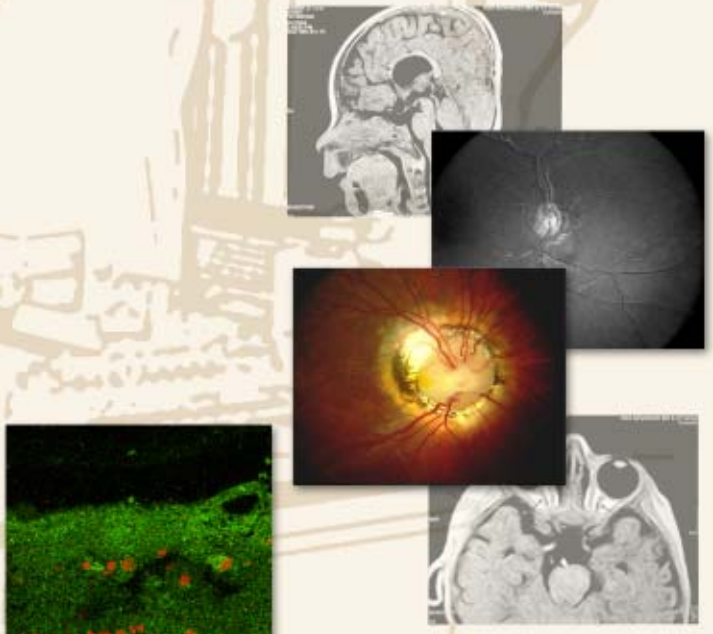
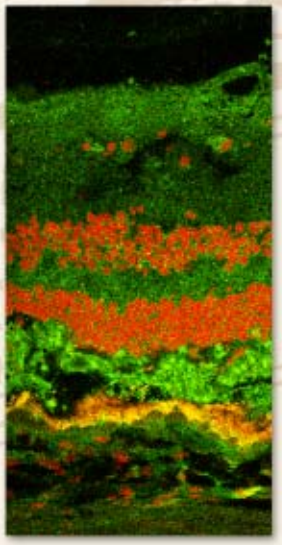
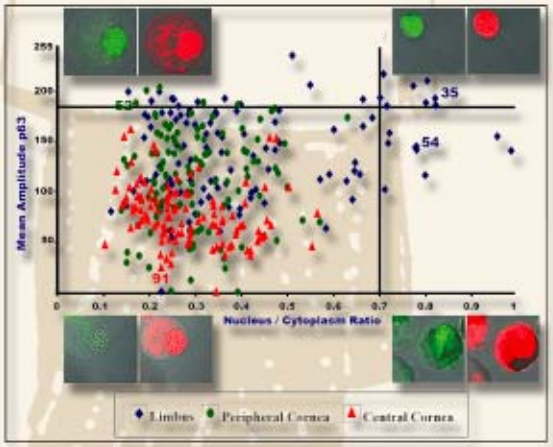
ARAVIND EYE RESEARCH INSTITUTE

Aravind Medical Research Foundation

Report 2005







30 years 1976-2006
a journey towards light

ARAVIND EYE CARE SYSTEM

ARAVIND EYE RESEARCH INSTITUTE

Aravind Medical Research Foundation

Report 2005

Though Aravind Eye Hospitals have been known for their service delivery, evidence and research have always been the platform on which service delivery models were built.

The research activities at Aravind began within a year of the establishment of the hospital leading to one of the first publications documenting barriers to accessing health care particularly eye care. Since then several research studies have taken place to provide evidence to directly influence service delivery models. Subsequently, research activities increased, leading to the formation of a separate organization known as Aravind Medical Research Foundation. Over the years, the spectrum of research activities also diversified and they now include basic research involving Genetics, Immunology, Microbiology, Cell Biology, Biochemistry and Molecular Biology as well as clinical trials to evaluate various intervention options.

*Aravind is currently in the process of establishing a new major centre for research-**Aravind Eye Research Institute**, to strengthen and integrate our activity on basic research, clinical research, epidemiology, clinical genetics, translational research and stem cell biology.*

Dr.P.Namperumalsamy, Vice-Chairman, Aravind Eye Care System (in the middle) and Dr.VR.Muthukkaruppan, Director - Research, Aravind Medical Research Foundation having discussion with Dr.Paul Sieving, Director, National Eye Institute, Bethesda, USA during the Indo-US workshop in February 2005

ARAVIND MEDICAL RESEARCH FOUNDATION (AMRF) STAFF LIST

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Dr. G. Venkataswamy, MS, FACS

Vice President
Dr. P. Namperumalsamy, MS, FAMS

Secretary & Treasurer
Mr. G. Srinivasan, BE, MS

Project Director
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Director – Research & Immunology
Dr. VR. Muthukkaruppan, MSc, Ph.D

Department of Genetics
Senior Scientist
Dr. P. Sundaresan, MSc, Ph.D

Department of Cell Biology
Senior Scientist
Dr. G. Sangiliyandi, MSc, Ph.D

Department of Molecular Biology
Senior Scientist
Dr. P. Sajithlal, MSc, Ph.D

PH.D PROGRAMME

The Tamilnadu MGR Medical University has recognised Aravind Eye Hospital as a centre for Ph.D. in Ophthalmology. Aravind's courses and Ph.D in Biomedical Sciences has been recognized by Madurai Kamaraj University. Four faculty members are recognised as supervisors and eight scholars are currently working for their Ph.D.

SCHOLARS WORKING FOR PH.D

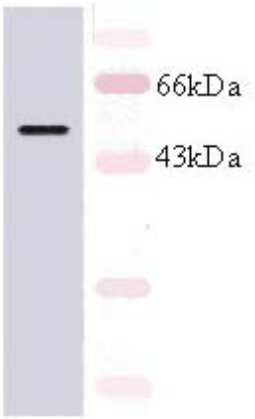
Name & Regn. year	Guide	Thesis title
Dr. SR. Rathinam 1-10-2000	Dr. P. Namperumalsamy	Studies on clinical presentation, diagnosis, long-term complications and management of infectious uveitis with references of Leptospirosis. **Submitted Thesis in December 2005.**
C. Gowri Priya 21-11-2002	Dr. VR. Muthukkaruppan	Aetiology and pathogenic Mechanism of uveitis associated with Leptospirosis.
P. Arpitha 25-11-2002	Dr. VR. Muthukkaruppan	Identification, characterization, maintenance and expansion in vitro of Human Corneal Epithelial Stem Cells.
G. Neethirajan 18-12-2002	Dr. P. Sundaresan	Molecular Analysis of PAX6 gene in Indian Aniridic patients.
J. Kanagavalli 24-12-2002	Dr. P. Sundaresan	Studies on Myocilin (TIGR/MYOC) gene mutations and its protein of Primary Open Angle Glaucoma patients inIndia.
B. Suganthalakshmi 26-11-2004	Dr. P. Sundaresan	Molecular Genetics of Diabetic Retinopathy.
J. Nallathambi 30-09-2004	Dr. P. Sundaresan	Involvement of Transcription factor genes PAX6/FOXL2 in various ocular anomalies.
R. Ramya Devi (2006)	Dr. G. Sajithlal	Differential Gene Expression in Age Related Cataract.
T. Amala Raja Sundari 02-11-2004	Dr. P. Sundaresan	Determination of Genetic makeup of Rubella Virus infecting children in South India.

