

PROJECT ACHIEVEMENTS DURING THE REPORTING PERIOD

Research Achievements

TEAM I (LONDON)

In the second year of the RetNet project (1st Jan 05 to 31st Dec 05) we consolidated the genetic mapping information of a new locus (RP31) for autosomal dominant RP (adRP) to chromosome 9 and published this work in the journal of Human Genetics. Subsequently we undertook positional cloning for the novel chromosome 9 adRP gene by large scale sequencing of all relevant genes in the genetic interval (a 15Mb region containing over 50 genes) and have successfully identified the RP31 gene. Extensive confirmatory and functional genomic work for this gene is currently ongoing and will comprise a significant part of work for the 3rd year of the RetNet project. Additionally we genetically mapped a large French adRP family to chromosome 3q and found a previously unreported rhodopsin mutation which is a 9bp deletion from nucleotide position 615 to 623 in exon3. In parallel we are also undertaking a total genome screen for adRP in a large English family in which all previously known loci for adRP have already been excluded. This indicates the possibility of finding another new adRP locus in due course. As part of the ongoing functional studies of adRP genes, we have created a mouse Knock-In model carrying a heterozygous A216P mutation in one of the splicing factor genes (PRPF31). This particular change has previously been described in one of our RP11 families. The mice are viable and at the moment they are at the colony expansion stage. The murine retinas will be investigated by ERG and histological studies at different ages (3, 6, 12 months) for the possibility of photoreceptor degeneration. We have also been working on an ex-vivo splicing assay, trying to understand the disease mechanism of RP involving the splicing factors. These studies will continue in the following year of the project.

TEAM II (DUBLIN)

We have effectively delivered AAV subretinally to both postnatal and adult mice, achieving extensive and exclusive transduction of the outer nuclear layer (ONL). This technology has subsequently been utilised for the delivery of each of our therapeutic strategies. Papers describing the use of shRNA molecules to down-regulate rhodopsin and rds-peripherin genes have now been published by our group (Kiang et al; 2005 and Palfi et al; 2006) and in vivo studies in an AAV context are ongoing.

Initial studies into the therapeutic potential of p35 for the treatment of retinal degenerations have indicated p35 expression to have some protective effect in retinal explants exposed to an apoptosis inducing agent.

In respect to the RP10 form of retinitis pigmentosa, electroretinographic studies undertaken on 120 IMPDH1^{-/-} mice have demonstrated this to be an attractive target for therapeutic intervention. AAV.wtIMPDH1 2/5 has been injected into mice showing reduced ERG amplitudes and periodic electrophysiological assessments will be performed to evaluate changes in the responses. Preservation of ERG in such animals as a result of expression of wild type IMPDH1 protein could form part of a therapeutic strategy for prevention of the dominant form of disease in man.

TEAM III (TUEBINGEN)

Our work combines in silico analysis of ESTs and of algorithm predictions together with experimental validation of them through RNA Ligase Mediated Rapid Amplification of cDNA Ends (RLM-RACE, Ambion) which is designed to amplify cDNAs only from full length capped mRNA. The criteria of gene inclusion selects for retina or retinal cell type gene expression specificity, relationship of the gene with retinal diseases and comparison of expression pattern through microarray data analysis. In 2005 we have completed the analysis of forty genes and others thirty-four are in progress. Our results can be grouped in three categories: confirmation of previously described

5' UTR extensions, variable length extensions of their respective first exon. Shorted length of a non-coding first exon was also found for other two genes. Finally, a group of six genes shown new UTR exons, and the lacking of an annotated one. The obtained data are currently used to identify common as well as specific patterns and sequence motifs in retinal gene promoters by means of bioinformatics (in collaboration with the group of Olivier Poch). In addition we have generated reporter gene constructs to assess promoter function for CNGA3, OPA1 and OPTN.

