (eg. EYS and TOPORS) are novel and have not been reported by any other group or laboratory outside our consortium.

1.2.5 Component D: Therapy

Concerning the therapeutic component, EVI-GENORET consortium worked on the development of treatment strategies on the basis of the highly sophisticated RNA interference (RNAi) technology, comprising strategies for controlling gene expression, investigating the ways in which a diseased retina responds to therapeutic intervention and utilizing functional genomics as the source of new therapeutics for retinal disease. RNAi-based gene silencing procedures for rhodopsin, peripherin and IMPDH1 transcripts were successfully developed and validated *in vitro*. It was shown that following AAV-mediated sub-retinal delivery of a mutant human IMPDH1 gene in mice an aggressive retinopathy is induced. Co-delivery of shRNA molecules designed to ablate the human (and mouse) transcript resulted in extensive protection of photoreceptor structure and viability at a point where, in the absence of the shRNA suppressing molecules, the photoreceptor cells are completely destroyed.

Major achievements include the demonstration that exogenous application of RdCVF in a rat model of retinal degeneration not only protected retinal morphology, but most importantly also retinal function. This is of high relevance since other neuroprotective factors (e.g. CNTF) were shown to strongly and negatively influence retinal function.

In addition, several transcription factors were identified which may control expression of RdCVF and which may thus be potent targets for an artificial regulation of RdCVF gene expression using exogenous compounds targeting the activity of these transcription factors.

Furthermore, the application of the high content screening developed to identify RdCVF enabled the characterization of one fraction of Fructus Barbarum which was capable to protect retinal cells in an *in vitro* assay. This fraction most likely contains a compound with a potent neuroprotective activity.
The genetic inhibition of van Hippel Lindau (VHL) protein in photoreceptors cells led to the stabilization of HIF-alpha proteins and the activation of STAT3 in the normoxic retina.

In addition, genes shown to be differentially regulated by hypoxic preconditioning in wild type mice were similarly regulated in the normoxic VHL knockdown retinas. This is a major achievement since it provides proof of the principle to mimic hypoxic conditions in normoxia and is also an additional step in understanding the pathogenetical role of oxidative stress in retinal degeneration.

1.2.6 Component E: Functional Genomics

Systematic genomic analyses towards characterization and validation of pathways, networks and targets implicated in hereditary retinal degenerations were in the focus of the Functional gene analysis component. Survival and death of photoreceptors in degenerative diseases of the retina is controlled by a multitude of genes and endogenous factors. Some genes may be involved in the degenerative process itself and cause retinal degeneration upon mutation, whereas others may be part of an endogenous defense system. This is why the EVI-GENORET members concentrated on both, mechanisms of retinal degeneration and mechanisms of protection. Mutations causing retinal degeneration were analyzed on a systems level to reveal interrelationships between affected and non-affected genetic loci, as well as interactions within functional protein networks to determine the risk and penetrance of disease. Standardized experimental and operation procedures (SOPs) have been established for collection of biomaterial and human specimens, and generation of samples for genomic analysis. Data and biological pictures have been organized and indexed by portable standard informatics scripts and programs have been developed and distributed towards comprehensive data gathering and integration. A relational information network, RETSCOPE, facilitating compilation of complex data-set, biological pictures and experimental protocols was generated. This database served as a bioinformatics backbone of EVI-GENORET allowing comprehensive analysis of data by classical and original clustering programs, the comparison, cross-validation and evaluation of the data through in depth mining of public transcriptomic databases and transcription regulation predictions generated by comparative genomics (i.e. phylogenetic footprinting).

Photoreceptor protection *via* rod derived cone viability factor (RdCVF) was a main topic of research within the project. With RetChip a thematic oligochip array for genes of interest for retinal research was generated, allowing the analysis of mRNA expression patterns from retinal tissue in a SOP based work-flow. Tissue and cell-specific expression in the retina were studied at the level of certain human gene promoters (CNGA3, CNGB3, RDH12 and OPA1). Two of these promoters were characterized in detail in *in vitro* and *in vivo* systems which allowed the identification of:

i) alternative transcription initiation sites and their use in different retinal cell types,
ii) sequence segments that enhance or suppress transcription and
iii) specific transcription factors directly involved in the regulation of these genes.

Transcriptional regulation in healthy and degenerating retinal tissue has focused on the analysis of transcriptional regulation patterns and of regulatory mechanisms concentrating on the Rd1 mouse model. This work resulted in a comprehensive data warehouse on transcriptional pattern associated with normal mouse retina development and the temporal development of transcriptional patterns associated with retinal degeneration.

Mapping of transcription initiation and termination sites and identification of promoter sequences for selected cone photoreceptor genes has been another major activity elaborated. Transcriptional patterns associated with the onset and progression of retinal degeneration in the Rd1 mouse have been systematically studied and analyzed. Lebercilin, a new gene associated with Leber's Congenital Amaurosis, was identified and characterized as a ciliary protein involved in protein transport processes between inner and outer segment of photoreceptors.

Several groups within EVI-GENORET focussed on the role of Müller glia cells in neuroprotection of photoreceptors. It has been demonstrated that leukemia inhibitory factor (LIF) extends the lifespan of injured photoreceptors *in vivo* in two models of retinal degeneration. Several new neurotrophic molecules were identified further establishing Muller cells as major players that control an intrinsic program of protective mechanisms to support photoreceptor cell survival and to preserve vision in the injured retina. Proteomic expression profiles of discrete retinal cells and compartments as well as large sets of protein-protein interactions mainly focusing on photoreceptor cells were generated.

Major progress was made to quantitatively assess the impact of mutations as found in patients with retinal degenerations on protein interaction and function. To our knowledge, this is the first time that the impact of mutation on a given protein quantitatively on a proteomic scale was assessed.

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Within the frame of the project, more than 30 training courses and 45 symposia or expert talks have been held. Tight relationship with patient organizations has been built helping the tracking of patients for clinical studies and facilitating the dissemination of treatment and basic educational materials to the patients.

1.3.1 Project Website and Logo

The EVI-GENORET Database and Secure Website is mainly dedicated to integrate the large amount of biological and clinical heterogeneous data provided by the consortium members. First the **database centralizes and organizes the documents** related to SOPs, SEPs and various lab experiment resources such as antibodies, primers, DNA samples, etc.

The system wants to act as a data warehouse for **patient data** as well as a node connecting remote patient databases hosted in other consortium centers. Tools were developed to integrate, as automated as possible, the heterogeneous formats of clinical data provided by different clinicians. This concerns for example the integration of Excel files (JavOO) or the direct connection to distant databases as well as the creation of complex relational databases allowing cross queries within all available information.

Many specific developments have been set up to integrate and interconnect all components of the consortium. Starting from ImAnno, the *in situ* hybridization image annotation tool created for the component B Development for the study of the mouse embryo development, we are able to query or diffuse the information of their 1667 genes all over the EVI-GENORET Database. In the same way the proteomics and transcriptomics information provided by the component E Functional Genomics has been be dynamically incorporated in the data network. A special effort has been done to analyze and verify the codification and description of the mutations of the LCA genes from the component C: Genetics.

GenoretGenes has been developed within WP14 and centralizes all information about “retinal genes”. This database is totally integrated and acts as a gene knowledge base for the EVI-GENORET Database. In the same way most of the functionalities provided by RetinoBase, a retina specific transcriptomic database developed within RetNet and WP12, are also directly available within the EVI-Genoret Database. As RetinoBase became more and more popular it was necessary to integrate ownership and access rights for the sensitive data hosted in the database.

All these tools are available through the **EVI-GENORET Database Website.** During the progression of the project the system was adapted taking into account the volume of data and the increasing complexity of their interconnections. So, to provide an attractive and user friendly interface, a new design of the website was developed.

The EVI-GENORET Database users have nowadays the possibility to **query, filter and process** the large amount of heterogeneous data provided by the web site.

A new tool, called **PipeWork**, has been developed allowing the user to create, manage and evaluate his own flowcharts. It provides a set of processing elements which can be easily connected together by the user as on a blackboard. Each PipeWork can be stored, retrieved, updated, splited, and reused for any other similar query. In addition it is possible to merge

several PipeWorks by simply connecting outputs of one to the adequate inputs of another. Of course, reuse and sharing should allow PipeWork to be a great collaborative tool.

The Genoret Database is a big and complex system with various topics, entities and concepts. In order to explain its functions and keep track of its architecture we created **WikiGenoret**, a MediaWiki powered "Wiki". It contains today around 100 pages.

The **EVI-GENORET Database and Secure Website** was developed also considering the following aspects:

1) the database was designed also to handle "administrative" parts of the project, the function of a scientific and administrative documents exchange platform, wanted to be the central reference knowledge sharing tool of the project.

2) to develop many add-ons, not only after a specific request of the consortium members, but also anticipating their needs.

Beside the project management tools **very useful tools have been developed and promoted** such as datafiles upload, online deliverables and reporting repositories, articles and publications sharing, forums, training and meeting organisation and reporting.

EVI-GENORET Database and Secure Website can be accessed (only with a password) under the following URL http://www-genoret.u-strasbg.fr/genoret/

For further details and requests please contact Raymond Ripp (Raymond.Ripp@ igbmc.fr) or Olivier Poch (Olivier.Poch@igbmc.fr)

1.4.1 Conclusions

EVI-GENORET was the largest consortium ever funded by the European Commission in the field of vision research combining synergistic efforts of researchers, clinicians, industrials and patient organizations.

This project obtained unique data resulting from population genetics, clinical and experimental phenotyping, biology of development and functional genomics. The successful integration of these data in a new type of database provides unique knowledge and clues to identify new therapeutic targets aiming at developing new therapies for the devastating retinal diseases.

Equipped with the EVI-GENORET database, researchers will be more effective in translating fundamental findings into an improved classification of disease in both clinical and biological terms, and identifying novel therapeutic targets and treatment strategies.

During the lifespan of this project, existing collaborations have been strengthened and new collaborations have been initiated, demonstrating that EVI-GENORET has played a key role in structuring and promoting the European Vision Research Community.

2 Dissemination and use

Name: T. Wheeler Schilling, O. Lorentz ; Participant:1, 24 ; Work Package: WP 17

Planned/actual Dates	Type	Type of audience	Countries addressed	Size of audience	Partner responsible /involved
11-15/06/2006	ISCEV	Research	**World**	300	24
6-10 /09/2006	ISCOB meeting	Research	**World**	300	24
24/09/ 2006	D.O.G. (Berlin, Germany)	Research	**EU**	150	1 and 24
November 2006	Posters	Research	**Worldwide**	150	24
2/2007	Flyers	Research	**EU**	n/a	1, 24
2/2007	EVi-Genoret Penballs and Gimmick	Research/General Public	**EU**	250	1
Potsdam March 2007	Meeting and Course	Research	**International**	100	1
2-3 / 07 / 2007	EVI-GENORET / EUROHEAR	Research / General public/ EU representatives	**Europe**	200	24
Regularly running	Direct e-mailing: Regular Newsletter	Researcher / Clinicians	**International**	250	**1**
May 2007 ARVO / USA	Presentation of the EVI-Genoret project	Research	**World**	300	24
July, 2007, Paris	Hearing and Seeing Meeting- Press conference	Research, Clinicians	**International**	40	24
2-3 / 07 / 2007	Conference / Media briefing EVI-GENORET / EUROHEAR	Research / General public/ EU representatives	**Europe**	200	24
July 2007	VIDEO DVD production	Research / General public / EU Commission/ Media	**International**	unknown	24
March 2008	EVI-Genoret newsletter	Research	**EU**	unknown	1
April, 2008	ARVO	Research	**International**	>1000	1, 24
November 2008	Lifecompentence portal	Research / General public / EU Commission/ Media	**International**	Unknown	1, 24
February 2009	**Online news**	Research / General public / EU Commission/ Media	**International**	Unknown	1, 24

Planned/actual Dates	Type	Type of audience	Countries addressed	Size of audience	Partner responsible /involved
March 2009	EVI-GENORET final meeting	Research / Commission	**EU**	100	1, 24

Name: S. Aymé ; Participant:2a ; Work Package (WP): WP17, WP18, WP11, WP18

Planned /actual Dates	Type	Type of audience	Countries addressed	Size of audience	Partner responsible /involved
2005	Educational materials concerning research with animal and human subjects	Young researchers	EU or EVI Genoret partnering countries	-	WP 18
2006	Publication of educational materials on www.orpha.net (Orphanet, Rare Disease Information Portal) and www.evi-genoret.org	Orphanet and EVI-GENORET website audiences	EU or EVI Genoret partnering countries	-	WP 18
2007	Presentation at Central Training Course Potsdam 2008 "Ethics in medical research"	Participants of the ProRetina Research Colloquim	EVI Genoret partnering countries	50	WP 18 and WP19
2008	Publication of educational materials on www.orpha.net	Orphanet and EVI-GENORET website audiences	EU		WP 18