ONGOING PROJECTS

MOLECULAR GENETICS OF PRIMARY OPEN ANGLE GLAUCOMA IN INDIAN POPULATION AND STRUCTURE-FUNCTION ANALYSIS OF MYOCILIN PROTEIN

Investigators	:	Dr. P. Sundaresan Dr. S.R. Krishnadas
Collaborators	:	Dr. S. Krishnaswamy, School of Biotechnology, Madurai Kamaraj University
Research Scholars	:	J. Kanagavalli Eswari Pandaranayaka
Funded by	:	Indian Council of Medical Research, New Delhi

The purpose of this study is to screen for mutations in Myocilin gene and functional analysis of Myocilin protein in vitro. The function of Myocilin protein is not clear. Cloning, over expression and purification of recombinant human Myocilin protein have been achieved. Myocilin clone in pRSET was used and coding region was recloned into different expression vector, followed by over expression in *E.coli*. The myocilin protein from Pet20b + in Rosetta (DE3)pLysS was solubilised and affinity purified using the Histidine tag. Myocilin in soluble form does not aggregate or form oligomers. Purified Myocilin is recognized by polyclonal antibody in the western blot. The yield is approximately 16mg of purified protein from one litre of culture. The wildtype and mutant myocilin is now crystallized to understand the structure – function in relation to glaucoma.



Western blot analysis of over expressed, solubilised and purified recombinant human myocilin protein (55 kDa)

Currently mutation have been created in Myocilin gene in vitro which was identified in glaucoma patients at the hospital. The expression of mutant Myocilin gene in cultured trabecular meshwork cells is being studied.

Dr.P. Sundaresan, Senior Scientist and his students interacting with the Singapore National Eye Centre faculty

NOVEL MOLECULAR DIAGNOSTICS FOR EYE DISEASES: SCREENING OF GLAUCOMA GENE (MYOC, OPTN, CYP1B1 AND OPTC) MUTATIONS IN SOUTH INDIAN POPULATION

Principal Investigator : Dr. VR. Muthukkaruppan

Co-Investigators : Dr. P. Sundaresan
Dr. S.R. Krishnadas

Research Scholars : J. Nallathambi
R. Ramya Devi
B. Hemadevi

Funded by : Council of Scientific and Industrial Research, under NMITLI programme

The purpose of this study was to screen mutations in *OPTN*, *MYOC* and *OPTC* genes in 190 glaucoma patients (POAG) and 100 normal controls.

In *OPTN* gene, one mutation in nine POAG patients have been identified. In *OPTC* gene four mutations were identified, one among them was novel (R229H). In *MYOC* gene, five mutations, two exonic polymorphisms and one promotor polymorphism were identified. Screening of *CYP1B1* gene in 100 POAG samples identified three mutations. In addition, Exon 2 and 3 of *CYP1B1* gene were screened for mutations in 95 PCG samples by direct sequencing. Six mutations and six polymorphisms in CYP1B1 gene including one novel mutation and one novel polymorphism have been identified .

STUDIES ON THE GENETICS OF INHERITED ANIRIDIA IN INDIAN POPULATION

Prinicipal Investigator : Dr. P. Sundaresan

Co-Investigators : Dr. P. Vijayalakshmi
Dr. S.R. Krishnadas

Research Scholar : G. Neethirajan

Funded By : Indian Council of Medical Research (ICMR)

The purpose of this study was to investigate genotype/phenotype correlations in familial aniridia patients with PAX6 mutations in Indian population. Total genomic DNA was isolated from peripheral blood from patients after informed consent. The coding exons of the human PAX6 gene were amplified by PCR, SSCP, heteroduplex analysis, allele specific PCR and restriction digestion followed by automated sequencing. Three new PAX6 mutations (c.710delC, c.1174delTG, c.397ins5) and one reported mutation (c.1080C>T) in four out of seven unrelated familial aniridic pedigrees have been identified. The mutations detected in aniridia patients result in premature termination of translation derived from mutant allele. Three novel and one reported mutations in PAX6 gene was added in familial aniridia to the existing spectrum of mutations in Indian population.

SCREENING FOR MUTATIONS IN CRYBA1 AND CRYGC GENES IN CATARACT PATIENTS IN SOUTHERN INDIA

Investigators : Dr. Reena Chandrashekar
Dr. P. Vijayalakshmi

Research Scholars : R. Ramyadevi
B. Hemadevi

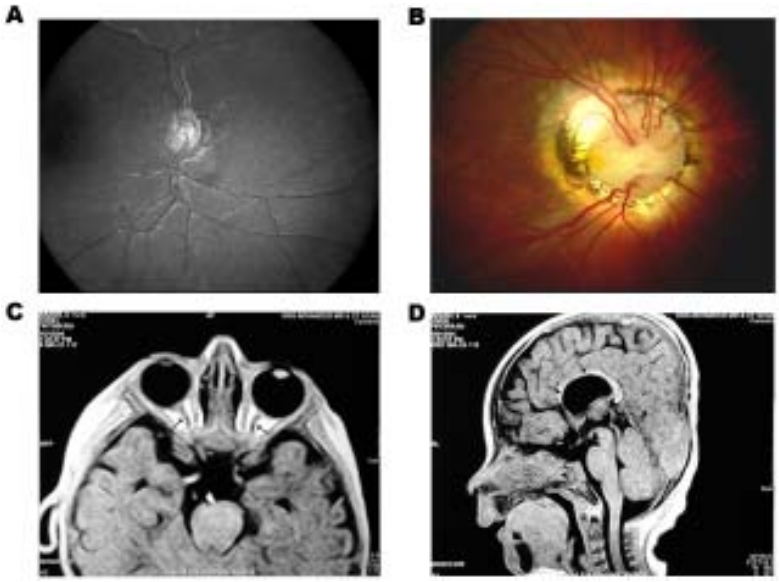
We have screened for mutations in 41 probands with family history and 109 sporadic cases. A 5' Donor splice site mutation was identified in a four-generation family with eleven affected members having lamellar opacities. In addition, two novel and three reported polymorphisms were identified in CRYBA1. Analysis of CRYGC revealed one novel and two reported polymorphisms.