TEAM IV (NAPLES)

We selected 126 murine and 106 human EST clusters with eye-predominant expression for analysis by RT-PCR and RNA in situ hybridisation (ISH). A first group of 32 murine and 31 human clusters was analysed by RT-PCR. Expression was determined in different tissues of CD1 mice (eye, retina, brain, heart, lung, liver, kidney) and on cDNA from mouse eyes at different developmental stages (E12.5, E14.5, E16.5, P0, P8, adult). For the human clusters, RT-PCR was performed on cDNA from human tissues (kidney, muscle, lung, liver, fetal brain and retina). All murine and human clusters analysed were strongly expressed in the retina. Cryosections have been prepared from CD1 mice and human eye bulbs from cornea donors. Probes were synthesized either by PCR amplification on genomic DNA or from BMAP/IMAGE clones. Expression analysis by RNA ISH on cryosections is currently ongoing. We have also selected 9 murine microRNAs that were either cloned exclusively from eye-derived tissues (RNA. 2003. 9:175) or reported to be expressed in the zebrafish eye (Science. 2005. 309:310). For these miRNAs, we have ordered LNA-modified probes from Exiqon and we are currently performing expression analysis both by whole-mount and cryosection ISH.

TEAM V (PARIS)

RdCVF is a rod derived cone viability factor. It is expressed by rod cells. The protein exists in 2 forms: a short and a long one and has 33% similarity to Thioredoxin-1. The specific objective of my project is to identify RdCVF interaction proteins. As first step, I demonstrated the expression of the long isoform of the protein in cones enriched cultures (chicken). Contrarily, the chicken cones do not express a short isoform. The 2nd step is to find the protein partners of RdCVF using 2-hybrid system. According to previous studies, ASK1 interacts with Thioredoxin. I showed this interaction and I have also tested the interaction between ASK1 & RdCVF long form and short form. Both forms do not interact. Screening a cone library cDNA with RdCVF didn't show any colony. The question of the protein expression in the MAV203 yeast strain had emerged. In order to be sure that RdCVF sequence is actually in the right reading frame, I transfected COS cells with plasmid containing RdCVF. Western Blot identified RdCVF in the cell lysates, which means that its sequence was in the correct reading frame (Short stay in Nijmegen). To be sure that RdCVF does not interact with ASK1, I used other vectors and yeast strains providing by the Nijmegen group. As previous, no interaction was shown. Immunoprecipitation and Gel shift assay of MAV203 yeast strain showed that RdCVF isn't expressed. Furthermore, RT-PCR showed that probably the mRNA isn't transcribed.

TEAM VI (STRASSBURG)

The Laboratoire de BioInformatique et Génomique Intégrative in Strasbourg performed the transcriptomics data analysis of GDNF, CNTF and Diltiazem target genes in rd1 mice (task T6/1 and milestone M6/1), comparative genomics of GDNF CNTF and Diltiazem target genes (T6/2) and the creation of a dedicated database for transcriptomics data (T6/3).

In order to provide high quality results we have evaluated various modes for analyzing microarray data and developed novel methods for attributing a quality index to every measurement with the aim of identifying regulated target genes combined with a universal quality index. By limitation of the false discovery rate (FDR) in statistical tests we defined the list of differentially regulated target genes due to injection of neuroprotective agents. We have further investigated these targets using RetScope, a comprehensive annotation platform dedicated to retinal target validation. We have initiated developing a relational database (RETINOBASE) dedicated to retina-related transcriptomic experiments (from human and animal models) with unified normalisation and threshold calculation. The data are contributed from RetNet partners (9 microarray projects), data from public sources (3 projects) and selected publications (4 projects). RETINOBASE allows fast and flexible query options across multiple platforms to investigate gene regulation.