Name: F. Behar-Cohen ; Participant:2b ; Work Package (WP):WP9, WP17

Planned /actual Dates	Type	Type of audience	Countries addressed	Size of audience	Partner responsible /involved
3-4 March, 2005	EVI-Genoret Kick-off Meeting	Research	**International**	100	2b
13-15 March, 2006	1st EVI-Genoret Annual Meeting	Research	**International**	100	2b
18-21 March 2007	EVI-Genoret Midterm Review eeting	Research	**International**	100	2b
10-11 March, 2008	3rd EVI-Genoret Annual Meeting	Research	**International**	100	2b
5-6 March, 2009	4th EVI-Genoret Annual Meeting	Research	**International**	100	2b

Name: O. Goureau ; Participant: 2c ; Work Package (WP): WP5 and WP6

Planned /actual Dates	Type	Type of audience	Countries addressed	Size of audience	Partner responsible /involved
2007	**Conferences** Oral presentation (ICER meeting, 11-2006, Argentina)	Research	International	500	2
2007	**Posters** May 2007, ARVO meeting, (Florida, USA)	Research	International	1000	2
2008	**Posters:** October 2008, ICER meeting, Beijing	Research	International	500	2

Name: C. Hamel ; Participant:2d ; Work Package (WP): WP7, WP15

Planned /actual Dates	Type	Type of audience	Countries addressed	Size of audience	Partner responsible /involved
3-4 March, 2005	EVI-Genoret Kick-off Meeting	Research	**International**	100	2b
13-15 March, 2006	1st EVI-Genoret Annual Meeting	Research	**International**	100	2b
18-21 March 2007	EVI-Genoret Midterm Review eeting	Research	**International**	100	2b
10-11 March, 2008	3rd EVI-Genoret Annual Meeting	Research	**International**	100	2b
5-6 March, 2009	4th EVI-Genoret Annual Meeting	Research	**International**	100	2b

Ben Salah S, Kamei S*, Sénéchal A*, Lopez S, Bazalgette C, Bazalgette C, Malrieu-Eliaou C, Zanlonghi X, Hamel CP (2008). Novel KCNV2 mutations in cone dystrophy with supernormal rod electroretinogram. Am J Ophthalmol. 2008 Jun;145(6):1099-106. Epub 2008 Apr 9.*

Name: Josseline Kaplan, MD, PhD; Participant: 2e; Work Package (WP): WP7 Component C

Exploitable Knowledge (description)	**Exploitable product(s) or measure(s)**	**Sector(s)** of application	Timetable for commercial use	Patents or other IPR protection	**Owner** & Other Partner(s) involved
Comprehensive survey of NPHP6/CEP290 mutations in Leber congenital amaurosis (LCA) and genotype-phenotype correlations		Medical	None	None	2e
Identification of a novel LCA gene		Medical	None	None	2e

Perrault I, Delphin N, Hanein S, Gerber S, Munnich A, Kaplan J, Rozet JM. Is there a reason to study genes responsible for Joubert syndrome (JBTS) or Senior Loken syndrome (SNLS) in patients affected with isolated Leber congenital amaurosis (LCA)? Article in preparation.

Papon JF, Perrault I, Coste A, Hanein S, Delphin N, Gerber S, Kaplan J, Rozet JM, Escudier E. Nasal ciliary abnormalities in LCA patients with CEP290 mutations contrasting with the absence of clinical expression. J Med Genet 2009, submitted.

Kaplan J. Leber congenital amaurosis: from darkness to spotlight. Ophthalmic Genet. 29:92-8.2008.

Hanein S, Perrault, I, Gerber S, Delphin N, Benezra D, Shalev S, Carmi R, Feingold J, Dufier JL, Munnich A, Kaplan J, Rozet JM, Jeanpierre M. Population history and infrequent mutations : how old is a rare mutation ? GUCY2D as a worked example. Eur J Hum Genet 16:115-23, 2008.

Name: T. Leveillard ; Participant:2f ; Work Package (WP): WP11, WP12

Planned /actual Dates	Type	Type of audience	Countries addressed	Size of audience	Partner responsible /involved
3-4 March, 2005	EVI-Genoret Kick-off Meeting	Research	**International**	100	2b
13-15 March, 2006	1st EVI-Genoret Annual Meeting	Research	**International**	100	2b
18-21 March 2007	EVI-Genoret Midterm Review eeting	Research	**International**	100	2b
10-11 March, 2008	3rd EVI-Genoret Annual Meeting	Research	**International**	100	2b
5-6 March, 2009	4th EVI-Genoret Annual Meeting	Research	**International**	100	2b

Retina Research Colloquium “Rod-derived Cone Viability Factor, on the way for a therapy of retinitis pigmentosa” Postdam April 7th 2006

Séminaire annuel des Professeurs de Biochimie et Biologie Moléculaire. « Identification de Rod-derived Cone Viability Factor, un espoir thérapeutique pour les dégénérescences rétiniennes » Evian May 11th 2006

CRP Santé « RetChip, A retinal cDNA microarray ». Luxembourg May 12th 2006

Hôpital Salpetrière « Analyse protéomique de la rétine de souris rd1, un modèle de dégénérescence rétinienne ». Paris May 18th 2006.

International Society for Ocular Cell Biology. “Neuroprotection of Cone Photoreceptors” Cambridge September 2006

International Congress of Eye Research “PHOTORECEPTOR INTERACTIONS IN RETINITIS PIGMENTOSA: THE ROD-CONE VIABILITY FACTOR” Buenos Aires, October 2006

RETNET annual meeting “Functional Genomics of the Retina in Health and Disease” Venezia, November 20th 2006

EVI-GENORET therapeutic component meeting “Therapeutics using agents derived from funtional genomics” Tubingen Novemnber 29th 2006

Pasteur Institute “Rod-derived Cone Viability Factors defines a novel family of trophic factors” Paris December 5th 2006

Name: F. Mascarelli ; Participant: 2g ; Work Package (WP): 12

Planned/actual Dates	Type	Type of audience	Countries addressed	Size of audience	Partner responsible /involved
3-4 March, 2005	EVI-Genoret Kick-off Meeting	Research	**International**	100	2g
13-15 March, 2006	1st EVI-Genoret Annual Meeting	Research	**International**	100	2g
ECONAG 2006: 27-30 Nov 2006	Poster	Research	**AUSTRIA**	400	2g
18-21 March 2007	EVI-Genoret Midterm Review Meeting	Research	**International**	100	2g
ARVO: 6-10 May 2007	Poster	Research	**USA**	1000	2g
10-11 March, 2008	3rd EVI-Genoret Annual Meeting	Research	**International**	100	2g
5-6 March, 2009	4th EVI-Genoret Annual Meeting	Research	**International**	100	2g

Name: S. Picaud ; Participant:2h ; Work Package (WP): WP3

Exploitable Knowledge (description)	**Exploitable product(s) or measure(s)**	**Sector(s)** of application	Timetable for commercial use	Patents or other IPR protection	**Owner** & Other Partner(s) involved
1. New Eye examination device	equipment	Medicine	2008-2009	A patent application is under investigation	**2h**
1. Prevention of Vigabatrin toxicity		1. Medical		A patent application was filed	**Owner: Picaud**

Posters & Talks
Kolomiets B, Sahel JA and Picaud S. Single-unit activity and visual response characteristics in retinal ganglion cells of ex vivo retina recorded using 3D MEA microelectrode array recordings in mice MEA 2006 Proceedings, Edited by BIOPRO Baden-Wuerttemberg. (2006) p95-96.
Kolomyets B, Sahel JA, Picaud S. Analysis of the ON light responses in retinal ganglion cells from isolated mouse retina using multi-electrode recordings. ARVO annual meeting 2006, poster 3108.

Publications
Guyomard J.-L, Linderhom P., Salzman J., Paques M., Simonutti M., Bertrand D., Renaud P., Safran A., Sahel J., Picaud S. *Evolution of the Electrode Impedance on Subretinal Implants in Dystrophic P23H Rats. ARVO annual meeting 2006, poster 1072.*
Picaud S., Kolomiets B., Sahel J.A. *Multi-electrode array recording: A technique to assess pharmacological effects on retinal information processing by recording ganglion cell light responses in the ex vivo retina. ISOT annual meeting, Germany, 2006.*
Paques M, Guyomard JL, Simonutti M, Roux MJ, Picaud S, Legargasson JF, Sahel JA. *Panretinal, high-resolution color photography of the mouse fundus. Invest Ophthalmol Vis Sci. 2007 Jun;48(6):2769-74.*

Jammoul F*, Wang Q*, Nabbout R, Coriat C, Duboc A, Simonutti M, Dubus E, Craft C M, Ye W, Collins S D, Dulac O, Chiron C, Sahel J A, Picaud S. *Taurine deficiency is a cause of vigabatrin-induced retinal phototoxicity* *Annals of Neurology (2009) 65:98-107.* **equal contribution*
Guyomard JL, Rosolen SG, Paques M, Delyfer MN, Simonutti M, Tessier Y, Sahel JA, Legargasson JF, Picaud S *A low cost and simple imaging technique of the anterior and posterior segments: eye fundus, ciliary bodies, irido-corneal-angle.* *Invest Ophthalmol Vis Sci. (2008) 49, 5168-74.*
Wang Q, Jammoul F, Duboc A, Gong J, Simonutti M, Dubus E, Craft C, Ye W, Sahel JA, Picaud S *Treatment of epilepsy: the GABA-transaminase inhibitor, vigabatrin, induces neuronal plasticity in the mouse retina* *Eur J Neurosci (2008) 27, 2177–2187.*

Name: J. Sahel ; Participant:2i ; Work Package (WP): WP1, WP2, WP11, WP17

Planned /actual Dates	Type	Type of audience	Countries addressed	Size of audience	Partner responsible /involved
3-4 March, 2005	EVI-Genoret Kick-off Meeting	Research	**International**	100	2i
13-15 March, 2006	1st EVI-Genoret Annual Meeting	Research	**International**	100	2i
18-21 March 2007	EVI-Genoret Midterm Review Meeting	Research	**International**	100	2i
10-11 March, 2008	3rd EVI-Genoret Annual Meeting	Research	**International**	100	2i
5-6 March, 2009	4th EVI-Genoret Annual Meeting	Research	**International**	100	2i

Publications

Audo I, Robson AG, Holder GE, Moore AT. *The negative ERG: clinical phenotypes and disease mechanisms of inner retinal dysfunction. Surv Ophthalmol. 2008 Jan-Feb;53(1):16-40.*
Joint publication by partners: Paris, London

Audo I, Vanakker OM, Smith A, Leroy BP, Robson AG, Jenkins SA, Coucke PJ, Bird AC, De Paepe A, Holder GE, Webster AR*. Pseudoxanthoma elasticum with generalized retinal dysfunction, a common finding? Invest Ophthalmol Vis Sci. 2007 Sep;48(9):4250-6.*

Name: S. Bhatthacharya ; Participant:3a ; Work Package (WP):WP7, WP15, WP17

Planned/actual Dates	Type	Type of audience	Countries addressed	Size of audience	Partner responsible /involved
May 06, Oct 06, Nov 06	Talks, BRPS branch meetings	RP patients and family members	**UK**	30-50	3a
May 2006	ARVO Conference	Research	**International**	500+	3a
July 2006	University Meeting	Research	**Greece**	30+	3a
Nov 2006	Genetic Plan Sevelle Andulucia	Research & Lay public	**Spain**	200+	3a
Feb 2007	Keynote address, Indian	Research	**India &**	400+	3a

Planned/actual Dates	Type	Type of audience	Countries addressed	Size of audience	Partner responsible /involved
	Soc Human Genetics		**International**		
May 2007	Talk, ARVO Conference	Research	**International**	500+	3a, 4a, 4e
Oct 2007	Poster, Americal Soc Human Genetics	Research	**International**	500+	3a
July 2006	Genoret WP7 meeting	Research	**Greece**	20	3a
Oct 2006 Nov 2006 March 2006	Neurotrain meeting Retnet meeting Neurotrain & Retnet	Research Research Research	**Munich** **Venice** **Berlin**	30 40+ 50+	3a 3a 3a

Publications:

Henderson RH, Waseem N, Searle R, van der Spuy J, Russell-Eggitt I, Bhattacharya SS, Thompson DA, Holder GE, Cheetham ME, Webster AR, Moore AT. An assessment of the apex microarray technology in genotyping patients with Leber congenital amaurosis and early-onset severe retinal dystrophy. Invest Ophthalmol Vis Sci. 2007 Dec;48(12):5684-9

Chakarova CF, Papaioannou MG, Khanna H, Lopez I, Waseem N, Shah A, Theis T, Friedman J, Maubaret C, Bujakowska K, Veraitch B, Abd El-Aziz MM, Prescott de Q, Parapuram SK, Bickmore WA, Munro PM, Gal A, Hamel CP, Marigo V, Ponting CP, Wissinger B, Zrenner E, Matter K, Swaroop A, Koenekoop RK, Bhattacharya SS. Mutations in TOPORS cause autosomal dominant retinitis pigmentosa with perivascular retinal pigment epithelium atrophy. Am J Hum Genet. 2007 Nov;81(5):1098-103. Epub 2007 Sep 26.