INVOLVEMENT OF TRANSCRIPTION FACTOR GENE PAX6 IN VARIOUS CONGENITAL OCULAR ANOMALIES IN INDIAN POPULATION

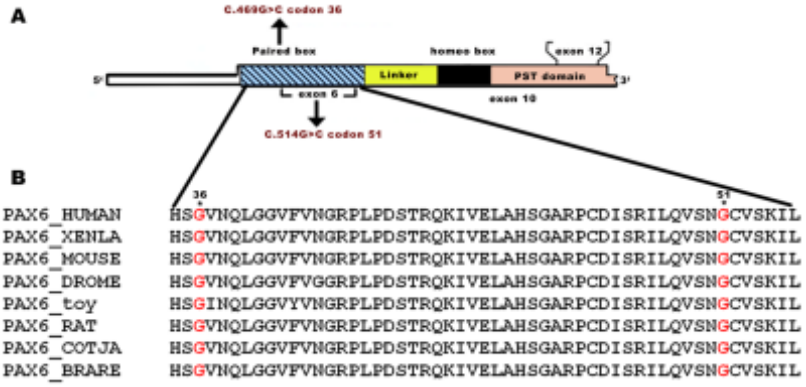
Investigators : Dr. P. Sundaresan
Dr. Shashikant Shetty Bhoja
Dr. P. Vijayalakshmi

Research Scholar : J. Nallathambi

Funded By : Indian Council of Medical Research (ICMR)



Fundus photography and the MRI scan report of the affected probands
A*- Ophthalmoscopic appearance of a 4-year-old male boy showing abnormally small optic nerve head which is surrounded by a yellowish mottled peripapillary halo boarded by a dark pigment ring (double ring sign).* ***B****-A six-year-old boy showed the fundus picture of optic disc coloboma with large wafer like defect, enlarged disc funnel shaped excavation surrounded by an elevated annulus of chorioretinal pigmentary disturbance. Blood vessels emerge from the rim of excavation like a spokes of wheel,* ***C****-MRI scan photograph of axial view (T_1 WI) shows thinning of optic nerves in proband ONH 4-1 (Arrow),* ***D****-MRI scan picture (Saggital view T_1 WI) shows the congenital absence of septum pellucidum with hypogenesis of corpus callosum (Arrow).*



Graphical representation of PAX6 gene and amino acid conservation analysis of PAX6 protein
A*- Graphical representation of* PAX6 *gene shows the location of nucleotide changes in paired box.*
B*-Amino acid sequence alignment of the human PAX6 paired domain (codons 34-57) homologs [DROME- Drosophila Pax-6 homologs eyeless, toy – twin of eyeless] and other species. The G36 and G51 shown in red are highly conserved.*

PAX6, a paired box transcriptional factor is considered as the master control gene for morphogenesis of the eye. Mutations in this gene have been associated not only with aniridia but also with various eye abnormalities including the globe and optic nerve anomalies. The purpose of this study is to carry out the genetic analysis of PAX6 gene in order to correlate with the spectrum of PAX6 mutations with various ocular manifestations in Indian population. In this study two novel PAX6 mutation was identified in patients with congenital optic nerve malformation (c.469G>C, c.514G>C). The aim is to understand the significance of this gene in ocular pathogenesis. It has been proposed to establish genetic counselling especially for sporadic probands affected with congenital ocular anomalies.

IDENTIFICATION OF CANDIDATE GENES AND SCREENING FOR MUTATIONS OF GENES ASSOCIATED WITH TYPE II DIABETIC RETINOPATHY

Investigators : Dr. P. Sundaresan
Dr. P. Namperumalsamy
Dr. R. Kim

Research Scholar : B. Suganthalakshmi

Funded by : TIFAC-CORE, Department of Science and Technology

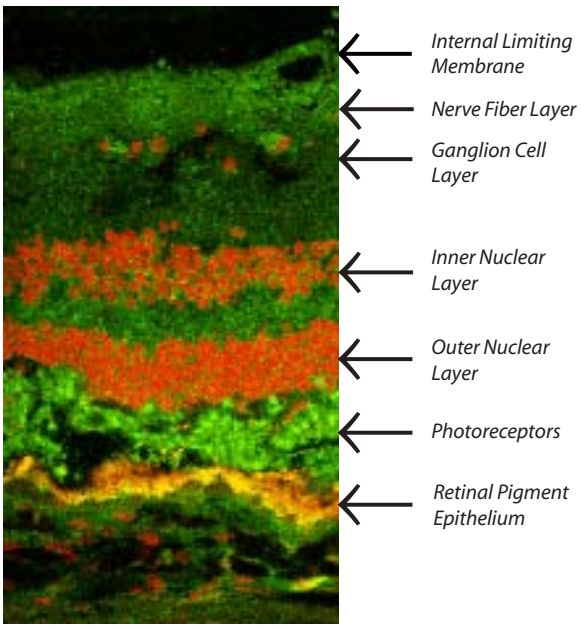
The aim of the study is to identify the genetic variations in the genes associated with diabetic retinopathy. One hundred and twenty diabetic retinopathy (DR) and ninety diabetic non retinopathy (DNR) patients have been screened for mutations in VEGF (5' UTR & Promoter region), ALR (Promoter region) and eNOS (Intron 4 region) genes. Five reported and two novel polymorphisms in Indian DR populations have been identified. Distributions of genotype, allele and haplotype frequencies were calculated and compared between DR and DNR using logistic regression analysis, X2 test and Monte Carlo analysis for VEGF and eNOS gene polymorphisms. All these data suggests that three heterozygous polymorphisms in VEGF gene were significantly associated with diabetic retinopathy when compared with diabetic non-retinopathy in Indian populations.

Genome wide sib-pair linkage analysis will be performed to identify the novel genetic loci, associated with diabetic retinopathy using 3-4 generation families in which the family members have been affected by diabetes with or without retinopathy.