TEAM VII (NIJMEGEN)

Exudative vitreoretinopathy/microcephaly

We ascertained a female patient with exudative vitreoretinopathy/microcephaly and mild mental retardation carrying a large de novo chromosome 6 inversion. Employing FISH of chromosome 6 BAC clone DNAs, we were able to characterize the breakpoints in greater detail. It appears that this genomic rearrangement not only consists of an inversion but also of a microduplication of 60 kb. Identification of the exact breakpoints of the inversion and duplication(s) will show which of the genes located at the breakpoints can be considered as candidates for the observed phenotype. Two promising candidate genes located at the breakpoint were tested in 3 other unrelated patients with microcephaly and vitreoretinopathies, but no causative variants were identified. In the coming months we will employ Southern blot and MLPA analysis to fine map the duplicated/inverted chromosomal segments.

Wagner disease

Despite an accurate assignment of the Wagner disease gene at 5q14 several years ago, causal defects were not found up to recently. Detailed haplotype analysis of six large Wagner disease families and one erosive vitreoretinopathy family revealed a common Dutch founder haplotype in four Wagner disease families, which, surprisingly, also was found in the erosive vitreoretinopathy family. This suggests that the same mutation underlies Wagner disease and erosive vitreoretinopathy. The critical region is located between D5S626 and D5S107, spanning a 3-cM/2-Mb chromosomal region.

Recently a Japanese group reported on the identification of a splice site mutation in CSPG2/Versican, a gene residing in the critical region and previously excluded as the causal gene due to the absence of pathologic variants in the open reading frame and flanking splice sites by dr. G. Black and colleagues (Manchester). The defect identified resulted in an apparently benign 39-nt in-frame deletion in exon 8.

Sequence analysis of the CSPG2/Versican gene in our families revealed an intron 7 splice site sequence variant (c.4004-5T>C) in the four Wagner disease families carrying the Dutch founder haplotype, and changes in the same splice site (c.4004-5T>A and c.4004-1G>A) in two other unrelated Wagner disease families. Qualitative RT-PCR of mRNA isolated from venous blood of patients revealed the activation of a cryptic

splice site in exon 8 and the skipping of 39 nucleotides in CSPG2/Versican splice variants V0 and V1 in patients carrying the latter two variants. No mutations were found in other parts of this gene.

Sequence analysis of the DNA of 250 control individuals (500 chromosomes) did not show an intron 7/exon 8 splice site variant as observed in the Wagner disease patients. Real-time quantitative RT-PCR of mRNA from patients revealed a CSPG2/Versican mRNA isoform balance shift which most strikingly resulted in the upregulation of the V2 (> 40 fold increase) and V3 (> 10 fold increase) isoforms. Sequence analysis of 10 recently collected families, six of which through a collaboration with the RETNET partner dr. B. Wissinger, Tuebingen and two of which through a collaboration with dr. G. Black, Manchester, is underway. We hypothesize that many mutations will be found deep in the sizeable introns 7 (15 kb) and intron 8 (3 kb).

TEAM VIII (LUND)

The project studies the mechanisms behind retinal degeneration, for instance by using the rd1 mouse, which serves as a model for the human hereditary disease Retinitis pigmentosa (RP). During 2005 we have gathered evidence that calpains, calcium-activated proteolytic enzymes, seem to be involved in rd1 retinal degeneration. We could for instance unequivocally show that calpain enzymes are activated in degenerating photoreceptor cells. The calpain finding has resulted in a conference abstract, as a joint RETNET effort with partners 3 and 10, and a regular scientific article, now in press, with partner 10. Our studies have also identified another possible rd1 degeneration effector: poly(ADP-ribose) polymerase (PARP). Although having important roles in DNA repair, PARP may also be involved the execution of apoptosis. We now suggest that PARP indeed is overactivated in the dying rd1 photoreceptors. Other parts of the research dealt with proteomic and transcriptomic analyses of differences between rd1 retinas and their wild-type counterparts. We could show that both calcium-calmodulin kinase II and several isoforms of protein kinase C are abnormally active in the rd1 retina, including in the degenerating photoreceptors themselves, which are all novel findings. Both studies, one of them in collaboration with RETNET partner 10, are in press.