Chakarova, C.F., Papaioannou, M.G., Khanna, H., Lopez, I., Waseem, N., Shah, A., Theis, T., Friedman, J., Maubaret, C., Bujakowska, K., Veraitch, B., Abd El-Aziz, M.M., Prescott, Q., Parapuram, S., Bickmore, W.A., Munro, P.M/G/, Gal. A/, Hamel, C.P., Marigo, V., Ponting, C.P., Wissinger, B., Zrenner, E., Matter, K., Swaroop, A., Koenekoop, R.K. and Bhattacharya, S.S. (2007).

Mutations in TOPORS Cause Autosomal Dominant Retinitis Pigmentosa with Perivascular RPE Atrophy. Am J Hum Genet, 81: 1098-1103.

Abd El-Aziz MM, Barragan I, O'Driscoll CA, Goodstadt L, Prigmore E, Borrego S, Mena M, Pieras JI, El-Ashry MF, Safieh LA, Shah A, Cheetham ME, Carter NP, Chakarova C, Ponting CP, Bhattacharya SS, Antinolo G. (2008)

EYS, encoding an ortholog of Drosophila spacemaker, is mutated in autosomal recessive retinitis pigmentosa. Nat Genet. 40: 1285-1287.

Name: Bird/Moore/Webster ; Participant:3c ; Work Package (WP): WP1, WP2,WP17

Planned/actual Dates	Type	Type of audience	Countries addressed	Size of audience	Partner responsible /involved
April 2007	Poster presentation	Research and Medicine	**USA / International**	50	3c
September 2006	Meeting / Talk	General public	**UK**	300	3c
May 2006	Talk	General public and patients	**UK**	100	3c
May 2006	Poster presentation	Ophathalmologists	**UK / International**	200	3c
April 2006	ARVO poster presentation	Research and Medicine	**International**	1000	3c
Februar 2006	Talk	Research and Medicine	**UK**	100	3c
March 2006	Lecture	Ophthalmologists	**Sweden / International**	100	3c
March 2006	Lecture	Research and Medicine	**USA / International**	200	3c
September	Lecture (Cambridge)	Research and	**UK /**	300	3c

Planned/actual Dates	Type	Type of audience	Countries addressed	Size of audience	Partner responsible /involved
2006		Medicine	**International**		
September 2006	Lecture	Research and Medicine	**UK / International**	200	3c
June 2006	Lecture (Singapore)	Research and Medicine	**Asia / International**	1500	3c
October 2006	Lecture (EVER)	Research and Medicine	**International**	500	3c
October 2006	Lecture (Newcastle)	Research and Medicine	**UK / International**	200	3c
January 2007	Lecture (Columbia University, New York)	Research and Medicine	**USA / International**	250	3c

Publications:

Audo I, Robson A, Holder G, Moore AT. The negative ERG: clinical phenotypes and disease mechanisms of inner retinal dysfunction. Survey Ophthalmol 2008 Jan-Feb;53(1):16-40

Audo I, Vanakker OM, Smith A, Leroy BP, Robson AG, Jenkins SA, Coucke PJ, Bird AC, De Paepe A, Holder GE, Webster AR. Pseudoxanthoma elasticum with generalized retinal dysfunction, a common finding? Invest Ophthalmol Vis Sci. 2007 Sep;48(9):4250-6.

Henderson RH, Waseem N, Searle R, van der Spuy J, Russell-Eggitt I, Bhattacharya SS, Thompson DA, Holder GE, Cheetham ME, Webster AR, Moore AT. An assessment of the apex microarray technology in genotyping patients with Leber congenital amaurosis and early-onset severe retinal dystrophy. Invest Ophthalmol Vis Sci. 2007 Dec;48(12):5684-9

Moradi P, Moore AT. Molecular genetics of infantile-onset retinal dystrophies. Eye. 2007;21:1344-51.

Robson AG, Michaelides M, Luong VA, Holder GE, Bird AC, Webster AR, Moore AT, Fitzke FW. Functional correlates of fundus autofluorescence abnormalities in patients with RPGR or RIMS1 mutations causing cone or cone rod dystrophy. Br J Ophthalmol. 2008 Jan;92(1):95-102.

Michaelides M, Chen LL, Brantley MA Jr, Andorf JL, Isaak EM, Jenkins SA, Holder GE, Bird AC, Stone EM, Webster AR. ABCA4 mutations and discordant ABCA4 alleles in patients and siblings with bull's-eye maculopathy. Br J Ophthalmol. 2007 Dec;91(12):1650-5.

Name: Stephen E Moss ; Paricipant: 3e ; Work Package (WP): WP10

Planned /actual Dates	Type	Type of audience	Countries addressed	Size of audience	Partner responsible /involved
3-4 March, 2005	EVI-Genoret Kick-off Meeting	Scientists at GENORET meeting	EU member states	100	3d, 3e
13-15 March, 2006	1st EVI-Genoret Annual Meeting	Scientists at GENORET meeting	EU member states	100	3d, 3e
18-21 March 2007	EVI-Genoret Midterm Review Meeting	Scientists at GENORET meeting	EU member states	100	3d, 3e
10/11 March 2008	Poster	Scientists at GENORET meeting	EU member states	100	3d, 3e
March 2009	Presentation	Scientists at GENORET meeting	EU member states	100	3d, 3e

Name: Eberhart Zrenner; Participant: 4a; Work Package (WP):WP1, WP 2, WP16, WP17, WP19

Exploitable Knowledge (description)	**Exploitable product(s) or measure(s)**	**Sector(s)** of application	Timetable for commercial use	Patents or other IPR protection	**Owner** & Other Partner(s) involved
Standardized Case Report Form for MRD	CRF for MRD	Medical	none	none	
Standardized Case Report Form for AMD	CRF for AMD	Medical	None	None	
Phenotypic database for AMD	Phenotypic data; Pool of patients for clinical trials	Clinical trials on AMD	None	None	
Phenotypic database for MRD	Phenotypic data; Pool of patients for clinical trials	Clinical trials on MRD	None	None	
Enhanced ERG technologies	Submicrovolt ERG Signal to Noise Ratio assessment	Clinical trials on MRD	None	None	4a
Enhanced ERG software	ERG explorer DICOM; standard for ERG data	Clinical trials; ERG device manufacturers	Within 2009 (open source)	IP protected by open source definitions	4a
Enhanced imaging	Multimodal Mapper (MMM)	Enhanced retinal diagnostic by combining functional and morphological imaging	Within 2009 Open source software or cooperation with device manufacturers	To be negotiated	4a

Publications	
POSTER: THE ARVO 2006 ANNUAL MEETING / FORT LAUDERDALE 04/29/2006 - 05/04/2006 **The Phenotype of Early-Onset Retinal Degeneration in Persons with *RDH12* mutations** Gal, Andreas Schuster, Andreas R. Janecke, Robert Wilke, Eduard Schmid, Debra A. Thompson, Gerd Utermann, Bernd Wissinger and Eberhart Zrenner	
Almudena Avila-Fernandez1, Rosa Riveiro-Alvarez1, Elena Vallespin1, Robert Wilke2, Ignacio Tapias3, Diego Cantalapiedra1, Jana Aguirre-Lamban, Ascension Gimenez, MJ Trujillo-Tiebas, Carmen Ayuso Genotype-phenotype correlation in seven CERKL mutated Spanish families with Autosomal Recessive Retinitis Pigmentosa	*Invest Ophthalmol Vis Sci. 2008. In press*
Rosa Riveiro-Alvarez, Elena Vallespin, Robert Wilke, Blanca Garcia-Sandoval, Diego Cantalapiedra, Jana Aguirre-Lamban, Almudena Avila, Mª Jose Trujillo-Tiebas, Carmen Ayuso Molecular analysis of ABCA4 and CRB1 genes in one mixed Spanish family segregating Stargardt disease and Autosomal Recessive	*Mol Vis. 2007. In press*

Retinitis Pigmentosa.	
Vallespin E, Cantalapiedra D, Riveiro-Alvarez R, Avila-Fernández A, Gimenez A, Lopez-Martinez MA, Trujillo-Tiebas MJ, Ramos C, Ayuso C Mutation screening in 299 Spanish families with retinal dystrophies using a Leber Congenital Amaurosis genotyping microarray: mutations vs polymorphisms..	*Invest Ophthalmol Vis Sci. 2007 Dec;48(12):5653-61. / PMID: 18055816*
Kitiratschky VB, Grau T, Bernd A, Zrenner E, Jägle H, Renner AB, Kellner U, Rudolph G, Jacobson SG, Cideciyan AV, Schaich S, Kohl S, Wissinger B. ABCA4 gene analysis in patients with autosomal recessive cone and cone rod dystrophies	*Eur J Hum Genet. 2008 Feb 20; [Epub ahead of print]*
Langrová H, Jägle H, Zrenner E, Kurtenbach A. The multifocal pattern electroretinogram (mfPERG) and cone-isolating stimuli.	*Vis Neurosci. 2007 Nov-Dec;24(6):805-16.*
Chakarova CF, Papaioannou MG, Khanna H, Lopez I, Waseem N, Shah A, Theis T, Friedman J, Maubaret C, Bujakowska K, Veraitch B, Abd El-Aziz MM, Prescott de Q, Parapuram SK, Bickmore WA, Munro PM, Gal A, Hamel CP, Marigo V, Ponting CP, Wissinger B, Zrenner E, Matter K, Swaroop A, Koenekoop RK, Bhattacharya SS. Mutations in TOPORS cause autosomal dominant retinitis pigmentosa with perivascular retinal pigment epithelium atrophy	*Am J Hum Genet. 2007 Nov;81(5):1098-103. Epub 2007 Sep 26.*
Messias A, Gekeler F, Wegener A, Dietz K, Kohler K, Zrenner E. Retinal safety of a new fluoroquinolone, pradofloxacin, in cats: assessment with electroretinography.	*Doc Ophthalmol. 2007 Oct 2; [Epub ahead of print]*
Ziemssen F, Lüke M, Messias A, Beutel J, Tatar O, Zrenner E, Bartz-Schmidt KU; Tuebingen Bevacizumab Study Group. Safety monitoring in bevacizumab (Avastin) treatment: retinal function assessed by psychophysical (visual fields, colour vision) and electrophysiological (ERG/EOG) tests in two subgroups of patients.	*Int Ophthalmol. 2007 Jul 20; [Epub ahead of print]*
Reinhard J, Messias A, Dietz K, Mackeben M, Lakmann R, Scholl HPN, Apfelstedt-Sylla E, Weber BHF, Seeliger MW, Zrenner E, Trauzettel-Klosinski S (2007) Quantifying fixation in patients with Stargardt disease.	*Vision Res. 47:2076-85.*
Schuster A, Janecke AR, Wilke R, Schmid E, Thompson DA, Utermann G, Wissinger B, Zrenner E, Gal A. The phenotype of early-onset retinal degeneration in persons with RDH12 mutations.	*Invest Ophthalmol Vis Sci. 2007 Apr;48(4):1824-31.*
C. Bellmann, et al., "A Pan-European Approach for a Comprehensive Assessment of Patients With Age-Related Macular Disease (AMD),"	*Invest. Ophthalmol. Vis. Sci. 2007 48: E-Abstract 4539, 2007.*
R. Wilke et al. "Development of a pan-european database to provide phenotypic data of patients with retinal diseases"	*WC2006, Seoul, Korea*
Wilke R. "The EVI-Genoret Project"	*DOG Annual meeting, 2008, Berlin*
E. Troeger, et al, "REUSABILITY IN PATIENT REGISTRIES - Implementation of a Generic Extensible Web-based Patient Registry System,"	*International Joint Conference on Biomedical Engineering Systems and Technologies (BIOSTEC),Porto, 2009.*
E. Zrenner et al. "A pan-European patient registry for retinal dystrophies and age related macular degeneration"	*EVER meeting 2007*
Wilke R., et al. "Objective Assessment of Retinal Functions in Subjects with Severely Impaired Retinal Function – part of the ERG standard of the European Vision Institute"	*DOG Annual meeting, Berlin 2008*
Prokofyeva E, Wilke R, Zrenner E. (2009) Prevalence and Incidence of Age-Related Macular Degeneration in Europe: Meta-Analysis Based on a Systematic Literature Review	*ARVO Annual Meeting, Fr. Lauderdale, FL, USA.*
Prokofyeva E., et al. (2009) An epidemiological approach to the estimation of the onset of central and peripheral hereditary retinal dystrophies in Central Europe.	*Graefe's Archive for Clinical and Experimental Ophthalmology. –accepted for publication.*
Prokofyeva E., et al. (2008) Distribution and clinical peculiarities of monogenic retinal dystrophies at the Center for Ophthalmology,	*EVER congress, Slovenia, Portoroz*