STUDIES ON THE PROANGIOGENIC AND VASCULAR GROWTH FACTORS IN RELATION TO THE PATHOGENESIS OF EALES' DISEASE AND DIABETIC RETINOPATHY

Investigators : Dr. VR. Muthukkaruppan
Dr. P. Namperumalsamy
Dr. Dhananjay Shukla
Dr. R. Anand Rajendran
Dr. G. Sangiliyandi

Research Scholar : P. Murugeswari



Confocal microscopic image of Normal Cadaver Retina showing VEGFR-2 positivity (green) in photoreceptors. Nuclei (red) stained with propidium iodide

Funded by : TIFAC-CORE, Department of Science and Technology

To assess the levels of Proinflammatory cytokines (IL-6, IL-8, IL-1B), Chemokine factor (MCP-1), Angiogenic growth factor (VEGF) Antiangiogenic factor (PEDF) in the vitreous, aqueous and serum of 25 Proliferative Diabetic retinopathy (PDR), 10 Eales' Disease and 25 Macular Hole (MH) patients. Our previous studies have been extended to more number of PDR patients and MH controls than earlier. Studies have also been carried out to compare diabetic retinopathy with Eales' Disease on those

patients who are not diabetic but have retinal neovascualization. Significant finding suggests that the diabetic retinopathy is also an inflammatory disease. This is based upon the following data.

Cytokine levels in vitreous

- Cytokines IL-6 and IL-8 were significantly higher in the vitreous of Proliferative Diabetic Retinopathy and Eales' than the Macular hole patients.
- VEGF in the vitreous was significantly higher in PDR and Eales'patients than MH.
- PEDF was significantly lower in PDR but not in Eales' when compared with MH patients.
- The Chemokine factor MCP-1 was significantly increased in the vitreous of Eales' disease and PDR than in MH patients.
- IL-1B showed no difference in the PDR and ED when compared with the MH patients.

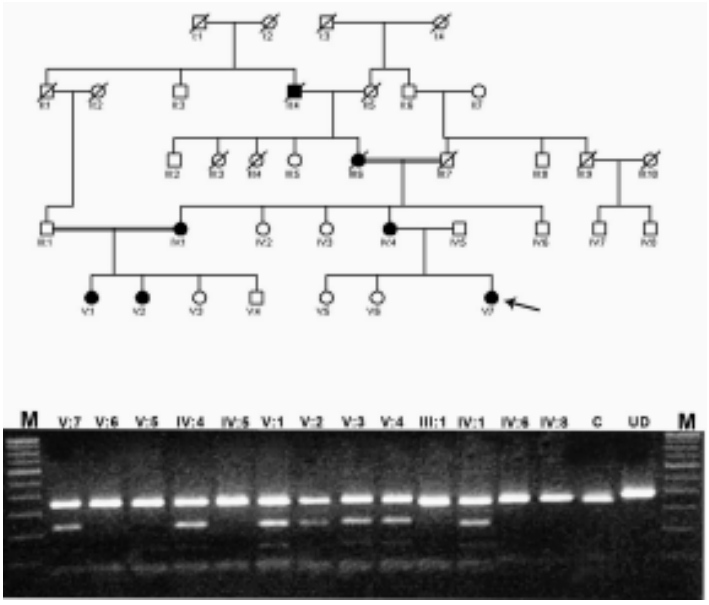
THE MOLECULAR GENETICS OF CONGENITAL CATARACT IN THE INDIAN POPULATION

Investigators : Dr. G. Sajithlal
Dr. P. Vijayalakshmi

Research Scholar : R. Ramyadevi

Funded by : Aravind Medical Research Foundation

RFLP Analysis - Connexin 46 (V28M)



M - 100bp ladder, C - Control, UD - Undigested

Congenital cataract is one of the most common eye abnormalities and often leads to blindness in infants. All three Mendelian forms of inheritance are observed in congenital cataract with autosomal dominant trait being the most common. In a developing country like India autosomal recessive forms of inheritance are also found in high frequency in the population involving consanguineous marriages.

Further it is still unclear what proportion of inherited cataract is associated with each of the gene mutations as there have been only few studies involving the systematic screening of all the candidate genes in a population.

More than 30 loci are associated with various forms of congenital cataract. Two novel missense mutations have been identified in all the affected members of two families out of 60 families studied. Interestingly it has been detected that same mutations in two unaffected individuals. Therefore, there is a possibility of modifier gene to delay the onset of cataract.

IMMUNOLOGY OF FUNGAL KERATITIS

Investigators : Dr. VR. Muthukkaruppan
Dr. N.V. Prajna
Dr. Lalitha Prajna

Research Scholars : M. Vasanthy
G. Rohini

Funded by : Allergan

Tear from fungal keratitis patients have been studied for the presence of infiltrating cells and inflammatory cytokines. This is a non-invasive procedure to collect 10µl of tear samples a few times from the same patient. Polymorpho nuclear leukocytes were the predominant infiltrating cells in tear from infected eye, in contrast to the absence in an infected fellow eye. IL-6 and IL-8 were significantly increased in the infected tear, but reduced after healing. This horizontal study indicates that the early inflammatory response could be studied using tear samples.

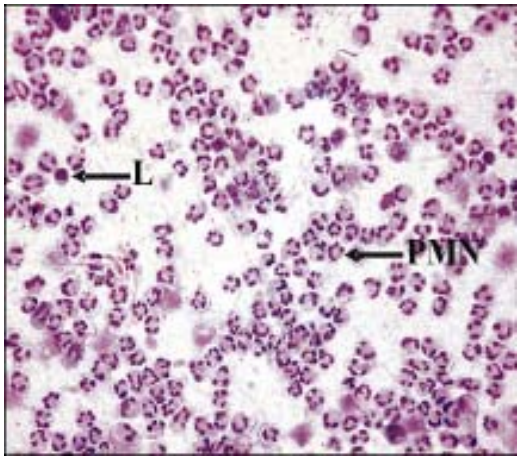
Additional studies were carried out to elucidate the levels of specific MMPs (MMP –8, -9)/ TIMPs (TIMPs –1, -2) in the Cornea [collected in perforated ulcers (TPK)], tear and serum. The levels of MMP-8 and MMP-9 were significantly elevated in the fungal corneal homogenates when compared to the cadaver corneal and the keratoconus corneal homogenates. The levels of TIMP-1 and TIMP-2 did not show significant modulations. No significant changes were observed in the levels of MMP-8, MMP-9 and TIMP-1, TIMP-2 in the tear and serum of fungal keratitis patients when compared with the keratoconus patients. Corneal melting and corneal tissue degradation observed in the fungal keratitis patients is possibly due to the significant elevation in levels of the matrix metallo proteinases 8 and 9.

