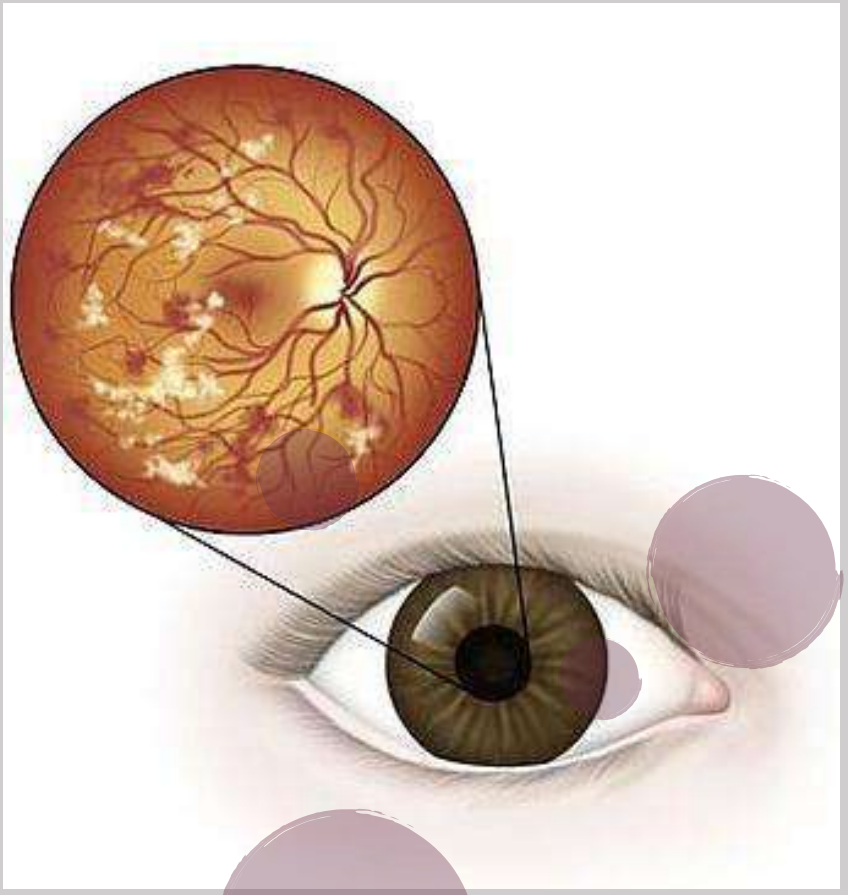
UPDATES ON OCULAR COMPLICATIONS OF DIABETES; A BENCH TO BEDSIDE REVIEW



Date:	**Friday 29 October**
Time:	**17-20:10**
Chairpersons	**Dr. Ali Hafezi-Moghadam , Dr. Zahra-Soheila Soheili, Dr. Farzad Pakdel**

	TIME	Name	Title	Duration (Minutes)*
1	**17:00 -17:10**	Dr. Hamid Ahmadieh IRAN	Greetings	10
2	**17:10 -17:40**	Dr. Ali Hafezi-Moghadam USA	Early diagnosis of diabetic complications in the eye	25+5
3	**17:40 -18:10**	Dr. Mehran Zarei-Ghanavati IRAN	A review of the effects of diabetes on cornea and ocular surface	25+5
4	**18:10 -18:40**	Dr. Ehsan Ranaei-Pirmardan USA	Diabetic cataract: A longitudinal phenotypic and cellular study of pathology formation in T2D animal model	25+5
5	**18:40 -19:10**	Dr. Hamid Safi IRAN	An overview on diabetic choroidopathy	25+5
6	**19:10 -19:40**	Dr. Sare Safi IRAN	Epidemiology of diabetic retinopathy	25+5
7	**19:40 -20:00**	Panel Discussion Dr. Ali Hafezi-Moghadam, Dr. Mehran Zarei-Ghanavati, Dr. Ehsan Ranaei-Pirmardan, Dr. Hamid Safi, Dr. Sare Safi, Dr. Farzad Pakdel		20
8	**20:00 -20:10**	Closing Dr. Hamid Ahmadieh, Dr. Zahra-Soheila Soheili, Dr. Farzad Pakdel		10

* SCIENTIFIC SESSION Presentations are 25 minutes in duration, followed by 5-minute discussion.