University of Tübingen.	
Prokofyeva E., et al. (2008) An epidemiological approach for the estimation of disease onset in inherited retinal dystrophies.	*106 DOG (German Ophthalmologic Society Congress), Berlin, Germany*
R. Wilke, et al., "Objective Assessment of Retinal Functions of Persons With Advanced Retinal Degeneration in Clinical Trials"	*Invest. Ophthalmol. Vis. Sci. 2008 49: E-Abstract 3810, 2008.*
T. Strasser, H. Jägle, T. Peters, E. Zrenner, and R. Wilke, "Evaluating the use of Continuous Wavelet Transformation for clinical routine,"	*Invest. Ophthalmol. Vis. Sci. 2009 E-Abstract 2009.*
R. Wilke et al. "Objective Assessment of Retinal Functions of Subjects with Advanced Retinal Degeneration in Clinical Trials"	*ISCEV annual meeting, 2008*
E. Prokofyeva, **R. Wilke**, G. Lotz, E. Tröger, T. Strasser, E. Zrenner "An epidemiological approach for the estimation of disease onset in Central Europe in central and peripheral monogenic retinal dystrophies"	*Graefe's Archive for Clinical and Experimental Ophthalmology; 2009 Mar 11. [Epub ahead of print]*
V.B. Kitiratschky, **R. Wilke**, A.B. Renner, U. Kellner, M. Vadala, D.G. Birch, B. Wissinger, E. Zrenner, and S. Kohl, "Mutation analysis identifies GUCY2D as the major gene responsible for autosomal dominant progressive cone degeneration"	*Invest Ophthalmol Vis Sci, May 16 2008.*
R. Riveiro-Alvarez, E. Vallespin, **R. Wilke**, B. Garcia-Sandoval, D. Cantalapiedra, J. Aguirre-Lamban, A. Avila-Fernandez, A. Gimenez, M.J. Trujillo-Tiebas, and C. Ayuso, "Molecular analysis of ABCA4 and CRB1 genes in a Spanish family segregating both Stargardt disease and autosomal recessive retinitis pigmentosa,"	*Mol Vis, vol. 14, pp. 262-7, 2008.*
Avila-Fernandez, R. Riveiro-Alvarez, E. Vallespin, **R. Wilke**, I. Tapias, D. Cantalapiedra, J. Aguirre-Lamban, A. Gimenez, M.J. Trujillo-Tiebas, and C. Ayuso, "CERKL mutations and associated phenotypes in seven Spanish families with autosomal recessive retinitis pigmentosa,"	*Invest Ophthalmol Vis Sci, vol. 49, (no. 6), pp. 2709-13, Jun 2008.*
E. Vallespin, D. Cantalapiedra, R. Riveiro-Alvarez, **R. Wilke**, J. Aguirre-Lamban, A. Avila-Fernandez, M.A. Lopez-Martinez, A. Gimenez, M.J. Trujillo-Tiebas, C. Ramos, and C. Ayuso, "Mutation screening of 299 Spanish families with retinal dystrophies by Leber congenital amaurosis genotyping microarray"	*Invest Ophthalmol Vis Sci, vol. 48, (no. 12), pp. 5653-61, Dec 2007.*
Schuster, A.R. Janecke, **R. Wilke**, E. Schmid, D.A. Thompson, G. Utermann, B. Wissinger, E. Zrenner, and A. Gal, "The phenotype of early-onset retinal degeneration in persons with RDH12 mutations"	*Invest Ophthalmol Vis Sci, vol. 48, (no. 4), pp. 1824-31, Apr 2007.*
Bernd A., et al. "The Phenotype in Patients With Mutations in the Rds/peripherin Gene"	*ARVO Annual meeting, Fort Lauderdale 2008*
Aguirre-Lamban J, Riveiro-Alvarez R, Maia-Lopes S, Cantalapiedra D, Vallespin E, Avila-Fernandez A, Villaverde-Montero C, Trujillo-Tiebas MJ, Ramos C, Ayuso C. Br J Molecular analysis of the ABCA4 gene for reliable detection of allelic variations in Spanish patients: identification of 21 novel variants..	*Ophthalmol. 2008 Nov 21*
Susana Maia–Lopes1, Jana Aguirre-Lamban2, Miguel Castelo–Branco1, Rosa Riveiro-Alvarez2, Carmen Ayuso2 & Eduardo Duarte Silva1,3 ABCA4 mutations in Portuguese Stargardt patients: identification of new mutations and its phenotypic analysis.	*Mol. Vis. accepted*
Vallespin E, Cantalapiedra D, Riveiro-Alvarez R, Avila-Fernández A, Gimenez A, Lopez-Martinez MA, Trujillo-Tiebas MJ, Ramos C, Ayuso C. Mutation screening in 299 Spanish families with retinal dystrophies using a Leber Congenital Amaurosis genotyping microarray: mutations vs polymorphisms.	*Invest Ophthalmol Vis Sci. 2007 Dec;48(12):5653-61. / PMID: 18055816*
Vallespin, E. López-Matínez, MA, Cantalapiedra, D., Riveiro-Alvarez, R., Aguirre-Lamban, J., Avila-Fernandez, A. Villaverde, C., Trujillo-Tiebas, M.J. and Ayuso, C. Frequency of CEP290 c.2991_1655A>G mutation in 175 Spanish	*Mol Vis. 2007 Nov 27;13:2160-2. PMID: 18079693*

families affected with Leber Congenital Amaurosis and early-onset Retinitis Pigmentosa.	

Name: Mathias W. Seeliger ; Participant: 4d ; Work Package (WP): WP3

Exploitable Knowledge (description)	**Exploitable product(s) or measure(s)**	**Sector(s)** of application	Timetable for commercial use	Patents or other IPR protection	**Owner** & Other Partner(s) involved
1. SLO imaging		service for the consortium			4d
2. ERG recording		service for the consortium			4d
3. Optomotor response		service for the consortium			4d
4. OCT imaging		service for the consortium			4d

Planned /actual Dates	**Type**	**Type of audience**	**Countries addressed**	**Size of audience**	**Partner responsible /involved**
2005	Publications	Research	world wide		4d
2006	Publications	Research	world wide		4d
2006	Oral presentations	Conference ISCEV	world wide	500	4d
2006	Oral presentations	Conference ARVO	world wide	1000	4d
2006	Posters	Conference ARVO	world wide	1000	4d
2006	Special interest group	Conference ARVO	world wide	300	4d
2007	Oral presentations	Swiss retina meeting	world wide	200	4d
2007	Posters	ARVO Conference	world wide	1000	4d, 2h
2007	Oral Presentations	Swiss Eye Research Meeting	world wide	200	4d
2007	Oral Presentations	ISCEV	world wide	500	4d
2007	Oral Presentations	DOG, Berlin	world wide	500	4d
2008	Oral Presentations	Swiss Eye Research Meeting	world wide	200	4d
2008	Posters	ARVO Conference	world wide	1000	4d
2009	Oral presentation	SERM	EUwide	100	4d

Publishable results

Kiang et al., Toward gene therapy for dominant disease: validation of an RNA-interference-based mutation-independent approach. Molecular Therapy, 12 (2005) 555-561.

Reinhard et al.: Quantifying fixation in patients with Stargardt disease. Vis. Res. 2007; 47: 2076 – 2085.

Chen et a.: Rb-mediated neuronal differentiation through cell cycle independent regulation of E2f3a. PLoS Biol 2007, 5: E179.

Paques et al.: Panretinal, high-resolution color photography of the mouse fundus. IOVS 2007, 48: 2769 – 2774.

Gong et al.: The toxicity of the PrP106-126 prion peptide on cultured photoreceptors correlates with the prion protein distribution in the mammalian and human retina. The American Journal of Pathology, Vol. 170, No. 4, April 2007,

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Dumelin C. et al. A portable albumin binder from a DNA-encoded chemical library. Angew. Chem. Int. Ed. 2008, 47, 3196 –3201.
Schaeferhoff K. et al. Comprehensive phenotypic and gene expression analysis in the conespecific photoreceptor function loss 1 (cpfl1) mouse mutant – a model for retinal neurodegenerations. 2009, submitted to Journal of Molecular Biology.
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Name: B. Wissinger ; Participant:4e ; Work Package (WP): WP12 / WP 14

Publications

Renner, A.B., Fiebig, B.S., Weber, B.H.F., Wissinger, B., Andreasson, S., Gal, A., Cropp, E., Kohl, S., Kellner, U. (2009) *Phenotypic variability and long-term follow-up of patients with known and novel PRPH2 (peripherin/RDS) gene mutations. Am J Ophthalmol 147:518-530*
Kitiratschky, V.B.D., Wilke, R., Renner, A.B., Kellner, U., Vadalà, M., Birch, D.G., Wissinger, B., Zrenner, E., Kohl, S. (2008) *Mutation analysis identifies GUCY2D as the major gene responsible for progressive autosomal dominant cone degeneration. Invest Ophthalmol Vis Sci 49 5015-5023*
Kitiratschky, V., Zabel, T., Nagy, D., Zrenner, E., Wissinger, B., Kohl, S., Jägle, H. (2008)*Cone and cone-rod dystrophy segregating in the same pedigree due to the same novel CRX gene mutation.*
Br J Ophthalmol 92: 1086-1091
Kitiratschky, V.B.D., Grau, T., Bernd, A., Zrenner, E., Jägle, H., Renner, A.B., Kellner, U., Rudolph, G., Jacobson, S.G., Cideciyan, A.V., Schaich, S., Kohl, S., Wissinger, B. (2008) *ABCA4 gene analysis in patients with autosomal recessive cone and cone rod dystrophies. Eur J Hum Genet 16: 812-819.*

Name: Jose Cunha-Vaz, E. Silva ; Participant: 5a ; Work Package (WP): WP1

Publications

Bernardes R., Santos T., Cunha-Vaz J: Increased-Resolution OCT Thickness Mapping of the Human Macula: A Statistically Based Registration. Invest. Ophthalmol. Vis. Sci; 2008; 49 (5): 2046-2052.
Bernardes R., Cunha-Vaz J.: Perspectives for multimodal imaging of the retina in disease. 8th EURETINA Congress, Vienna, Austria, May 22-25,2008 , 1:15-1:17.
Bernardes, R., Lobo C., Cunha-Vaz J.: Multimodal mapping of the macula. Ophthalmol. International, Summer 2008; 3 (2): 58-61.
Maia–Lopes S., Silva E., Reis, A., Silva M.F., Mateus C. & Castelo–Branco M. Retinal Function in Best Macular Dystrophy: Relationship Between Electrophysiological, Psychophysical and Structural Measures of Damage (2008) Investigative Ophthalmology and Visual Sciences 49(12):5553-60.
Maia–Lopes S., Silva E., Silva M.F., Reis, A. Faria P. & Castelo–Branco M. (2008) Evidence for widespread retinal dysfunction in patients with Stargardt disease and morphologically unaffected carrier relatives. Investigative Ophthalmology and Visual Sciences, 49(3):1191-9.
Silva MF, Maia-Lopes S, Mateus C, Guerreiro M, Sampaio J, Faria P, Castelo-Branco M. Retinal and cortical patterns of spatial anisotropy in contrast sensitivity tasks. (2008) Vision Research 48(1):127-35.
Maia-Lopes S., Mateus, C. Sebastião A.R., Nunes S., Reis, A. and Castelo Branco, M. Inhibition across the human retina in space and time: novel evidence for long range interactions. Under revision in The Journal of Neuroscience.