PATHOGENIC MECHANISM OF UVEITIS ASSOCIATED WITH PAST LEPTOSPIROSIS

Investigators : Dr. VR. Muthukkaruppan
Dr. S.R. Rathinam

Research Scholar : C. Gowri Priya

Funded by : Netherlands Foundation for Advancement of Tropical Research (WOTRO)



Giemsa stained cytospin preparation of aqueous humor cells showing predominant infiltration of Neutrophils (PMN) in leptospiral uveitis patients

Leptospiral aetiology of uveitis have been demonstrated on the basis of presence of antileptospiral antibody in the serum of these patients. Though bacteria could not be isolated, aqueous humor showed positivity for PCR. Selective infiltration of neutrophils in AH is demonstrated now. Significant levels of IL-6 and IL-8, the inflammatory cytokines were also observed. We are looking at the possibility of Lepto uveitis being mediated by endotoxin.

Arpitha interacting with Dr. Robert M. Lavker, Director of Dermatology Research, Northwestern University, Chicago during the Indo-US workshop on February 2005

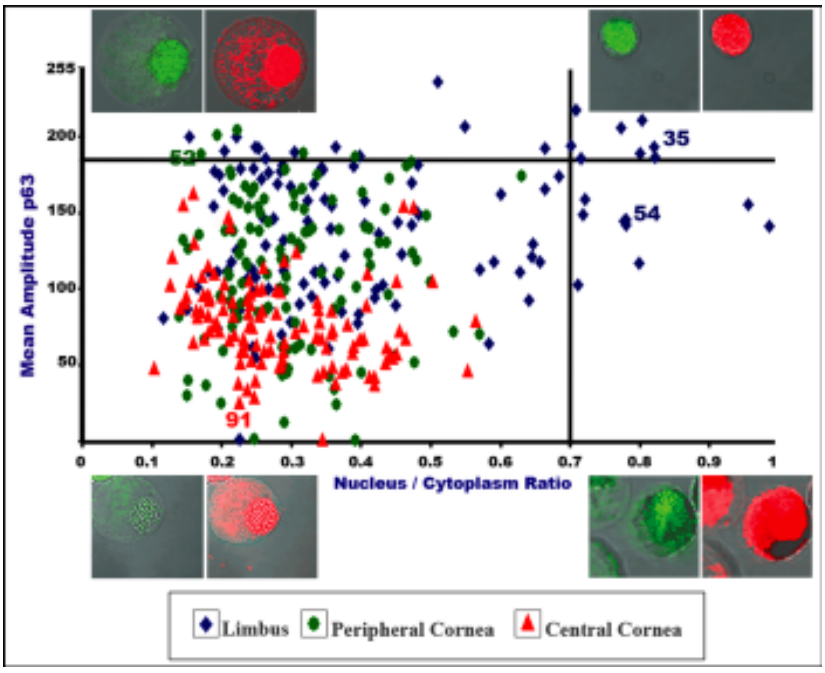
CHARACTERIZATION AND IN VITRO EXPANSION OF HUMAN CORNEAL EPITHELIAL STEM CELLS

Investigators : Dr. VR. Muthukkaruppan
Dr. M. Srinivasan
Dr. N.V. Prajna

Research Scholar : P. Arpitha (ICMR SRF)

Funded by : Aravind Medical Research Foundation

Corneal epithelial stem cells on the basis of high level of expression of P63 – a transcription factor and the high nucleocytoplasmic ratio have been identified. The cells in the upper right quadrant (Figure) are positive for cytokeratin-5 (epithelial cell marker), and negative for cytokeratin 3, connexin 43, 14-3-3 sigma and ki67 which are the characteristics of stem cells. Experiments are underway to understand the proliferative potential and label retaining property of the upper right cells.



A distinct group of small cells in the limbus with greater N/C ratio with high levels of p63 - Identified as stem cells in the upper right quadrant

POPULATION BASED SURVEILLANCE OF CONGENITAL RUBELLA SYNDROME (CRS) IN SOUTH INDIAN CHILDREN

Investigator : Dr. P. Vijayalakshmi

Collaborator : Dr. David Brown, Health Protection Agency, London

Funded By : World Health Organization

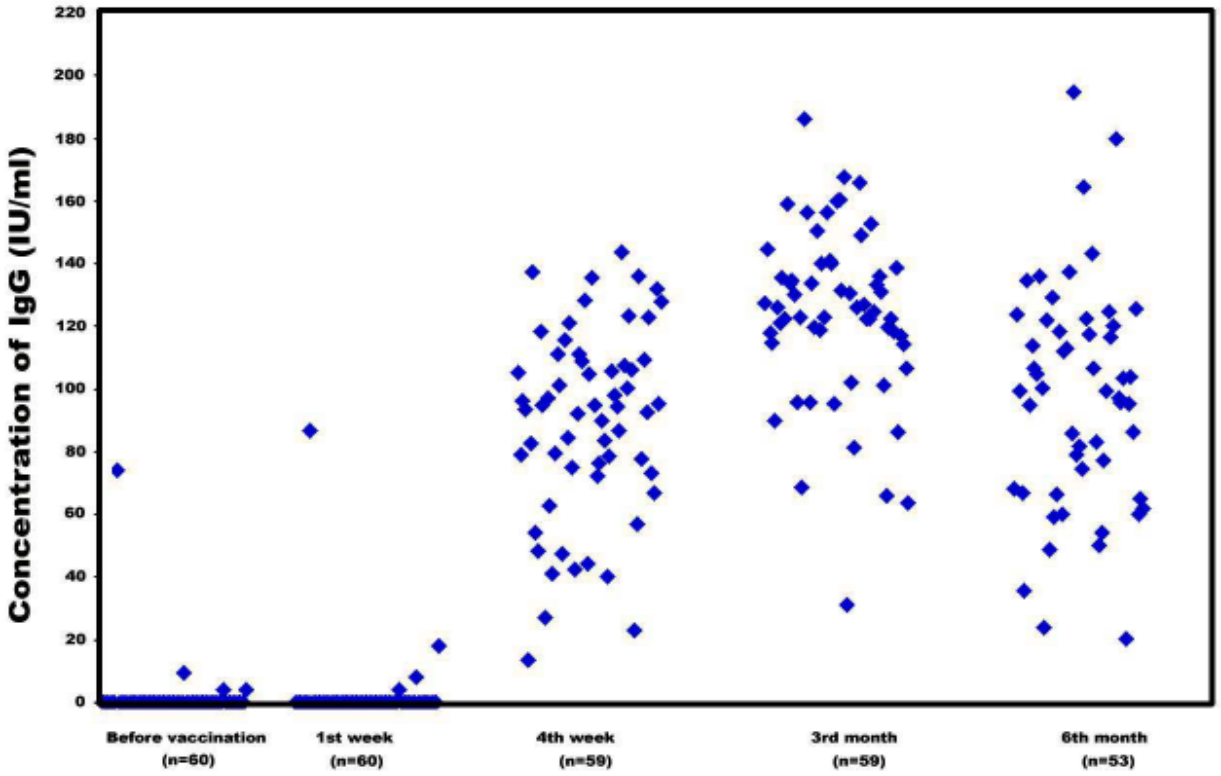
More than 50,000 children were screened and among 1090 suspected cases, 229 were clinically confirmed for CRS. Thus, the burden of CRS have been established in the South Indian population. Immune status of the CRS children (0-11 months) was studied and 44 sera were found to be positive for IgM anti - rubella antibody due to infection during early pregnancy.