TEAM IX (MUNICH)

Own previous results (Swiatek and Beer, Manuscript in prep.) indicate the presence of several small GTP binding proteins (monomeric GTPases) in photoreceptor cells. These molecular switches play a critical role in almost all cellular activities ranging from vesicular transport to signal transduction. In order to identify the main up- and downstream interacting partners of the small GTPase Rac, its wild-type and mutant forms have been cloned into a suitable vector enabling the expression of tagged Rac proteins, which are intended to use in pull-down experiments. Because the constitutively active form of Rac can rescue the degenerating photoreceptors (PRs) of rhodopsin null-mutant flies, we aimed at recapitulating these experiments in vertebrates. Adeno-associated viral particles were purified and used as a vehicle to deliver Rac genes into PR cells (cooperation with Peter Humphries's Lab, Trinity College, Dublin, Ireland). Age-related macular degeneration (AMD) is the leading cause of visual loss in elderly population. We have started studying expression and function of LOC387715, a gene associated with AMD encoding a protein of unknown function.

For further details see Annex I : Implementation Plan

Training and ToK

TRAINING AND TOK REPORT (01/01/2005-31/12/2005)

During the employment period of Dr. Cecilia Maubaret in the Department of Molecular Genetics, Institute of Ophthalmology, London, she received training in different methods of molecular genetic analysis. A comprehensive explanation of linkage analysis was presented to her since her work includes mapping of two adRP families. As a continuation of the linkage mapping exercise Cecilia took part in the recombination mapping using genomic microsatellite markers on the ABI 3100 automated sequencer running the genotyper software to exclude known loci and retrieve the putative disease loci. In the process she became familiar with the process of recombination events in the human genome. The standard procedures of designing oligonucleotide primers, PCRs and direct genomic DNA sequencing were part of her daily work. Furthermore, Cecilia has been actively involved in the preparation for the new RP11 mouse model, developing the genotyping strategy and learning mouse eye histology.

Kinga Bujakowska has started her PhD in Department of Molecular Genetics, Institute of Ophthalmology, London in December 2004. During this period she has undergone various training in the host institution as well as through RetNet collaborations. In our department she has familiarized herself with molecular genetics tools, such as molecular cloning and sequencing, as well as with cell culture and Western blotting. As part of the work on the new RP11 mouse model, she has received an accredited training in animal handling under the Animals Scientific Procedures Act 1986, completing modules 1-3. Kinga has learnt preparation of histological sections of mouse eyes and also she has been acquainted with the technique of hybridization in-situ during her RetNet exchange visit in TIGEM in Naples (Dr S. Banfi and Dr V. Marigo). Moreover Kinga has attended theoretical courses at the University College of London that include Introduction to Statistics and Bioinformatics courses.

In the past year, Dr. Naomi Chadderton has trained in Naples to optimise AAV purification and benefited from the opportunities presented by RETNET, as part of the laboratory exchange programme, to learn techniques for retinal explant culture in Prof. Theo van Veen's laboratory, Lund.

During the last year Dr. Valeria Roni has performed the following experimental procedures: isolation of RNA and DNA from human, established human cell lines; plasmid isolation; restriction endonuclease digestion of DNA; agarose gel electrophoresis; DNA gel extraction; retro- transcription of cDNA; Polymerase Chain Reaction (PCR); TA cloning of PCR products; dideoxy sequencing of plasmid DNA and PCR products; bacterial transformation; RNase Ligase Mediated Rapid

Amplification of cDNA Ends (RLM-RACE); In addition she used available public database information to perform in silico assemblies and analyse of 5' transcript termini. She has also performed computer-based techniques as: alignment and clustering of ESTs; interspecies gene comparisons; localization of transcription factors binding sites and genomic alignment of transcripts. Besides the lab-training she participated on progress reports and journal clubs of the laboratory and has presented her topic in a Seminar in the Eye Hospital monthly lecture.