Name: Sandro Banfi, Valeria Marigo ; Participant: 6 & 25 ; Work Package (WP): WP4

Planned/actual Dates	Type	Type of audience	Countries addressed	Size of audience	Partner responsible /involved
October 2006	Publications	Research	International		25
May 2006	Posters	Research	International		25
August 2007	Conference	Research, higher education	India	200	6
2007 (March, May, October)	Posters	Higher education, Research	Europe, US	Approx. 200	6
February 2008	Conference	Research	Italy	100	6
June 2008	Publications	Research	worldwide		6 and 25
October 2008	Posters	Higher education, Research	US, Europe	Approx. 200	6
May 2008	Poster at ARVO and at RD2008 and ICER	Researchers	International	thousands	25
June 2008	Posters at ISSCR	Researchers	International	hundreds	25
September 2008	Posters at RD2008 and ICER	Researchers	International	thousands	25

PUBLICATIONS

Trifunovic D, Karali M, Campogampiero D, Ponzin D, Marigo V, Banfi S. "A high-resolution RNA expression atlas of Retinitis Pigmentosa genes in the human and mouse retinas." Invest Ophthalmol Vis Sci, 2008, in press.

Marigo V. (2007) Programmed Cell Death in Retinal Degeneration: Targeting Apoptosis in Photoreceptors as Potential Therapy for Retinal Degeneration. Cell Cycle 6: 652-655.

Comitato A., Spampanato C., Chakarova C., Sanges D., Bhattacharya S.S., Marigo V. (2007) Mutations in splicing factor PRPF3, causing retinal degeneration, form detrimental aggregates in photoreceptor cells. Human Molecular Genetics 16: 1699-1707.

Allocca, M., Mussolino, C., Hoyos, M. G., Sanges, D., Iodice, C., Petrillo, M., Vandenberghe, L. H., Wilson, J. M., Marigo, V., Surace, E. M., Auricchio, A. (2007). Novel AAV serotypes efficiently transduce murine photoreceptors. Journal of Virology 81: 11372-11380.

Chakarova C.F., Papaioannou M.G., Khanna H., Lopez I., Waseem N., Shah A., Theis T., Friedman J. , Maubaret C., Bujakowska K., Veraitch B., Abd El-Aziz M.M., Prescott D.Q., Parapuram S., Bickmore W.A., Munro P.M.G., Gal A., Hamel C., Marigo V., Ponting C.P., Wissinger B, Zrenner E., Matter K., Swaroop A., Koenekoop R.K. Bhattacharya S.S. (2007) Mutations in TOPORS Cause Autosomal Dominant Retinitis Pigmentosa with Perivascular Retinal Pigment Epithelium Atrophy. The American Journal of Human Genetics 81: 1098-1103.

Giordano F., De Marzo A. Vetrini F., Marigo V. (2007) FGF and EGF differently affect differentiation of murine retinal stem cells in vitro. Molecular Vision 13: 1842-1850.

Trifunovic D, Karali M, Campogampiero D, Ponzin D, ***Banfi S,*** *Marigo V. A high-resolution RNA expression atlas of Retinitis Pigmentosa genes in the human and mouse retinas. Invest Ophthalmol Vis Sci 49(6):2330-6 (2008). Epub 2008 Feb 15.*

Name: Ronald Roepman ; Participant: 7a ; Work Package (WP): WP12, WP13, WP15

Planned/ actual Dates	Type	Type of audience	Countries addressed	Size of audience	Partner responsible /involved
29.02.2008	Invited lecture	patients + research	USA	100	7a
06.03.2008	Invited lecture	research	Germany	70	7a
03.06.2008	Invited lecture	research	Europe	500	7a
08.10.2008	Invited lecture	research	Italy	80	7a
24.10.2008	Invited lecture	research	USA	80	7a

Planned/ actual Dates	Type	Type of audience	Countries addressed	Size of audience	Partner responsible /involved
29.02.2008	Foundation Fighting Blindness 'Day of Science', San Diego, USA				
06.03.2008	Heinrich-Heine-University, Institute for Animal Developmental and Molecular Biology (EMT), Düsseldorf, Germany				
03.06.2008	European Society of Human Genetics, Annual meeting, Barcelona, Spain				
08.10.2008	TIGEM (Telethon Institute of Genetics and Medicine, Naples, Italy				
24.10.2008	Massachussets Eye and Ear Infirmary (MEEI), Harvard Medical School, Boston, USA				

Publications

van Wijk, E., Kersten, F.F.J., Kartono, A., Mans, D.A., Brandwijk, K., Letteboer, S.J., Peters, T.A., Märker, T., Yan, X., Cremers, C.W.R.J., Cremers, F.P.M., Wolfrum, U., Roepman, R., and Kremer, H.* (2009). Usher syndrome and Leber congenital amaurosis are molecularly linked via a novel isoform of the centrosomal ninein-like protein.* ***Hum. Mol. Genet.****, 18, 51-64.*equal senior authors*

Arts, H.H., Cremers, F.P.M., Knoers, N.V.A.M., and Roepman, R. (2009). Focus on Molecules: RPGRIP1. ***Exp Eye Res.****, 88, 332-333.*

Gorden, N., Arts, H.H., Parisi, M.A., Coene, K.L., Letteboer, S.J.F., van Beersum, S.E.C., Mans, D.A., Hikida, A., Eckert, M., Knutzen, D., Alswaid, A.F., Ozyurek, H., Dibooglu, S., Otto, E.A., Liu, Y., Davis, E.E., Hutter, C.M., Bammler, T.K., Farin, F.M., Dorschner, M., Topçu, M., Zackai, E.H., Rosenthal, P., Owens, K.N., Katsanis, N., Vincent, J.B., Hildebrandt, F., Rubel, E.W., Raible, D.W., Knoers, N.V.A.M., Chance, P.F., Roepman, R., Moens, C.B., Glass, I.A., and Doherty, D. (2008). CC2D2A is mutated in Joubert syndrome and interacts with the ciliopathy-associated basal body protein CEP290. ***Am. J. Hum. Genet.****, 83, 559-571.*

den Hollander, A.I., Roepman, R., Koenekoop, R.K., and Cremers, F.P.M. (2008). Leber congenital amaurosis: genes, proteins and disease mechanisms. ***Prog. Retin. Eye Res.****, 27, 391-419.*

Name: F. Cremers ; Participant: 7b ; Work Package (WP): WP12, WP15

Publications with EVI-Genoret acknowledged (2007-2008):

Arts, H.H., Doherty, D., van Beersum, S.E., Parisi, M.A., Letteboer, S.J.F., Gorden, N.T., Peters, T.A., Märker, T., Voesenek, K., Kartono, A., Ozyurek, H., Farin, F.M., Kroes, H.Y., Wolfrum, U., Brunner, H.G., Cremers, F.P.M., Glass, I.A., Knoers, N.V.A.M., and Roepman, R. (2007). Mutations in the gene encoding the basal body protein RPGRIP1L, a nephrocystin-4 interactor, cause Joubert syndrome. ***Nat. Genet.****, 39, 882-888.*

den Hollander, A.I., Koenekoop, R.K., Mohamed, M.D., Arts, H.H., Boldt, K., Towns, K.V., Sedmak, T., Beer, M., Nagel-Wolfrum, K., McKibbin, M., Dharmaraj, S., Lopez, I., Ivings, L., Williams, G.A., Springell, K., Woods, C.G., Jafri, H., Rashid, Y., Strom, T.M., van der Zwaag, B., Gosens, I., Kersten, F.F.J., van Wijk, E., Veltman, J.A., Zonneveld, M.N., van Beersum, S.E., Maumenee, I.H., Wolfrum, U., Cheetham, M.E., Ueffing, M., Cremers, F.P.M., Inglehearn, C.F., and Roepman, R. (2007). Mutations in LCA5, encoding the novel ciliary protein lebercilin, cause Leber congenital amaurosis. ***Nat. Genet.****, 39, 889-895.*

Gosens, I, van Wijk, E., Kersten, F.F., Krieger, E., van der Zwaag, B., Märker, T., Letteboer, S.J.F., Dusseljee, S., Peters, T., Spierenburg, H.A., Punte, I.M., Wolfrum, U., Cremers, F.P.M., Kremer, H., and Roepman, R. (2007). MPP1 links the Usher protein network and the Crumbs protein complex in the retina. ***Hum. Mol. Genet.****, 16, 1993-2003.*

Gosens, I., Sessa, A., den Hollander, A. I., Letteboer, S.J.F., Belloni, V., Arends, M. L., Le Bivic, A., Cremers, F.P.M., Broccoli, V., and Roepman, R. (2007). FERM protein EPB41L5 is a novel member of the mammalian CRB-MPP5 polarity complex. ***Exp. Cell. Res.****, 313, 3959-3970.*

Gloeckner, C.J., Boldt, K., Schumacher, A., Roepman, R., and Ueffing, M. (2007). A novel tandem affinity purification strategy for the efficient isolation and characterization of native protein complexes. ***Proteomics****, 7, 4228-4234 .*

Roepman, R. and Wolfrum, U. (2007). Protein complexes and networks in photoreceptor cilia. ***Subcell Biochem.****, 43, 209-235.*

Gosens, I., den Hollander, A.I., Cremers, F.P.M., and Roepman, R. (2008). Composition and function of the

Crumbs protein complex in the mammalian retina. ***Exp. Eye Res.****, in press.*

Name: Per Ekström, Participant: 8a ; Work Package (WP): WP 15

Planned/actual Dates	Type	Type of audience	Countries addressed	Size of audience	Partner responsible /involved
ARVO meeting April 30 - May 4, 2006	Poster	Research	International	8000	8a, 11a
ISOCB meeting Sep. 6 - 10, 2006	Posters	Research	International	200	8a, 11a
ICER meeting Oct. 29 - Nov. 3, 2006	Invited conference talk	Research	International	600	8a, 11a
Exp. Ophtalmology, Univ. Tübingen, Jan. 30, 2007	Invited talk	Research	Germany	40	8a, 11a
2007; Brain Res.	Publication	Research	International	-	8a, 11a
2007; J. Neurosci. Res.	Publication	Research	International	-	8a, 11a
ARVO meeting May 6-10, 2007	Poster	Research	International	8000	8a / 6b
ARVO meeting May 6-10, 2007	Poster	Research	International	8000	11a / 8a
ARVO meeting May 6-10, 2007	Poster	Research	International	8000	8a / 11a
2007; J. Neurosci.	Publication	Research	International	-	8a / 11a
2008; Mol. Neurobiol.	Publication	Research	International	-	8a/4a
2008; Invest Ophthalmol Vis Sci.	Publication	Research	International	-	8b
2009; J. Neurochem.	Publication	Research	International	-	8a/11a
ARVO meeting May 3-7, 2009	Abstract/ (Poster)	Research	International	-	8b/4a/4d
ARVO meeting May 3-7, 2009	Abstract/ (Poster)	Research	International	-	8a/11a

Publications:

Paquet-Durand F., Silva J., Johnson L., Talukdar T., Azadi S., van Veen T., Ueffing M, Hauck S., Ekström P.A.R. (2007). Poly(ADP-ribose) polymerase (PARP) is overactivated in rd1 mouse photoreceptors and contributes to their degeneration. Journal of Neuroscience, 27:10311-10319.

Sancho-Pelluz J, Arango-Gonzalez B, Kustermann S, Romero FJ, van Veen T, Zrenner E, Ekström P, Paquet-Durand F (2008). Photoreceptor cell death mechanisms in inherited retinal degeneration. Molecular Neurobiology, 38: 253-269.

Sancho-Pelluz J, Wunderlich KA, Rauch U, Romero FJ, van Veen T, Limb GA, Crocker PR, Perez MT (2008). Sialoadhesin expression in intact degenerating retinas and following transplantation. Invest Ophthalmol Vis Sci., 49:5602-10.

Paquet-Durand F, Hauck SM, van Veen T, Ueffing M, Ekström P (2009). PKG activity causes photoreceptor cell death in two retinitis pigmentosa models. Journal of Neurochemistry, 108:796-810.