Ali Hafezi-Moghadam, MD, PhD

Associate Professor of Radiology, Molecular Biomarkers Nano-Imaging Laboratory, Brigham and Women's Hospital, Department of Radiology, Harvard Medical School, Boston, MA, USA.

Biography

I am an Associate Professor in Radiology at Harvard Medical School and the Director of the Molecular Biomarkers Nano-Imaging Laboratory (MBNI) at the Brigham and Women's Hospital (BWH).

I received my undergraduate degree in sciences in Berlin Germany. I then studied medicine and completed my dissertation at the Freie Universität Berlin. My postdoctoral fellowship was in Biomedical Engineering at the University of Virginia in Charlottesville (UVA). Subsequently I joined the faculty at the Immune Disease Institute, an affiliate of the Harvard Medical School as an instructor. In 2003, I established my laboratory at Massachusetts Eye & Ear Infirmary (MEEI) and since 2010 at Brigham and Women's Hospital (BWH).

Early diagnosis of diabetic complications in the eye

Major obstacles to developing therapeutic approaches for diabetes complications are 1) the lack of biomarkers for tracking the onset, progression, and extent of tissue damage, and 2) insufficient knowledge of the effect of treatments on a cellular or molecular level in vivo. My laboratory focuses on the identification and non-invasive detection of molecular biomarkers for early diagnosis of diabetes complications before irreversible tissue damages occur.

In this lecture I will provide a chronological overview of my initial research in basic immunology that inspired the development of a non-invasive technology for assessment of diabetic retinopathy. The purpose of this talk is to provide trainees and fellows in the audience with one specific example of how basic research of today could impact the clinical practice in decades to come.

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The novel imaging technology, which I will discuss in detail could provide clinicians a powerful tool for screening and monitoring early molecular and cellular events in the organs of diabetic patients, as well as measuring early responses to therapeutic interventions in humans. This technique enables for the first time direct visualization of individual molecules associated with diabetes in the retina, reaches a sensitivity that rivals that of the most sensitive in vitro techniques, and provides live quantitative feedback on therapeutic success. In collaboration with leading colleagues in the audience, we established endothelial VEGFR-2 as a novel biomarker for early diagnosis of diabetic retinopathy. The select assembly of presenters covering the various tissues of the diabetic eye promises a productive discussion and generation of new ideas for research.

Mehran Zarei-Ghanavati, MD

Farabi Eye Hospital, Tehran University of Medical Sciences.

Biography

Mehran Zarei Ghanavati is an associate professor of ophthalmology at Farabi Eye Hospital; Tehran University of Medical Sciences. He completed his fellowships in external disease, cataract and anterior segment at Farabi Eye Hospital and cornea and artificial keratoplasty (supported by Helmerich Award-International Council of Ophthalmology) at Sussex Eye Hospital in Brighton, UK. His clinical focus is in ocular surface disease, lamellar keratoplasty, artificial keratoplasty and limbal stem cell transplantation.

A review of the effects of diabetes on cornea and ocular surface

DATE: Friday 29 October

TIME: 17:40 -18:10

Ehsan Ranaei-Pirmardan, PhD

Postdoctoral Researcher, Molecular Biomarkers Nano-Imaging Laboratory, Brigham and Women's Hospital, Department of Radiology, Harvard Medical School, Boston, MA, USA.

Biography

Ehsan Ranaei Pirmardan is a postdoctoral researcher at Brigham and Women's Hospital, Harvard Medical School, since November 2019. He received his PhD in molecular genetics from Tarbiat Modares University, Tehran, Iran in 2016. He did his PhD thesis at NIGEB, Dr. Soheili's lab, and gained a solid background in recombinant AAV-mediated gene transfer to the mouse eye and molecular/histological analysis. His research is in the field of ocular diseases with a special focus on molecular underpinnings of cellular aspects of diabetic cataract. He is interested in methods of early diagnosis of diabetic complications in the eye and in novel therapies pertaining to angiogenesis.