During the last year Ronald Carpio has performed the following experimental procedures: isolation of RNA and DNA from human, established human cell lines and mice; plasmid isolation; restriction endonuclease digestion of DNA; agarose gel electrophoresis; DNA gel extraction; retro-transcription of cDNA; Polymerase Chain Reaction (PCR); TA cloning of PCR products; subcloning; dideoxy sequencing of plasmid DNA and PCR products; bacterial transformation with plasmid DNA; retina whole mount in situ hybridization; RNase Ligase Mediated Rapid Amplification of cDNA Ends (RLM-RACE); cryosectioning of mouse retinal tissue. In addition he used available public database information to perform in silico assemblies and analyse of 5' transcript termini. He has also performed computer-based techniques as: alignment and clustering of ESTs; interspecies gene comparisons and measurement of their distances; localization of transcription factors binding sites and genomic alignment of transcripts. Besides the lab-training he participated on progress reports and journal clubs of the laboratory.

During the last year Dr. Marianthi Karali has performed the following experimental procedures: training in animal techniques; preparation of mouse and human tissues for cryopreservation and paraplast treatment; RNA in situ hybridization on sections; whole-mount in situ hybridization on mouse embryos; immunohistochemistry; bioinformatics

During the last year Dragana Trifunovic has performed the following experimental procedures: training in animal techniques; preparation of mouse and human tissues for cryopreservation; RNA in situ hybridization on sections; immunohistochemistry; immunofluorescence; basics of molecular cloning; bioinformatics

Over the last year in the laboratory in Paris, Ram Fridlich has had the opportunity to learn several new skills. At practical level, he had the chance to deal with: molecular biology (Gateway cloning method, Cesium chloride gradient RNA purification, purification of yeast nuclear proteins, yeast genetics, RT-PCR), biochemistry (Western Blot, immunoprecipitation), in situ Hybridisation and two- hybrid system. In addition to the practical work, he learned how to use professional software as Vector NTI and GCG. During this year he did 3 presentations in front of the laboratory staff and he also attended several presentations given by invited scientists from all over the world. Speaking French each day really improved his French skills and contributed to his integration into the French society and culture.

Ravi Kiran Reddy was trained in tools for design of relational databases, in particular Power designer version 9.0 and SYBASE and their use for designing and visualisation of physical entity relationship models in retinobase. He further learnt PostgreSQL, a sophisticated open-source Object-Relational Database management system to build the retinobase. In order to query the relational database created with the tools above R.K.R. was trained in using Structured Query Language(SQL) for querying the database. Finally, he learned C language to use arrays and pointers for the development of faster algorithms.

Dr. Wolfgang Raffelsberger continued his training in bioinformatics and biostatistics in our laboratory. In particular, he was trained in advanced statistical analysis for multiple hypothesis testing and controlling the false discovery rate. In order to perform fast, efficient and automated statistical analysis he received training in multiple types of using R and programming statistical procedures in R. In the context of a platform wide use of these procedures he also was initiated in installation and maintenance of BioConductor packages on a Linux server-cluster for the entire IGBMC.

In the context of target gene annotation W.R. received further training in use of the bioinformatic resources at the University of Southern California (UCSC).

Dr. Arijit Mukhopadhyay

Practical training: RNA isolation and handling; quantitative and qualitative reverse transcription-polymerase chain reaction; genotyping using fluorescently labeled markers; sequence analysis; genome browser applications; fluorescence in situ hybridization data interpretation. Theoretical training: Literature seminars (weekly); research theme discussions (weekly); Nijmegen Centre for Molecular Life Sciences graduate school seminars & symposia; manuscript writing skills.

Konstatinos Nikopoulos

Practical training: Sequence analysis and sequence data analysis; genotyping using fluorescently labeled markers; RNA isolation and handling; quantitative and qualitative reverse transcription-polymerase chain reaction. Preparation of presentations for workdiscussions.