Name: Vescovi AL , Fiocco R ; Participant: 9a ; Work Package (WP): 5

Exploitable Knowledge (description)	**Exploitable product(s) or measure(s)**	**Sector(s)** of application	Timetable for commercial use	Patents or other IPR protection	**Owner** & Other Partner(s) involved
1. transgenic GFP and wt neural stem cell lines		1. research	NA	NA	**Vescovi (owner)**

Planned /actual Dates	**Type**	**Type of audience**	**Countries addressed**	**Size of audience**	**Partner responsible /involved**
2007	TV programs (talk show)	General public	**IT**	10-15% share	Vescovi
2008	Press	General public	**IT**		Vescovi
2008	Press	General public	**IT**	10% share	Vescovi
2008	Conference	Research	**worldwide**		Vescovi
2008	Publications	Research	**worldwide**		Vescovi

Name: Veronica van Heyningen ; Participant: 10a ; Work Package (WP): WP6

Exploitable Knowledge (description)	**Exploitable product(s) or measure(s)**	**Sector(s)** of application	Timetable for commercial use	Patents or other IPR protection	**Owner** & Other Partner(s) involved
Creation of PAX6 YAC reporter transgenic mouse	PAX6 expressing cells fluoresce green with GFP eg ciliary body stem cells	Medical research	No plans for commercial use	No patent plans	**10a**

Planned /actual Dates	**Type**	**Type of audience**	**Countries addressed**	**Size of audience**	**Partner responsible /involved**
05/05/08	European Congress of Endocrinology	Research in different discipline	European	150	Partner 10a
31/08/08	European Life Sciences Organisation	Research, postgraduates	European	40	Partner 10a
25/09/08	Conference	School children	India	1000	Partner 10a
	Publications	Research	Worldwide	?	Partner 6a and 25
ongoing	Project web-site – Mutation database for PAX6, SOX2 and OTX2	Human Genetics Research and clinical delivery	Worldwide	?	Partner 10a
Planned/ actual Dates	Type	Type of audience	Countries addressed	Size of audience	Partner responsible /involved
2008	Trifunovic et al Invest Ophthalmol Vis Sci. 2008 Jun;49(6):2330-6.	Research	All	?	6a, 25
2009/ 2010	Publications planned – probably 2	Scientific reports	All	Developm ental	10a

Planned /actual Dates	Type	Type of audience	Countries addressed	Size of audience	Partner responsible /involved
				biology community	

Name: A. Wright ; Participant: 10b ; Work Package (WP): WP8

Planned /actual Dates	Type	Type of audience	Countries addressed	Size of audience	Partner responsible /involved
March 06	**Invited talk** 1. C1QTNF5 is mutated in late-onset retinal macular degeneration and interacts with complement factor H XXI International Complement Workshop, Beijing	Research	**China**	~500	10b
March 06	Disease Mechanism of Retinal Degeneration University Of Durham, UK	Research	**UK**	100	10b
Oct 06	**Posters** 1. Oct. 2006 XXI International Complement Workshop, Beijing, China				10b
	2. May 2006 Annual meeting of Association for Research in Vision and Ophthalmology, Fort Lauderdale, USA				
	3. Apr. 2006 Retinal degeneration: illuminating molecular complexities of the retina, Potsdam, Germany				
2007 May	Conference: 11th Annual Vision Research Conference, Fort Lauderdale, Florida,	Research	**Global**	100 approx	10b
2007	Conference: Royal College of Surgeons, Edinburgh, The Eye Symposium 2007 "Science to Surgery".	Research / Clinicians	**UK**	120 aprox	10b
2007	Eye Genetics Group, University of Manchester.	Research	**UK**	30 approx	10b
April 2007	John Scrimgeour Non-Clinical Lecture: Insights into the pathogenesis of age-related macular degeneration, Western General Hospital, Edinburgh	Research	**UK**	100 approx	10b
2008	Lab. of Marius Ueffing	Research		20 approx	10b
12 Feb 2008	Conference: TIGEM, Naples, Italy on	Research	**Global**	100 approx	10b
20 Feb 2008	Conference: 2008 Institute of Ophthalmology, London			100 approx	10b

Name: Marius Ueffing ; Participant: 11a ; Work Package (WP): WP13

Planned/ actual Dates	Type	Type of audience	Countries addressed	Size of audience	Partner responsible /involved
5.4. 2006	Conference Charité, Meeting „Molecular Interactions“, Berlin	Research and Higher Education	**Germany**	70	**11**
14.4.2006	Conference RIKEN, Center for Developmental Biology, Kobe, Japan	Research	**Japan and International**	200	**11**
17.4.2006	Conference Tokyo Medical and Dental University, Tokyo, Japan	Research and Clinic ?	**Japan and International (?)**	100	**11**
18.4.2006	Conference Institute for Clinical Medicine and Research, Jikei Univ., Kashiwa, Japan	Research and Clinic ?	**Japan and International (?)**	100	**11**
8.5.2006	Conference Proteome Information Exchange Meeting‘, Münster	Research	**Germany International**	300	**11**
29.6.2006	Conference Medical Research Council, Edinburgh, UK	Research & Clinic	**International**	500	**11**
22.7.2006	Conference KFG Retreat der Univ. Tübingen, Freudenstadt	Research and Higher Education	**Germany**	40	**11**
6.10.2006	Conference EVER Annual Meeting, Faro, Portugal	General public Research Higher education	**International**	200	**11**
31.10.2006	Conference ICER International Congress, Buenos Aires, Argentinien	General public Research Higher education	**International**	500	**11**
27.11.2006	Conference EMBL Heidelberg	Research Higher education	**Germany International**	200	**11**
12.12.2006	Conference BMBF Koordinatorentreffen Berlin	Research Higher education	**Germany**	100	**11**
20.12.2006	Conference Becton Dickinson Diagnostics Advisory Board Meeting, Martinsried	Research & Clinic	**Germany**	150	**11**
May 2008	ARVO conference, Invited talk in Special Interest Group, Mueller glia in Health and Disease	Research	**international**	300	**11a**
May 2008	ARVO conference, presentation	Research	**international**	150	**11a**
May 2007	ARVO conference, Poster	Research	**international**		**11a**
April 2008	ProRetina Meeting, poster	Research	**international**	200	**11a**
May 2008	KHUPO, Korea, invited talk	Research	**international**	300	**11a**
September 2008	Max-Plank Institute, Dortmund, Invited talk	Research	**national**	50	**11a**
October	3. ESF Conference on	Research	**international**	500	**11a**

Planned/ actual Dates	Type	Type of audience	Countries addressed	Size of audience	Partner responsible /involved
2008	Functional Genomics, invited talk				
07.07.08	Publication	Research	**international**		**11a**
06.02.09	Publication	Research	**international**		**11a**

Publications

Stefanie M. Hauck, Christian J. Gloeckner, Margaret E. Harley, Stephanie Schoeffmann, Karsten Boldt, Per A.R. Ekström and M. Ueffing "Identification of paracrine neuroprotective candidate proteins by a functional assay-driven proteomics approach", Mol Cell Proteomics.2008 Jul;7(7): 1349-61

Johanna Zipplies, Stefanie M. Hauck, Stephanie Schoeffmann, Barbara Amann, Manfred Stangassinger, Marius Ueffing and Cornelia A. Deeg "Serum PEDF Levels Are Decreased in a Spontaneous Animal Model for Human Autoimmune Uveitis" J Proteome Res. 2009 Feb 6;8(2):992-998.

Name: Gal, Andreas ; Participant: 12a ; Work Package (WP): WP 8

Publications

A. Schuster, A. R. Janecke, R. Wilke, E. Schmid, D. A. Thompson, G. Utermann, B. Wissinger, E. Zrenner, and A. Gal. The phenotype of early-onset retinal degeneration in persons with RDH12 mutations. Inv. Ophthalmol. Vis. Sci., 48, 1824-1831 (2007).

I. Kurth, D.A. Thompson, K. Ruther, K.L. Feathers, J.D. Chrispell, J. Schroth, C.L. McHenry, M. Schweizer, S. Skosyrsky, A. Gal, and C.A. Hubner.. Targeted disruption of the murine retinal dehydrogenase gene Rdh12 does not limit visual cycle function. Mol. Cell. Biol., 27, 1370-1379 (2007).

C.F. Chakarova, M.G. Papaioannou, H. Khanna, I. Lopez, N. Waseem, A. Shah, T. Theis, J. Friedman, C. Maubaret, K. Bujakowska, B. Veraitch, M.M. El-Aziz, Q. de Prescott, S.K. Parapuram, W.A. Bickmore, P.M. Munro, A. Gal, C.P. Hamel, V. Marigo, C.P. Ponting, B. Wissinger, E. Zrenner, K. Matter, A. Swaroop, R.K. Koenekoop, and S.S. Bhattacharya. Mutations in TOPORS cause autosomal dominant retinitis pigmentosa with perivascular retinal pigment epithelium atrophy. Am. J. Hum. Genet., 81:1098-103 (2007).

J. Neidhardt, E. Glaus, B. Lorenz, A. Gal, W. Berger: Identification of novel mutations in X-linked retinitis pigmentosa families and implications for diagnostic testing. Mol. Vis., 14:1081-1093 (2008)

A.B. Renner, A. Gal, B. Wissinger, U. Kellner: Long-term follow-up of the phenotype of periphe-rin/RDS gene mutations. Am. J. Ophthalmol., 147:518-530 (2009)

C. Schob, C.F. Chakarova, S. Bhattacharya, A. Gal, S. Kindler: Mutations in TOPORS: a rare cause of autosomal dominant retinitis pigmentosa in continental Europe? Ophthalmic Genet., in press (2009)

J.D. Chrispell, K.L. Feathers, A. Gal, D.A. Thompson
RDH12 activity and effects on retinoid processing in the murine retina.
J. Biol. Chem., accepted for publication

Name: Christian Grimm, C. Remé ; Participant:13a ; Work Package (WP): WP11

Planned /actual Dates	Type	Type of audience	Countries addressed	Size of audience	Partner responsible /involved
06.05.-11.05.2007	ARVO Meeting Ft Lauderdale USA	Research	**International**	5000	**13a**
31.03.2008	Symposium of the Center for Integrative Human Physiology, Zürich, Switzerland	Research and Higher Education	**Switzerland**	150	**13a**
27.03.2008	Symposium of the Center for Clinical Research, Zürich, Switzerland	Research	**Switzerland**	80	**13a**
25.11. –	Meeting; Hypoxia, form	Research	**Internationa**	150	**13a**

Planned /actual Dates	Type	Type of audience	Countries addressed	Size of audience	Partner responsible /involved
30.11.02 007	integrative biology to human disease		**l**		
14.02.-15.02.20 08	Swiss Eye Research Meeting Brunnen Switzerland	Research	**Switzerland**	100	**13a**
May 2008	Invited Seminar	Research	**Germany**	50	**13a**
June 2008	Conference; Symposium Zurich	Research	**Internationa l**	80	**13a**
July, 2008	Seminar	Research	**Germany**	40	**13a**
Aug, 2008	Seminar	Research	**Germany**	20	**13a**
Sept, 2008	Conference; RD2008, Chengdu, China	Research	**internationa l**	150	**13a**
Oct, 2008	Seminar	Research	**Germany**	20	**13a**
Jan, 2009	Seminar	Research	**Germany**	50	**13a**

Markus Thiersch, Wolfgang Raffelsberger, Rico Frigg, Marijana Samardzija, Andreas Wenzel, Olivier Poch and Christian Grimm *(accepted) Analysis of the retinal gene expression profile after hypoxic preconditioning identifies candidat genes for neuroprotectionBMC Genomics*

Grimm C., Wenzel A., Samardzija M., Thiersch M. (2007)*Mechanisms of cell death and neuroprotection in retinal degenerationsIn: Brain and retina in degenerative diseases of childhood, by Schmitt B., Kohlschütter A., Neubauer B., Plecko-Startling B. (Edts.) SPS Verlagsgesellschaft, Heilbronn, Germany. pp 170-180.*

Joly, S., Lange, C., Thiersch, M., Samardzija, M., Grimm, C. *(2008)Leukemia inhibitory factor extends the lifespan of injured photoreceptors in vivo. J. Neurosci. 28, 13765-13774.*

Thiersch, M., Raffelsberger, W., Frigg, R., Samardzija, M., Wenzel, A., Poch, O., Grimm, C *(2008) Analysis of the retinal gene expression profile after hypoxic preconditioning identifies candidate genes for neuroprotectionBMC Genomics, 9:73*

Name: F. Holz, H. Scholl; Participant: 14a & 14b; Work Package (WP): WP1

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Schmitz-Valckenberg S, Fleckenstein M, Helb HM, Charbel Issa P, Scholl HPN, Holz FG (2009) In-vivo imaging of foveal sparing in geographic atrophy secondary to age-related macular degeneration. Invest Ophthalmol Vis Sci. 51: in press. (IF 3,8)

Charbel Issa P, van der Veen RL, Stijfs A, Holz FG, Scholl HPN, Berendschot TTJM (2009) Quantification of reduced macular pigment optical density in the central retina in macular telangiectasia type 2. Exp Eye Res: published online. (IF 2,7)

Charbel Issa P, Bolz HJ, Ebermann I, Domeier E, Holz FG, Scholl HPN (2009) Characterization of severe rod-cone dystrophy in a consanguineous family with a splice site mutation in the MERTK gene. Brit J Ophthalmol 93: in press. (IF 2,5)

Finger RP, Charbel Issa P, Fimmers R, Holz FG, Rubin GS, Scholl HPN (2008) Reading performance is reduced due to parafoveal scotomas in patients with macular telangiectasia type 2. Invest Ophthalmol Vis Sci. 50:1366-70. (IF 3,8)

Pauleikhoff D, Scheider A, Wiedmann P, Gelisken F, Scholl HPN, Roider I, Mohr A, Zlateva G, Xu X. (2008) Neovaskuläre altersabhängige Makuladegeneration in Deutschland. Beinträchtigung der Lebensqualität und ihre finanziellen Auswirkungen [Neovascular age-related macular degeneration in Germany: Encroachment on the quality of life and the financial implications.] Ophthalmologe 105: published online. (IF 0,8)

Scholl HPN, Charbel Issa P, Walier M, Janzer S, Pollok-Kopp B, Börncke F, Fritsche LG, Chong NV, Fimmers R, Wienker T, Holz FG, Weber BHF, Oppermann M (2008) Systemic complement activation in age-related macular degeneration. PLoS ONE 3(7):e2593.