Diabetic cataract: A longitudinal phenotypic and cellular study of pathology formation in T2D animal model

Diabetes is a major risk factor for cataract, the leading cause of blindness worldwide. There is an unmet need for a realistic model of diabetic cataract for mechanistic and longitudinal studies, as existing models do not reflect key aspects of the complex human disease. Here, we introduce and characterize diabetic cataract in the Nile grass rat (NGR, Arvicanthis niloticus), an established model of metabolic syndrome and type 2 diabetes (T2D). We conducted a longitudinal study of cataract in over 88 NGRs in their non-diabetic, pre-diabetic, and diabetic stages of metabolism. Oral glucose tolerance test (OGTT) results distinguished the metabolic stages. Diverse cataract types were observed in the course of diabetes, including cortical, posterior subcapsular (PSC), and anterior subcapsular (ASC), all of which succeeded a characteristic dotted ring stage in all animals. The onset ages of diabetes and cataract were 44 ± 3 vs 29 ± 1 ($P < .001$) and 66 ± 5 vs 58 ± 6 (not significant) weeks in females and males, respectively. Histological analysis revealed fiber disorganization, vacuolar structures, and cellular proliferation and migration in cataractous lenses. The lens epithelial cells (LECs) in non-diabetic young NGRs expressed the stress marker GRP78, as did LECs and migrated cells in the lenses of diabetic animals. Elucidating mechanisms underlying LEC proliferation and migration will be clinically valuable in prevention and treatment of posterior capsule opacification, a dreaded complication of cataract surgery. Marked changes in N-cadherin expression emphasized a role for LEC integrity in cataractogenesis. Apoptotic cells were dispersed in the equatorial areas in early cataractogenesis. Our study reveals diverse cataract types that spontaneously develop in the diabetic NGR, and which uniquely mirror the cataract and its chronic course of development in individuals with diabetes. We provide mechanistic insights into early stages of diabetic cataract. These unique characteristics make NGR highly suited for mechanistic studies, especially in the context of metabolism, diabetes, and aging.

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TIME: 18:10 -18:40

Hamid Safi, MD

Ophthalmic Research Center, Research Institute for Ophthalmology and Vision Science, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

Biography

Hamid Safi is a clinical researcher and laboratory scientist at Research Institute for Ophthalmology and Vision Science at Shahid Beheshti University of Medical Science. He completed his vitreoretinal fellowship at Shahid Beheshti University of Medical Science in 2021. He also received his Master of Public Health from Tehran University of Medical Sciences in 2012. He is currently working as a vitreoretinal specialist and surgeon at Imam Hossein Medical Center. His main area of research interest is vitreoretinal disease especially diabetic retinopathy and choroidal disease of the eye.

An overview on diabetic choroidopathy

The choroid is a vascular layer of the eye that lies between the retina and the sclera. With a dense network of blood vessels, it provides oxygen and nourishment to the outer layers of the retina, including the retinal pigmented epithelium and photoreceptors, and the only source of metabolic exchange for the avascular fovea. Histological and imaging based studies in diabetic patients demonstrated several choroidal changes. Choroidal abnormalities are common in patients with diabetes mellitus. The choroidal abnormalities in diabetic eyes include microaneurysms, dilatation and obstruction of the choriocapillaris, vascular remodeling with increased vascular tortuosity, vascular dropout, areas of vascular non-perfusion and choroidal neovascularization. The recent focus on choroidal thickness revealed significant differences in contrast to the normal population. However, understanding choroidal manifestations of diabetic eye disease remains a real challenge, and this gap is hindering efforts towards better defining choroidal evaluation as a predictive factor for disease evolution and treatment response. It is clear that choroidal changes are present in patients with diabetes mellitus. However, it remains unclear whether these changes are predictive, modulatory, causative or independent factors for diabetic retinopathy.