SERO SURVEY ON THE IMMUNE STATUS OF HEALTH CARE PERSONNEL AGAINST RUBELLA IN AN EYE HOSPITAL

Investigators : Dr. VR. Muthukkaruppan
Dr. P. Vijayalakshmi

Research Scholar : T. Amala Rajasundari

Funded by : ORBIS project



IgG Antibody Profile in individuals vaccinated for Rubella Virus

In order to determine the proportion of health care workers who are at risk of rubella infection, 500 female and 81 male health care personnel (15 – 40 years) were screened for rubella specific IgG and IgM antibodies. It was identified that 493 were IgG positive and 22 both IgG and IgM positive. Sixty-six personnel (laboratory staff, physicians, housekeepers) were seronegative.

Seronegative workers were vaccinated with monovalent rubella vaccine (RA27/3) and their immune response was followed for six months. All developed good protective (IgG) immunity. Therefore, we recommend that in order to reduce the risk of contracting hospital based rubella infection, vaccination of health care workers against rubella may be carried out at the start of their employment.

RESEARCH ADVISORY COMMITTEE

Aravind Medical Research Foundation has been approved as a Scientific and Industrial Research Organization (DSIR), Government of India. Aravind Research programmes are reviewed by a Research Advisory Committee consisting of the following members.

RESEARCH ADVISORY COMMITTEE MEMBERS

Dr. G. Venkataswamy, Founder Chairman, Aravind Eye Care System

Dr. P. Namperumalsamy, Vice Chairman, Aravind Eye Care System

Dr. A. Gnanam, Former Vice Chancellor, Pondicherry University

Dr. K. Dharmalingam, Sr. Professor & Head, Department of Genetic Engineering, Madurai Kamaraj University, Madurai

Dr. C.N. Paramasivan, Deputy Director, Tuberculosis Research Centre, Indian Council of Medical Research

Dr. L. Thayumanavan, Gastroenterologist, Vadamalayan Hospitals

Dr. K. Ananda Kannan, Former Vice Chancellor, The TN Dr. MGR Medical University

Mr. G. Srinivasan, Hony. Secretary & Treasurer, Aravind Eye Care System

Dr. VR. Muthukkaruppan, Director – Research, Aravind Medical Research Foundation

INSTITUTIONAL REVIEW BOARD

All the research projects undertaken by AMRF and by other components of Aravind Eye Care System are critically evaluated for ethical issues by the Institutional Review Board (IRB) which has the following members.

INSTITUTIONAL REVIEW BOARD MEMBERS

Chairman

Dr. K. Dharmalingam, Sr. Professor & Head, Department of Genetic Engineering, Madurai Kamaraj University, Madurai

Member Secretary

Dr. S.R. Rathinam, Chief, Uvea Clinic, Aravind-Madurai

Members

Mr. V. Sarangapani, Advocate, Madurai

Ms. Shobana Ramachandran, Managing Director, TVS Sri Chakra Ltd, Madurai

Dr. T.S. Chandrasekaran, Ophthalmologist, Gandhi Nagar, Madurai

Dr. C. Srinivasan, AICTE, Emeritus Professor, Department of Material Sciences, Madurai Kamaraj University, Madurai

Dr. L. Thayumanavan, Sr. Gastroenterologist, Vadamalayan Hospital, Madurai

MAJOR EVENTS 2005

MEMORANDUM OF UNDERSTANDING

Prof.Dr.Ang Chong Lye, Director, Singapore National Eye Centre; Dr.DonaldTan, Director, Singapore Eye Research Institute; Ms.Charity wai, Chief operating officer, Singapore National Eye Centre with Aravind Medical Research Foundation faculty

BETWEEN SINGAPORE NATIONAL EYE CENTRE AND ARAVIND EYE CARE SYSTEM

The research team from Singapore Eye Research Institute visited Aravind Medical Research Foundation and MOU for collaborative studies was signed on September 2005.

The major objectives are

- Continue Medical Education, Basic and Clinical research in Ophthalmology.
- Agree to work together to develop and garner the human and financial resources for joint projects.

Projects considered

a. Tear proteomics study in fungal keratitis patients.
b. Clinical and genetics studies in glaucoma.
c. Epidemiological studies in myopia.

INDO-US VISION RESEARCH SCIENTISTS JOINT GROUP VISIT

Some of the visitors having discussion in the AMRF laboratory during the Indo-US workshop

The Aravind Eye Hospital hosted a joint Working group of Indo US Vision research scientists under the aegis of the Association for Vision and Ophthalmology (ARVO) and the National Eye Institute, USA. 50 Vision Research Scientists from 18 reputed US Universities including Harvard and Duke, visited four Premier Eye Care institutes in India.

This joint exercise was hosted by Dr. Namperumalsamy, Director of the Aravind Eye Care System and was jointly chaired by Dr. Paul Kaufman who is the the Executive Vice President of ARVO, Dr. Paul Sieving and Leon Ellewin of the NEI and Dr. Balasubramaniam, Director of Ophthalmic research at LVPEI. The emphasis in this collaborative effort, according to Dr. VR. Muthukkaruppan, who leads ophthalmic research at the Aravind Eye Care System in Madurai was translating breakthrough in the laboratory to influence potential cure for blinding eye diseases prevalent in the country (Bench to Bedside applications).