Fleckenstein M, Charbel Issa P, Helb HM, Schmitz-Valckenberg S, Scholl HPN, Holz FG (2008) OCT correlates of lines of increased autofluorescence in macular dystrophy and PPRCA. Arch Ophthalmol. 126:1461-1463. (IF 3,2)

Fleckenstein M, Charbel Issa P, Helb HM, Schmitz-Valckenberg S, Finger RP, Scholl HPN, Löffler KU, Holz FG (2008) High resolution spectral domain-OCT imaging in geographic atrophy associated with age-related macular degeneration. Invest Ophthalmol Vis Sci 49:4137-4144. (IF 3,8)

Charbel Issa P, Finger RP, Holz FG, Scholl HPN (2008) Eighteen month follow-up of intravitreal bevacizumab in type 2 idiopathic macular telangiectasia. Brit J Ophthalmol 92:941-5. (IF 2,5)

Helb HM, Charbel Issa P, Fleckenstein M, Schmitz-Valckenberg S, Scholl HPN, Holz FG (2008) Confocal SLO angiography and fundus autofluorescence imaging combined with high-speed, high-resolution, spectral domain optical coherence tomography. Acta Ophthalmol Scand. [in press]

Charbel Issa P, Scholl HPN, Gaudric A, Massin P, Kreiger AE, Schwartz S, Holz FG (2008) Macular full-thickness and lamellar holes in type 2 idiopathic macular telangiectasia. Eye [published online]

Fleckenstein M, Charbel Issa P, Fuchs HA, Finger RP, Helb HM, Scholl HPN, Holz FG (2008) Discrete lines of increased fundus autofluorescence in retinal dystrophies and functional correlate on microperimetry. Eye [in press]

Helb HM, Charbel Issa P*, Berendschot TT, Scholl HPN, Holz FG (2008) Abnormal Macular Pigment Distribution in Type 2 Macular Telangiectasia. Retina [in press]*

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Ladewig MS, Karl SE, Hamelmann V, Helb HM, Scholl HPN, Holz FG, Eter N. (2008) Combined intravitreal bevacizumab and photodynamic therapy for neovascular age-related macular degeneration. Graefes Arch Clin Exp Ophthalmol. 246:17-25.

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Reinhard J, Messias A, Dietz K, Mackeben M, Lakmann R, Scholl HPN, Apfelstedt-Sylla E, Weber BHF, Seeliger MW, Zrenner E, Trauzettel-Klosinski S (2007) Quantifying fixation in patients with Stargardt disease. Vision Res. 47:2076-85.

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Holz FG, Bindewald-Wittich A, Fleckenstein M, Dreyhaupt J, Scholl HPN, Schmitz-Valckenberg S, FAM-Study Group (2007) Progression of Geographic Atrophy and Impact of Fundus Autofluorescence Patterns in Age-related Macular Degeneration. Am J Ophthalmol 143: 463-472.

Ebermann I, Walger M, Scholl HPN, Charbel Issa P, Lüke C, Nürnberg G, Lang-Roth R, Becker C, Nürnberg P, Bolz HJ (2007) Truncating mutation of the DFNB59 gene causes endocochlear hearing impairment and central vestibular dysfunction. Hum Mutat. 28: 571-577.

Ebermann I, Scholl HPN, Charbel Issa P, Becirovic E, Lamprecht J, Jurklies B, Millan JM, Aller E, Mitter D, Bolz H (2007) A novel gene for Usher syndrome type 2: mutations in the long isoform of whirlin are associated with retinitis pigmentosa and sensorineural hearing loss. Hum Genet. 121: 203-211.

Name: C. Fasser ; Participant: 16a ; Work Package (WP): WP17, WP18

Planned/actual Dates	Type	Type of audience	Countries addressed	Size of audience	Partner responsible /involved
3-4 March, 2005	EVI-Genoret Kick-off Meeting	Research	**International**	100	16
13-15 March, 2006	1st EVI-Genoret Annual Meeting	Research	**International**	100	**16**
September 2006	Press release(press/radio/TV	General Public	**German speaking**	n/a	**16**
October 17-22, 2006	Organisation of the Conference: 14th Retina International World Congress in Rio de Janeiro (Brazil)	Patients / General / Researcher / Clinicians	**International**	1000	**16**
18-21 March 2007	EVI-Genoret Midterm Review Meeting	Research	**International**	100	**16**
10-11 March, 2008	3rd EVI-Genoret Annual Meeting	Research	**International**	100	**16**
5-6 March, 2009	4th EVI-Genoret Annual Meeting	Research	**International**	100	**16**
Regularly running	Direct e-mailing: Regular Newsletter	Patients / General / Researcher / Clinicians	**International**	3000	**16**

Name: Frank Mueller, Participant: 17a¸Work Package (WP) 15

Planned /actual Dates	Type	Type of audience	Countries addressed	Size of audience	Partner responsible /involved
3-4 March, 2005	EVI-Genoret Kick-off Meeting	Research	**International**	100	17a
13-15 March, 2006	1st EVI-Genoret Annual Meeting	Research	**International**	100	17a
July 8th – 12th 2006	Poster, Conference FENS, Vienna, Austria	Research	**International**	>1000	17a
August 28th 2006	Lecture, Workshop Virtual Institute of Biohybridtechnology, Aachen, Germany	Research	**Germany**	40	17a
18-21 March 2007	EVI-Genoret Midterm Review Meeting	Research	**International**	100	17a
March 30th 2007	Poster, Conference Pro-Retina Research Colloquium	Research	**International**	ca. 150	17a
10-11 March,	3rd EVI-Genoret Annual Meeting	Research	**International**	100	17a

Planned /actual Dates	Type	Type of audience	Countries addressed	Size of audience	Partner responsible /involved
2008					
5-6 March, 2009	4th EVI-Genoret Annual Meeting	Research	**International**	100	17a

Poster: G. Knop, A. Brombas, A. Mataruga, U.B. Kaupp, F. Müller „ON- and OFF-retinal ganglion cells show altered light responses upon targeted deletion of the HCN1-channel gene"; Biannual Meeting FENS, July 8th – 12th 2006, Vienna, Austria

Lecture: F. Müller "Molecular Analysis of the first Steps in Vision"; August 28th 2006, Workshop of the Virtual Institute for Biohybridtechnology, Aachen

Poster: D. Kaschuba, A. Brombas, F. Müller „Optical and electrophysiological recording of light responses in the mouse retina". Pro Retina Research Colloqium, March 30th- 31st, 2007, Potsdam, Germany

Name: U. Chakravarthy ; Participant: 19a ; Work Package (WP): WP1

Publications

The list of publications which would not have been possible without EVIGENORET funding is shown below

Hughes AE, Orr N, Esfandiary H, Diaz-Torres M, Goodship T, Chakravarthy U. A common CFH haplotype with deletion of CFHR1 and CFHR3 is associated with a lower risk of age-related macular degeneration. Nat Genetics 2006, 38:1173-7

Hogg RE, Woodside JV, Gilchrist SE, Graydon R, Fletcher AE, Chan W, Knox A, Cartmill B, Chakravarthy U. Cardiovascular Disease and Hypertension Are Strong Risk Factors for Choroidal Neovascularization. Ophthalmology 2007, epub ahead of print.

Hughes AE, Patterson CC, Esfandiary H, Hogg RE, McConnell V, Silvestri G, Chakravarthy U. Neovascular age-related macular degeneration risk based on CFH, LOC387715/HTRA1, and smoking. PLoS Med. Epub 355 ahead of print. Dec 2007

Moutray T, Alarbi M, Mahon G, Chakravarthy U. Relationships between clinical measures of visual function, fluorescein angiographic and OCT features in patients with subfoveal CNV. Br J Ophthalmol. 2008 Mar;92(3):361-4.

McKay G, Silvestri G, Patterson C, Hogg RE, Chakravarthy U, Hughes AE. Further assessment of the Complement Component 2 and Factor B region associated with Age-related Macular Degeneration. Invest Ophthalmol., 2009; 50:533-9

McKay GJ, Silvestri G, Orr N, Chakravarthy U, Hughes AE. VEGF and age-related macular degeneration. Ophthalmology. 2009 Jun;116(6):1227.e1-3

Hogg RE, Woodside JV, Gilchrist SE, Graydon R, Fletcher AE, Chan W, Knox A, Cartmill B, Chakravarthy U. Cardiovascular Disease and Hypertension Are Strong Risk Factors for Choroidal Neovascularization. Ophthalmology 2007, epub ahead of print.

Hughes AE, Patterson CC, Esfandiary H, Hogg RE, McConnell V, Silvestri G, Chakravarthy U. Neovascular age-related macular degeneration risk based on CFH, LOC387715/HTRA1, and smoking. PLoS Med. 2007 Dec;4(12):e355

Name: O. POCH ; Participant: 20a ; Work Package (WP): WP14

Exploitable Knowledge (description)	**Exploitable product(s) or measure(s)**	**Sector(s)** of application	Timetable for commercial use	Patents or other IPR protection	**Owner** & Other Partner(s) involved
Knowledge of gene promoter	PromAn Program	Medical	2008		IGBMC CNRS ULP
Retinal transcriptome	RetChip	Medical	2008		EVI-GENORET consortium

Exploitable Knowledge (description)	**Exploitable product(s) or measure(s)**	**Sector(s)** of application	Timetable for commercial use	Patents or other IPR protection	**Owner** & Other Partner(s) involved
Transcriptomic knowledge	GxDb: Tools, algorithms and database dedicated to transcriptomic data	Medical	2009		IGBMC IDV
Proteomic knowledge	iDOUBT	Research	2009		IGBMC IBMC
Genoret Database		Research			EVI-GENORET
17/10/08	*Poster GxDb Cancéropôle du Grand-Est*	Medical and Research	*Vittel (France)*	*200*	Poidevin
17 and 18/02/09	*Joint Meeting IGBMC-IBMC*	Research	*Mont St Odile (France)*	*300*	Poch, Ripp

Planned/ actual Dates	**Type**	**Type of audience**	**Countries addressed**	**Size of audience**	**Partner responsible /involved**
2007 . Jan 25-26	Joint Meeting IGBMC-IBMC	Research	Mont St Odile France	300	20a, 20c
2006 Jul 5-7	Conference: JOBIM 2006	Research	Bordeaux (France)	400	20a
2006 Jun 12-14	IFBM 2006 Meetings India	Research	**International**	60	20a
2006 Aug 30-31 Sep 1	Conference: Automated function prediction San Diego (US)	Research	**International**	300	20a
2008/04	Posters	ARVO (research)	**International**	2000	20a

Publications:

RETINOBASE: a web database, data mining and analysis platform for gene expression data on retina. *Ravi Kiran Reddy Kalathur,[1] Nicolas Gagniere,[1] Guillaume Berthommier,[1] Laetitia Poidevin,[1] Wolfgang Raffelsberger,[1] Raymond Ripp,[1] Thierry Léveillard,[2] and Olivier Poch[1] BMC Genomics. 2008; 9: **208**.*

iDOUBT: the open loop of in silico DNA analysis. *Y-N Anno, E. Harle, P. Carbon, O. Poch and O. Lecompte. manuscript in preparation.*