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TIME: 18:40 -19:10

Sare Safi, PhD

Ophthalmic Research Center, Research Institute for Ophthalmology and Vision Science, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

Biography

Sare Safi is an assistant professor at Shahid Beheshti University of Medical Sciences (SBMU) and is the research director of the Research Institute for Ophthalmology and Vision Science (WHO Collaborating Center for Eye Care and Prevention of Blindness in Iran). She received her PhD degree in Optometry from SBMU in 2017. Sare is the Executive Officer of the Ophthalmic Knowledge Management Unit at the SBMU. She is also an Executive Editor of the Journal of Ophthalmic and Vision Research. Her main area of research interests is ophthalmic epidemiology and public health for eye care.

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Epidemiology of diabetic retinopathy

Diabetes mellitus affected 463 million people worldwide in 2019 and is predicted to achieve 700 million by 2045. A pooled global prevalence of diabetic retinopathy (DR), the leading cause of preventable blindness among the working population, was reported to be about 22.27% in 2020. The “Middle East and North Africa” and “Central Europe, Eastern Europe, and Central Asia” super regions have the highest and lowest crude prevalence of DR among people aged 50 years and more, respectively. This complication accounted for 3% of the total burden of blindness among the population aged 50 years or more. Blindness due to DR can be prevented at three levels. Primary prevention is focused on avoiding or delaying the onset of DR. Secondary prevention includes the strategies to prevent the progression of DR. Tertiary prevention is focused on preventing blindness due to DR. This level of prevention is concentrated on clinical ophthalmology and timely laser photocoagulation, the intravitreal anti-vascular endothelial growth factors, and surgery. It is recommended to shift the prevention of blindness due to DR from the tertiary prevention approach toward the secondary and primary prevention strategies.

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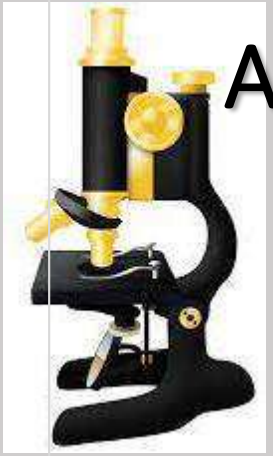
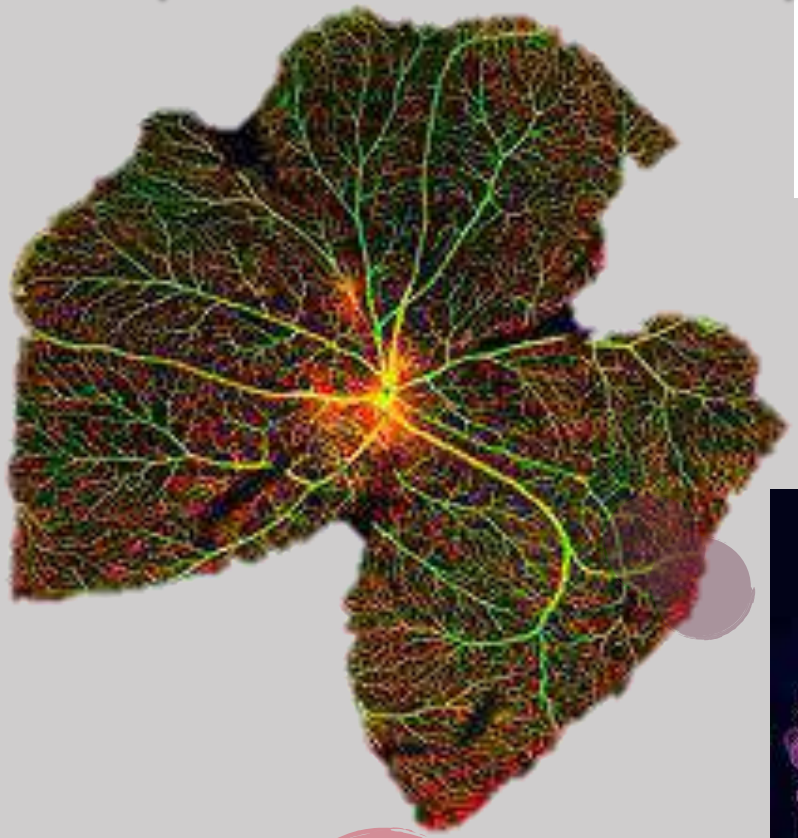
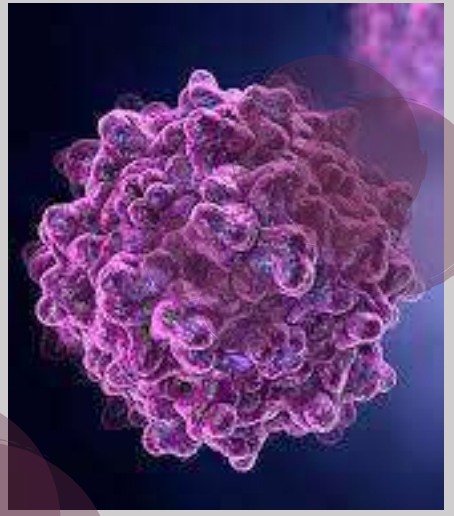