This endeavour for the first time brought under a single umbrella Vision Research scientists from reputed eye institutes in India and the US to discuss and explore possibilities of collaborative research in vision sciences and ophthalmology amongst scientists.

MAJOR CONFERENCES & TRAINING PROGRAMMES ATTENDED

WHO STEERING COMMITTEE SUBGROUP MEETING

London, October 12-13

The Subgroup Meeting of the WHO Steering Committee on Epidemiology and Field Research was convened at the Health Protection Agency (HPA), London to review findings of the WHO-sponsored Aravind Eye Hospital study of congenital rubella syndrome (CRS). This is the largest prospective study of CRS conducted anywhere in the world during the past 30 years, and a huge amount of data has been obtained during the 5 years of the study.

The meeting was opened by Dr. Brown, Director, Virus Reference Department, who welcomed the participants to the Centre for Infections, HPA, London. As the Virus Reference Department of HPA, London has served as the reference laboratory for the Aravind Eye Hospital CRS study since 2001; the meeting is being hosted at their Centre. For this meeting, Steering Committee officers who served in their usual capacities were: Dr. Vesikari, Chair; Dr. Slack, Rapporteur; Dr. Robertson, Secretary.

From Aravind Eye Care System, Dr. P. Vijayalakshmi, Principal Investigator of the Aravind CRS study; Mr. Karthick Prakash, the biostatistician for the study; and Miss. Amala, Ph.D student, who has conducted the serological testing at the Aravind Rubella Research Laboratory attended the meeting. Mr Featherstone, Project Leader for the WHO Global Measles and Rubella Laboratory Network attended the meeting because of the global importance of the Aravind CRS study.

Dr.P.Vijayalakshmi, Mr.Karthick Prakash, Ms.Amala with Dr.Susan Robertson and others in the WHO Steering Committee Meeting

63rd All India Ophthalmological Society Conference

Bhuvaneshwar, Orissa, January 13-16

Dr. Sundaresan

- *Diagnosis of Ophthalmic genetic diseases*

Dr.Sundaresan with the other participants at the AIOS conference

Society for Human and Animal Mycology –National conference

Hyderabad, January 17–21

Dr. Lalitha Prajna

– *Susceptibility patterns of antifungal agents to filamentous fungi from corneal ulcers*

International symposium on human origin and genetics (Genes, evolution and complex disease)

(Organized by National Centre for Biological Sciences) Bangalore, February 17-19

Three junior research fellow students from Aravind Medical Research Foundation attended the symposium and presented posters on the following topics at the conference.

R. Ramyadevi

- *A Novel Connexin 46 gene mutation associated with Autosomal Dominant Congenital Cataract.*

J. Nallathambi

- *Effects of PAX6 mutation in various Congenital eye malformations.*

B. Suganthalakshmi

- *Is Aldose Reductase promoter polymorphism strongly associated with Diabetic retinopathy?*

Hands on training

Sankara Nethralaya, Chennai, June 20 -July 19

Ms. S. Ananthi, Microbiology Lab underwent one month summer school hands on training in molecular biology and virology techniques which was conducted by Sankara Nethralaya.

Indian Eye Research group

LV Prasad Eye Institute, Hyderabad, July 29-31

Dr. P. Sunderasan, Senior Scientist, Department of Genetics, Aravind-Madurai participated.

Papers Presented

R. Ramyadevi

- *A Novel Missense Mutation in Connexin 46 Gene Mutation Associated with Autosomal Dominant Congenital Cataract*

S. Ananthi

- *Antibacterial activity of the fourth generation fluoroquinolones against Ocular pathogens*

Arpitha Parthasarathy

- *Analysis of Isolated Human Limbal Epithelial Cells for P63 expression levels and Nucleus/Cytoplasm ratio – A cue for the Identification of Stem cells*

Balasubbu Suganthalakshmi

- *Prevalence of VEGF and ENOS gene polymorphism in Type 2 Diabetic Retinopathy*

Poster Presentations

Dr. Lalitha Prajna

- *Susceptibility of filamentous fungi isolated from corneal keratitis to Amphotericin B, Natamycin, Caspofungin, Itraconazole, Voriconazole, and Posaconazole*

J. Nallathambi

- *PAX6 Missense Mutations in Congenital Optic Nerve Malformations*

Thanapal Amala Rajasundari

- *Serosurvey on the Immune Status of Health Care Personnel against Rubella in an Eye Hospital*

Boomiraj Hemadevi

- *A Novel HSF4 Mutation causes Autosomal Recessive Congenital Lamellar Cataract*

P. Murugeswari

- *Imbalance of Growth Factors and Anti-Angiogenic Factors in Proliferative Diabetic Retinopathy Patients*

53rd Annual conference of the TNOA - Sight@Height 2005

Sterling Holiday Resorts, Kodaikanal, August 12-14

Dr. Sundaresan

Ophthalmic Genetics: Bench to Bedside applications:

- *Would gene therapy work in ophthalmology?*

WHO – sponsored workshop on Good Clinical research Practices for Ethics Committee

JIPMER, Pondicherry, October 18-19

The Central Drugs Standard Control Organization (CDCSCO), Govt. of India in collaboration with WHO conducted a series of national workshops all over the country on various aspects of "Good Clinical research Practices". One such workshop was, exclusively for Ethics Committee Members. Of 113 nominees from various parts of south India, 39 members from of various institutes were selected.

From Aravind Dr. Rathinam, Member Secretary of Institutional review board of Aravind Eye Hospital attended this training programme. The areas covered were Evolution of Ethics, Good Clinical Practice, Informed Consent, special ethical issues in clinical research, Schedule Y. Proper functioning of committees, responsibilities of investigators, Standard Operating Procedure (SOP), legal issues and GCP guidelines.

All India Conference of Medical Microbiology

Chennai, October 20-22

Dr. Lalitha Prajna

- *Molecular Speciation and antibiotic sensitivity patterns of Nocardia isolated from Corneal Ulcers*

Dr. Lalitha Prajna received an award for Indian Association of Medical Microbiologists (IAMM) Silver Jubille Prize for the best paper published in Bacteriology in the Indian Journal of Medical Microbiology for the year 2004-2005.