Theoretical training: Module

Translational Research Course Theme

3 days (1 ECTS), developed for a topmaster programme: various aspects of translational research, ranging from molecule to patient care were discussed. Current state-of-the-art technologies were introduced and their application in various inherited and acquired (cancer) disorders, including target gene discovery, gene expression profiling, mutation scans, genomic profiling, imaging and bio-informatics. In addition, applications in (pre-symptomatic) screening and genetic counselling were reviewed.

Dr. Francois Paquet-Durand has in the period continued his acquiring of techniques needed to perform scientific investigations towards the scientific objectives. Apart from accomplishing methods related to analyses of protein expression and enzymatic activities in histological sections, there has also been ample training in various types of electrophoresis and accessory methodologies. Other training activities have dealt with the retinal explant technique and application of potential neuroprotective compounds. During a summer course the fellow has supervised and guided a PhD student in a cell biology training. In addition to these practical aspects, the fellow was introduced to the theoretical background of research in retinal degeneration, for instance by his partaking in group tutorials.

Tanuja Talukdar is an ESR and started only very late in the previous reporting period. In the light of this, the fellow has for the major part of the current reporting period focused on getting supervised hands-on experience of basic, standard laboratory techniques. However, there has also been training in more specialised methods for protein expression and enzymatic activities in for instance histological sections. In addition, the fellow has been trained in animal care and handling, including preparation of eye samples. With respect to other skills, the fellow has received training in assembling and presenting reports of her own work. There has also been education on the science behind retinal degenerations in the form of group tutorials.

For Dr.

Elia K Humphries a short term exchange to Peter

Humphries lab (Trinity College, Dublin, Ireland) was implemented from November 29 to December 7 in 2005 aimed at preparing AAV particles to be used in our later experiments. The triple transfection of the appropriate HEK cell lines providing additional viral genes was carried out by Naomi Chadderton. The plasmid encoding the V12 mutant form of Rac and used in this experiment was prepared in GSF lab. He was deeply involved in the collection of viral particles using several rounds of density gradient centrifugation. Besides, he get acquainted with the methods used to introduce the viral particles into the subretinal space (injections performed by Arpad Palfi) and with the subsequent histological processing of the injected eyes.

Training Courses (for details see Annex2: Training and TOK)

(1) RetNet BioInformatics Course March 7-9, 2005

Organized by RetNet Group VI: Laboratoire de BioInformatique et
Génomique
Intégrative,
IGBMC, 1 rue Laurent Fries, 67404 Illkirch, France
Topic: BioInformatics in Genomics
Objective: Gaining basic knowledge in current bioinformatic procedures in Genomics, transmission of practical skills for (basic) procedures

(2) RetNet: General Management Tutorial & Research Colloquium April 5th-April 10th, 2005
Organized by the European Vision Institute (Brussels, Belgium) in Potsdam, Germany

A. General Management tutorial

Topic: Soft skills refer to a very diverse range of abilities such as: self-awareness, analytical thinking, leadership skills, team-building skills, flexibility, ability to communicate effectively, creativity, problem-solving skills, listening skills, diplomacy and change-readiness. Soft skills represent one of the fundamental attributes that the new knowledge-based economy seems to be demanding from scientists.

Course 1: Managing Time at Work

Course 2: Emotional Intelligence

Course 3: Managing Change and Transition

Course 4: A Touch of Persuasion

Course 5: Developing you Creativity

Course 6: Understanding Differences across Cultures

B. Research Colloquium: Pro Retina, Retinal Degeneration

Session 1: The functional Retina

Session 2: Degeneration of photoreceptors and the retinal pigment epithelium

molecular mechanisms

Session 3: The retinal proteome: new proteins

new views

Session 4: Animal Models

Session 5: Therapeutic strategies in hereditary retinal degeneration

(3) Training Courses in

Tübingen,
26.09.-30.09.2005

A. Non-scientific tasks

Course 1: The Craft of Scientific Presentations

Course 2: Basic Legal Awareness

Course 3: Ethics in Research

B. Scientific Lectures and Workshops

Title: Identification of Disease Genes and Analysis of Disease Gene Products

Content: 11 Lectures and five different workshops

Lab-Exchanges:

All Young Researchers performed Lab Exchanges (Short Term Exchanges) in 2005 (for details see Annex2: Training and TOK)

Management

RETNET- MANAGEMENT REPORT (01/01/2004-31/12/2005)

ORGANISATION AND IMPLEMENTATION OF WEBPAGE

Creation and establishment of the RETNET

RETNET- MANAGEMENT REPORT (01/01/2004-31/12/2005)

ORGANISATION AND IMPLEMENTATION OF WEBPAGE

Creation and establishment of the RETNET webpage (URL; online: 12/01/2004)

Establishment of the Internal Site of the webpage; Passwords delivered (26/05/2004)

This Secure Part of the webpage serves also as storage site for several kinds of documents like meetings minutes and presentations; guidelines for reporting; RTN Contract; Network Handbook; fellows scientific reports and career development plans. Exclusively the network participants can have access there and download the necessary documents at each time

Establishment of the Discussion forum of the webpage; (15/11/2004; online 06/12/2004)

Implementation of contact addresses (01/11/2004) and credit to the EC (01/11/2004)

Daily update and evolution of the webpage <http://www.euro-ret.net>

Revision and new structure of the Internal Site of the homepage (27/12/2005)

ORGANISATION AND IMPLEMENTATION OF MEETINGS

RETNET Kick-off-meeting (09/03/2004 London, UK)

Participated by all Principal Investigators; Agenda and Minutes available

RETNET Intermediate Business Meeting (05/05/2004 Tuebingen, Germany)

Participated by SC Prof. Bhattacharya & MC Dr. Wheeler-Schilling; Agenda and Minutes available
RETNET First network meeting (25/05/2004 Neuherberg, Germany)

Participated by all Principal Investigators; Agenda and Minutes available
Coordinators meeting for FP6 RTNs (30/09/2004 Brussels, Belgium)

Participated by the SC Prof. Bhattacharya; MC Dr. Wheeler-Schilling excused
RETNET First annual network meeting (20/10/2004 Brussels, Belgium)

Participated by PI, SAC, EC-SO and YR employed; Agenda and Minutes available

REMARK: Programme for the meetings 2005 are available (24/11/2004)

RETNET Project Steering Committee (08/04/2005 Potsdam, Germany)

Participated by PSC; Agenda and Minutes available

RETNET Second annual network meeting (09-12/06/2005 Stockholm, Sweden)

Participated by PI, SAC, EC-SO and YR employed; Agenda and Minutes available

ORGANISATION AND IMPLEMENTATION OF RECRUITMENT

Creation and establishment of advertisement (12/01/2004) and standard recruitment procedure

Creation and collection of the respective job-descriptions

Publication of advertisements (22/01/2004); Nature, Medcor, EMJL, Hum-MolGen, individual by PI; documentation available

Publication of advertisements (monthly updates; 20/02/2004); MC-opportunities, RET-network

Central collection and processing of applications (a total of 172 received applications from 25 countries; 82% male applicants, 18% female applicants); statistics available . Databank with the applications available in the Internal Site of the Webpage.

REMARK: The recruitment process is still under its way (for details refer to the respective tables).

At the beginning of 2005, it is anticipated to fill all vacant positions according to the plan.