An overview of ocular gene delivery; from laboratory techniques to data analysis





Date: **Thursday 28 October**

Time: **15-18:20**

Chairpersons: **Dr. Hamid Ahmadieh, Dr. Zahra-Soheila Soheili, Dr. Farzad Pakdel**

	TIME	Name	Title	Duration (Minutes)*
1	**15:00 -15:10**	Dr. Farzad Pakdel IRAN	Greetings	10
2	**15:10 -15:40**	Dr. Ehsan Ranaei-Pirmardan USA	Practical approaches to the ocular gene delivery in pre-clinical research	25+5
3	**15:40 -16:10**	Dr. Hamid Latifi-Navid IRAN Dr. Narges Zolfaghari IRAN Dr. Somayeh Piroozmand IRAN	An overview of AAV virus production, intra ocular injection, and manipulation of the transduced retina	25+5
4	**16:10 -16:40**	Dr. Tahmineh Motevasseli IRAN	How to start working with ImageJ?	25+5
5	**16:40 -17:40**	Dr. Mozhgan Rezaei-Kanavi IRAN	Applications of ImageJ in Cytological and Histological Investigations	55+5
6	**17:40 -18:10**	Dr. Fatemeh Suri IRAN	Choroidal parameters analysis in OCT images	25+5
7	**18:10 -18:20**	Closing Dr. Hamid Ahmadieh, Dr. Zahra-Soheila Soheili		10

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Ehsan Ranaei-Pirmardan, PhD

Postdoctoral Researcher, Molecular Biomarkers Nano-Imaging Laboratory, Brigham and Women's Hospital, Department of Radiology, Harvard Medical School, Boston, MA, USA.

Biography

Ehsan Ranaei Pirmardan is a postdoctoral researcher at Brigham and Women's Hospital, Harvard Medical School, since November 2019. He received his PhD in molecular genetics from Tarbiat Modares University, Tehran, Iran in 2016. He did his PhD thesis at NIGEB, Dr. Soheili's lab, and gained a solid background in recombinant AAV-mediated gene transfer to the mouse eye and molecular/histological analysis. His research is in the field of ocular diseases with a special focus on molecular underpinnings of cellular aspects of diabetic cataract. He is interested in methods of early diagnosis of diabetic complications in the eye and in novel therapies pertaining to angiogenesis.

Practical approaches to the ocular gene delivery in pre-clinical research

In recent years, the eye is at the forefront of gene therapy studies. Since the FDA approved the first gene therapy drug for a form of congenital blindness, there have been numerous studies focused on developing novel ocular gene delivery systems and therapies. In these studies, new information has been revealed about the benefits and limitations of various drug delivery routes to the different parts of the eye. The aim of this workshop is to present a short history of ocular gene therapy and provide a practical review of gene delivery methods in preclinical studies.

DATE: Thursday 28 October

TIME: 15:10 -15:40

Narges Zolfaghari, PhD

Department of Molecular Medicine, National Institute of Genetic Engineering and Biotechnology, Tehran, Iran.