Ms.Ananthi with Dr.H.N.Madhavan, Head of Microbiology Department, Sankara Nethralaya, Chennai and other participants

PUBLICATIONS

INVESTIGATIVE OPHTHALMOLOGY AND VISUAL SCIENCE

2005 OCT; VOL. 46 (10): 3631-3636

Arpitha, P; Namperumalsamy, P; Prajna, NV; Srinivasan, M; Muthukkaruppan, VR

- *High Expression of p63 Combined with a Large N/C Ratio Defines a Subset of Human Limbal Epithelial Cells: Implications on Epithelial Stem Cells*

MOLECULAR VISION

2005 OCT; VOL. 11: 846-52

Ramya Devi, R; Reena, C; Vijayalakshmi, P

- *Novel mutations in* GJA3 *associated with autosomal dominant congenital cataract in the Indian population*

2005 (In Press)

Suganthalakshmi, B; Sundaresan, P; Anand, R; Kim, R; Mahalakshmi, R; Karthik Prakash, S; Namperumalsamy, P

- *Association of VEGF and eNos gene polymorphism in type 2 diabetic retinopathy*

2005 (In Press)

Nallathambi, J; Neethirajan, G; Shashikant, S; Vijayalakshmi, P; Sundaresan, P

- *PAX6 Missense Mutations Associated in patients with Optic Nerve Malformation*

INDIAN JOURNAL OF OPHTHALMOLOGY

2005; VOL. 53: 67–68

Srinivasan, M; Lalitha, P; Prajna, NV

- *Cluster of Cases of Mycobacterium Chelonei Keratitis following Penetrating Keratoplasty*

2005 (In press)

Lalitha, P; Amit, K; Kannan, M; Prajna, NV; Srinivasan, M

- *Herpes Simplex Keratitis and Visual impairment – a case series*

AMERICAN JOURNAL OF OPHTHALMOLOGY

2005; VOL. 139: 837–846

Haripriya, A; Lalitha, P; Minu M; Prajna, NV; Kim R; Shukla, D; Natchiar, G; Srinivasan, M

- *Nocardia Endophthalmitis after Cataract surgery: Clinicomicrobiological study*

INDIAN JOURNAL OF MEDICAL MICROBIOLOGY

2005; VOL. 23: 168–171

Smitha, S; Lalitha, P; Prajna, NV; Srinivasan, M

- *Susceptibility Trends of Pseudomonas Species from Corneal ulcers*

OPHTHALMOLOGY

2005; VOL. 112: 1884 – 1889

Lalitha, P; Rajagopalan, J; Karthick, P; Kim R; Prajna, NV; Srinivasan, M

- *Postcataract Endophthalmitis in South India: Incidence and Outcome*

EYE

2005 (In press)

Vasumathy, V; Lalitha, P; Velpandian, T; Ghose, S; Mahalakshmi, R; Kim, R

- *Vitreous and aqueous penetration of orally administered moxifloxacin in humans.*

ASIAN JOURNAL OF EXPERIMENTAL SCIENCES

2006; VOL. 20 Supplement, 15-28

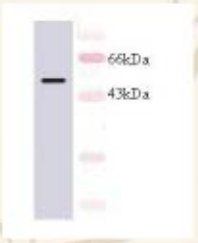
Suganthalakshmi, B; Anand, R; Kim, R; Namperumalsamy, P; Sundaresan, P

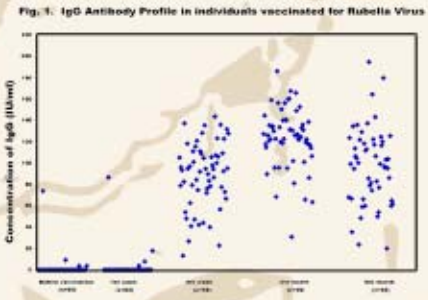
- *Emerging Patterns of Possible potential Candidate Gene Polymorphisms Associated with Diabetic Retinopathy - a review*

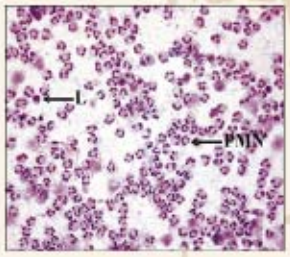
VISITS ABROAD

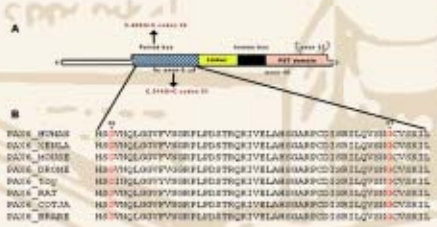
Dr. VR. Muthukkaruppan, Director-Research, Department of Immunology, Aravind Medical Research Foundation went to the US primarily to attend the ARVO Annual Meet at Fort Lauderdale. In the US he visited several institutes and met several eminent senior researchers and ophthalmologists.

- At ARVO 2005 Annual Meet at Fort Lauderdale, Florida, he presented a poster on 'Uveitis in patients with post leptospiral infection - Is it endotoxin mediated?'
- At Ocular Surface Center, Miami he held discussions with Dr. Schaffer Tseng on the importance of the amnion in ocular surface reconstruction.
- At Cullen Eye Institute, Baylon College of Medicine, Houston, he discussed human corneal epithelial stem cells with Dr. Pflugfelder and Dr. De-Quan Li. He also presented a paper on Aravind's recent studies on a new method of identification of corneal epithelial stem cells using confocal microscopy.
- At the Department of Ophthalmology, University of Wisconsin, Madison, he discussed two proposed collaborative projects with Dr. Paul Kaufman, Dr. Nadar, Sheibani and other senior staff. He also met Dr. Suresh Chandra, Dr. Chris Murphy of Veterinary School and Dr. Robert Auerback, his major professor for Ph.D.
- At the department of Dermatology, North Western University, Chicago, he discussed, with Dr. Robert Lauker, Director of Research, the latest method to functionally identify the human limbal stem cells
- At Wilmer Eye Institute, Baltimore he discussed the mechanism of inhibitory action of pigment epithelium derived factor (PEDF) in relation to diabetic retinopathy with Dr. Elia Duh. He discussed the limbal epithelial stem cells with Dr. Rof Chuck and clinical genetics of eye diseases with Irene Mauminee. To Dr. Sangili he spoke about the new projects which will be undertaken at Aravind.
- At National Eye Institute, Bethesda he discussed Uveitis with Dr. Chi-Chao Chan, and Dr. Nussenblalt. Here he presented a paper on 'Analysis of aqueous humor for infiltrating cells and cytokines in leptospiral uveitis patients'.
- At the Joslin Diabetic Centre and Beetham Eye Institute he met Dr. Paul Aiello, Dr. Jerry Cavalleralo and presented a paper on various research projects being carried out at Aravind Medical Research Foundation. He also discussed the collaborative projects on diabetic retinopathy with Dr. Aiello.









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