The thioredoxin-like protein RdCVFL interacts with Tau and inhibits its phosphorylation in the retina. *Fridlich R, Delalande F, Jaillard C, Lu J, Poidevin L, Cronin T, Perrocheau L, Millet-Puel G, Niepon ML, Poch O, Holmgren A, Van Dorsselaer A, Sahel JA, Léveillard T. Mol Cell Proteomics. 2009 Mar 11.*

The homeobox gene CHX10 regulates RdCVF promoter activity in inner retina. *S. Reichmann, R. Kiran Reddy, S. Lambard, A. Lardenois, R. Ripp, O. Poch, D. Zack, J. Sahel, T. Léveillard. manuscript submitted*

SM2PH-db: an interactive system for the integrated analysis of phenotypical consequences of missense variations in proteins involved in human monogenic diseases. *Friedrich A, Garnier N, Nguyen H, Bettler E, Deléage G, Poch O, Moulinier L. manuscript in preparation.*

Name: Raymond Ripp ; Participant: 20c ; Work Package (WP): WP16

Exploitable Knowledge (description)	**Exploitable product(s) or measure(s)**	**Sector(s)** of application	Timetable for commercial use	Patents or other IPR protection	**Owner** & Other Partner(s) involved
Annotation tool	ImAnno	Medical			All EVI-Genoret Participants

Planned / actual Dates	**Type**	**Type of audience**	**Countries addressed**	**Size of audience**	**Partner responsible /involved**
since 2006 Running	EVI-Genoret database	Genoret members	EU	120	20c
2006/2007	All component meetings	Genoret members	EU	120	20c
2007/2/22	Seminar IGBMC on the EVI-Genoret Database	Research	France	300	20c
2007/5	Poster at ARVO	Research	**International**	1000	20
2007/03/29	Potsdam Seminar	Students	**EU**	?	20c

Name: Carmen AYUSO ; Participant:22a ; Work Package (WP): WP2

Planned/actual Dates	**Type**	**Type of audience**	**Countries addressed**	**Size of audience**	**Partner responsible /involved**
ORGANIZATION OF CONFERENCES AND MEETINGS					
2 June 2006 Retina Madrid	Organization of VI Internacional Conference on Retinal Dystrophies	Research & Clinicians	**(international)**	150	22
2 June 2006 Retina Madrid	Organization of Special Simposium on Bardet Biedl Syndrome	Research, Clinicians & Patients	**(international)**	50	22
3 June 2006 Retina Madrid	Organization of VI Internacional Conference on Retinal Dystrophies	General Public	**(international)**	300	22
8th February 2007 FJD Madrid	Organization of 2nd Int Res Meeting	Research, Clinicians &	**(international)**	350	22
25th May 2007 FJD-FCR Madrid	Organization of Simposium on Genomic Medicine	Research, Clinicians &	**(international)**	150	22
26th June 2007 FJD Madrid	Organization of Clinical Trials and PGx meeting	Research, Clinicians &	**(SPAIN)**	300	22
PARTICIPATION AS A SPEAKER IN CONFERENCES AND MEETINGS					
18-21 May 2006 Lisboa	Conference Euretina Congress	Research & Clinicians	**(international**	300	22

Planned/actual Dates	Type	Type of audience	Countries addressed	Size of audience	Partner responsible /involved
2 Oct 2006 Vitoria	Conference Spanish RP Patients association	General Public	**(SPAIN)**	100	22
20-22 Oct 2006 Rio de Janeiro	Conference Retina Internation	Research & Clinicians	**(international**	300	22
25 Oct 2006 Madrid	2nd International Conference on Rare Diseases	Research & Clinicians	**(international**	35	22
23-25 Nov 2006 Barcelona	Conference Catal Ophthalm	Clinicians	**(SPAIN)**	200	22
25 Novt 2006 Madrid	Meeting participation Spanish RP Patients association	General Public	**(SPAIN)**	100	22
1-2 Febr 2007 Carmona, Sevilla	Meeting of Rare Diseases CIBER-ER	Research & Clinicians	**(SPAIN)**	50	22
ORGANIZATION and PARTICIPATION IN COURSES					
Sp Techn Org March 2006	Course for Techn Organization: Cytogenetics	Technicians	**(SPAIN)**	30	22
Sp Techn Org March 2006	Course for Techn Organization: Molecular Genetics	Technicians	**(SPAIN)**	30	22
24-28 Apr 2006 Valladolid	Hybrid Course ESGM	Research & Clinicians	**Europe (international)**	50	22
FUNDACION JIMENEZ DIAZ Madrid May 2006	Course for Nurses and specialists Orrganization: Cytogenetics	Research & Clinicians	**(SPAIN)**	30	22
Bertinoro (Italia), 24-28 Sept 2006	8TH COURSE IN MOLECULAR CYTOGENETICS AND DNA MICROARRAYS	Research	**Europe (international)**	30	22
25–29 Sep 2006. Madrid	Course Public Health School	Nurses	**(SPAIN)**	30	22
29 Nov 2006 Badajoz	Course on Advances on Genet	Research & Clinicians	**(SPAIN)**	50	22
12th Dec 2006 IOBA Valladolid	Ph Doct Course Organization	Research & Clinicians	**Europe (international)**	30	22
Feb 2007 Madrid	Ph Doct Course Bioethics	Research & Clinicians	**UNESCO (international)**	30	22
Feb 2007 Madrid	Ph Doct Course Genetics	Teachers Ministry of Education	**(SPAIN)**	30	22
Jan-June 2007	Superior Course on Genetic Conselling	University CEU	**(SPAIN)**	30	22

2007	*Publication: "Partial paternal uniparental disomy (UPD) of chromosome 1 in a patient with Stargardt disease."* *R.Riveiro-Alvarez, D.Valverde, I.Lorda-Sanchez, MJ Trujillo-Tiebas, D.Cantalapiedra, E.Vallespin J.Aguirre-Lamban, C.Ramos, C.Ayuso.*	*Molecular Vision 2007; 13:96-101 PMID: 17277736*
2007	*Publication: "MYO7A Mutation Screening in Usher Syndrome Type I Patients from Diverse Origins."*	*J Med Genet. 2007 Mar;44(3):e71.PMID:*

	Jaijo T, Aller E, Beneyto M, Najera C, Graziano C, Turchetti D, Seri M, Ayuso C, Baiget M, Moreno F, Morera C, Perez-Garrigues H, Millan JM.	*17361009*
2007	*Publication: "Spectrum of the ABCA4 gene mutations implicated in severe retinopathies from Spanish patients."* *Diana Valverde, Rosa Riveiro-Alvarez, Montserrat Baiget, Miguel Carballo, Guillermo Antiñolo, José Maria Millán, Blanca Garcia Sandoval, Carmen Ayuso.*	*Invest Ophthalmol Vis Sci. 2007 Mar; 48 (3):985-90. PMID: 17325136*
2007	*Publication: "SOX2 anophthalmia syndrome: twelve new cases demonstrating broader phenotype and high frequency of large gene deletions."* *Bakrania P, Robinson DO, Bunyan DJ, Salt A, Martin A, Crolla JA, Wyatt A, Fielder A, Ainsworth J, Moore A, Read SP, Uddin J, Laws D, Pascuel-Salcedo D, Ayuso C, Allen L, Collin JR, Ragge N.*	*Br J Ophthalmol. 2007;91:1471-6. PMID: 17522144*
2007	*Publication: "High prevalence of mutations in peripherin/rds in autosomal dominant macular dystrophies in a Spanish population."* *Imma Hernan, María José Gamundi, Marta Muntanyola, María José Trujillo, Blanca Garcia-Sandoval, Carmen Ayuso, Monserrat Baiget, Miguel Carballo*	*Mol Visión 2007; 13:1031-1037. PMID: 17653047*
2007	*Publication: "Gene symbol: CRB1."* *Vallespin E, Riveiro-Alvarez R, Cantalapiedra D, Aguirre-Lambam J, Avila-Fernandez A, Lopez-Gimenez-Pardo A, Trujillo-Tiebas MJ, Ayuso C.*	*Hum Genet. 2007 Apr;121(2):297-8. PMID: 17598245*
2007	*Publication: "Gene symbol: RP2."* *Villaverde-Montero C, García-Hoyos M, Giménez-Pardo A, Trujillo-Tiebas MJ, Baiget M, Ayuso C.*	*Hum Genet. 2007 Apr;121(2):289 PMID: 17598203*
2007	*Publication: "Gene symbol: CRB1."* *Vallespin E, Riveiro-Alvarez R, Cantalapiedra D, Aguirre-Lambam J, Avila-Fernandez A, Lopez-Gimenez-Pardo A, Trujillo-Tiebas MJ, Ayuso C.*	*Hum Genet. 2007 Apr;121(2):297-8. PMID: 17598198*
2007	*Publication: "Gene symbol: CRB1."* *Vallespin E, Millan JM, Riveiro-Alvarez R, Aguirre-Lamban J, Cantalapiedra D, Gallego J, Trujillo-Tiebas MJ, Ayuso C.*	*Hum Genet. 2007 Feb;120(6):914 PMID: 17438615*
2007	*Publication: "Gene symbol: CHM (REP-1). Disease: Choroideraemia."* *M.J.Trujillo-Tiebas; M.Garcia-Hoyos; N.Pérez-González; R.C.Narvaiza; J.M.Millán; C.Ayuso*	*Hum Genet. 2007 Feb. Temporary Accession #: M20070105/12.33.48.*
2007	*Publication: "Gene symbol: CRB1."* *Vallespin E, Millan JM, Riveiro-Alvarez R, Aguirre-Lamban J, Cantalapiedra D, Gallego J, Trujillo-Tiebas MJ, Ayuso C.*	*Hum Genet. 2007 Feb;120(6):914 PMID: 17438615*
2007	*Publication: "Gene symbol: CHM (REP-1). Disease: Choroideraemia."* *M.J.Trujillo-Tiebas; M.Garcia-Hoyos; N.Pérez-González; R.C.Narvaiza; J.M.Millán; C.Ayuso*	*Hum Genet. 2007 Feb. Temporary Accession #: M20070105/12.33.48.*
2007	*Publication: "Novel human pathological mutations. Gene symbol: CHM. Disease: choroideraemia."* *Villaverde C, Trujillo-Tiebas MJ, Garcia-Hoyos M, Narvaiza RC, Perez N, Guillén E, Ayuso C*	*Hum Genet. 2007; 121:648. PMID: 17879443*
2007	*Publication: "Novel human pathological mutations. Gene symbol: CHM. Disease: choroideraemia."* *Villaverde C, Trujillo-Tiebas MJ, Garcia-Hoyos M, Narvaiza RC, Perez N, Garcia-Sandoval B, Ayuso C.*	*Hum Genet. 2007; 121:648. / PMID: 17879444*
2007	*Publication: "Screening of the USH1G gene among Spanish patients with Usher syndrome."* *Elen Aller, T Jaijo, M Beneyto, C Najera, C Morero, H Perez-Garrigues, C Ayuso, J M Millan*	*Ophthalmic Genet. 2007; 28:151-5*
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Name: SMARAGDA KAMAKARI ; Participant:23a ; Work Package (WP): WP7

Exploitable Knowledge (description)	**Exploitable product(s) or measure(s)**	**Sector(s)** of application	Timetable for commercial use	Patents or other IPR protection	**Owner** & Other Partner(s) involved
Construction of a microarray chip for rapid/high throughput detection of unknown mutations in known retinal genes	Molecular diagnostics	Medical		A materials patent is planned	Partner 23 (owner) Component C partners

Planned /actual Dates	**Type**	**Type of audience**	**Countries addressed**	**Size of audience**	**Partner responsible /involved**
3-4 March, 2005	EVI-Genoret Kick-off Meeting	Research	**International**	100	23
13-15 March, 2006	1st EVI-Genoret Annual Meeting	Research	**International**	100	23
2007	Conference	Research	**International**		23/3a
2007	Posters	Research	**International**		23
18-21 March 2007	EVI-Genoret Midterm Review Meeting	Research	**International**	100	23
10-11 March, 2008	3rd EVI-Genoret Annual Meeting	Research	**International**	100	23
2009	Publications	Research	**International**		23
2008	Posters	Research	**International**		23
5-6 March, 2009	4th EVI-Genoret Annual Meeting	Research	**International**	100	23