COMMUNICATION AND DISSEMINATION STRATEGY

Quarterly newsletter to all participating project partners and young researchers

A total of 287 individual e-mail-contacts and 78 telephone calls were processed in 2004
 A relevant material (scientific, legal, administrative and financial) was distributed to the participants,
 RETNET handbook available (Version 0.5 02/04; current version 1.5 11/04); online availability of the whole documentation
 Publication of two press releases (in german language). IDW (13/02/2004) and
 Schwäbisches Tagblatt (14/02/2004); both releases are available on-line; information of two national journals,
 Der Ophthalmologe and
 Klinische Blätter der
 Augenkunde (both 16/02/2004)
 Poster presentation The European Retinal Research Training
 Network Brussels (30/09/2004)
 Organisation: Meetings/Communication strategy/FAQs/Guidelines for dissemination
 Monthly update of the CORDIS webpage and the
 respective vacancy tool
 REMARK: The RETNET coordinators realize the
 need for a more effective dissemination policy in 2005. All partners are involved and urged to spread
 the information on the network in their own countries under involvement of their respective PR
 support bodies by each institution.
 RETNET ball pens and ad notes have been designed
 and produced in March 2005. These have been distributed to all fellows and respective P.I. In
 addition they were distributed during appropriate meetings and conferences
 Article about the visit of the RETNET fellows at the University of Lund (Sweden, June 2005)
 appeared in the mag of the University of Lund (nr 7 / 2005). Available on line.
 In July 2005 RETNET baseball caps with embroidered RETNET logo. For all fellows, P.I. and
 coordinators
 In October 2005 a RETNET calendar 2006 was designed and printed. For all fellows, P.I.,
 coordinators and friends of RETNET
 Poster presentation, RETNET corporate-material and RETNET-info-flyers distribution at the CER
 2005, Brussels, November 2005

FINANCIAL MANAGEMENT

Update of the financial resources by partner in the
 RETNET handbook (available on-line)
 Cooperation with the respective financial bodies of each partner institution (FAQs)
 Organisation of audit certificates (and all problems in relation to this and the new form
 CÄ#))
 Processing of the financial resources of category F#
 for the partners; Reimbursement of travel cost and eligible expenses by the
 central budget.

GENERAL MANAGEMENT AND MISCELLANEOUS

Letter of confirmation: Organisation, check, distribution EC, Update personnel list; availability
 on-line
 Career Development plan: Organisation, check, availability on-line
 Welcome letter to all new recruited young fellows: Organisation, check
 Organisation, planning and check of the training courses 2005 (network-wide)
 Planning and check of the training courses 2005 (individual lab rotations)
 Organisation, planning and check of the First Annual Activity Report 2004 (23/12/2004)
 Organisation for submission of the First Annual Activity Report 2004 in time
 Brainstorming sessions for new innovative ideas to be implemented by
 RETNET (e.g. get in contact with other funded FP6
 RTNs; supporting team building measures)
 Design and development of an evaluation formulary.
 Statistical analysis and resum# of the evaluation formularies of 12 training
 courses

General Management Tutorial & Research Colloquium, April 5-10, 2005, Potsdam, Germany. Participated by all fellows. Agenda and assessments of the tutorial and colloquium available online
Training Courses in Tübingen, September 26-30, 2005. Agenda and assessments of the training available online.

Abbreviations: EC: European Community; FAQ: Frequent asked questions; MC: Managing coordinator; PI: Principal investigator; RETNET: European Retinal Research Training Network (MRTN-CT-2003-504003); RTN: Research Training Network; SAC: Strategic Advisory Committee; SC: Scientific coordinator; SO: Scientific officer; YR: Young researcher

DEVIATIONS/MODIFICATIONS TO THE ORIGINAL WORK PROGRAMME

Please indicate if the project

a) is, at this stage, being implemented as originally planned

If you answered b) or c) please include a detailed description of the modifications in the report (one page)

ADDITIONAL INFORMATION

Please indicate any additional information, which may be considered useful to assess the work done during the reporting period.

Attachments	Annex3_Publications_and_Conferences.pdf, Annex2_Training_and_TOK.pdf, Annex1_ImplementationPlan.pdf
Name	
Date	
Signature	