Biography

I am a PhD candidate at the Iranian national institute of genetic engineering and biotechnology (NIGEB). Since 2018, I have been studying for my PhD in molecular genetics at NIGEB. I am doing my PhD thesis in Dr. Soheili's lab. My thesis is about the role of miR-96 in the development of symptoms of diabetic retinopathy. My major technical abilities are molecular cloning, cell culture, gene delivery to the mice eyes using recombinant AAV2 viruses, STZ-induced diabetic mice model, and histological processing. My research interest area is novel anti-angiogenic therapies, especially in diabetic retinopathy disease.

Hamid Latifi-Navid, PhD

Department of Molecular Medicine, National Institute of Genetic Engineering and Biotechnology, Tehran, Iran.

Biography

Hamid Latifi-Navid is a PhD candidate in molecular genetics from the National Institute of Genetic Engineering and Biotechnology, Tehran, Iran. His research field in Dr. Soheili's lab is to design novel multi-target anti-angiogenic molecules and evaluate their function in the newborn mouse eye. Drug resistance in these molecules occurs slower than conventional therapeutic approaches. Moreover, He is interested in biological network analysis, computer-aided drug design, and artificial intelligence in drug discovery and development.

Somayeh Piroozmand, PhD

Department of Molecular Medicine, National Institute of Genetic Engineering and Biotechnology, Tehran, Iran.

Biography

Somayeh Piroozmand is a PhD candidate of Molecular Genetics in the Department of Molecular Medicine, National Institute of Genetics Engineering and Biotechnology, Tehran, Iran since 2018. She has started her PhD thesis in Dr.Soheili's laboratory two years ago and it is still going on. Her PhD thesis research project is about the evaluation of chimeric peptide carrier activity to efficiently transfer the anti-angiogenic gene in the newborn mouse eye. Her research interest is drug delivery systems into the eye and the function of anti-angiogenesis drugs to restrain pathologic angiogenesis in ocular diseases like Age-related macular degeneration and diabetic retinopathy.

An overview of AAV virus production, intra ocular injection, and manipulation of the transduced retina

The process of transferring and expressing a desired gene to cells or living animals has become a crucial approach in gene therapy. In recent years, the use of adeno-associated viruses (AAVs) has grown significantly in a wide range of gene therapy studies. This is due to the representation of several unique features by the AAV gene delivery system which involved safety, selective tissue tropism, high transduction efficiency, low immunogenicity, and a long stable gene expression.

This section provides an overview of the virus production process which involved plasmid extraction (maxipreparation), triple transfection, AAV production, collection of virus particles, purification, concentration, and titration.

In the next step, intra ocular injecting of the virus into the mice eyes will be examined, and finally, how to manipulate the transduced retina will be discussed.

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Tahmineh Motevasseli, MD

Retina fellowship, Labbafi-nejad medical center, Shahid Beheshti Medical University and Ophthalmic Research Center.

Biography

I am Tahmineh Motevasseli graduated from the Iran University of Medical Sciences and passed my ophthalmology residency at Shahid Beheshti Medical University. I have got the Iranian Board of ophthalmology and an award for a distinguished resident in 2016. In addition, I have passed the International Retina Clinical Research Fellowship program at the University of California San Diego (UCSD), Shiley Eye Center.

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How to start working with ImageJ?

ImageJ, as an image processing software developed at the National Institutes of Health, has been a very useful and simple tool in many research projects for quantification of the qualitative data presented in the captured images. In this workshop, multiple aspects of application of this software in ophthalmic research projects will be discussed.

DATE: Thursday 28 October

TIME: 16:10 -16:40

Mozhgan Rezaei-Kanavi, MD

Ocular Tissue Engineering Research Center, Research Institute for Ophthalmology and Vision Science, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

Biography

- Associate Professor of Ophthalmology and Ocular Pathology, Head of the Ocular Tissue Engineering Research Center at the Research Institute for Ophthalmology and Vision Science, Shahid Beheshti University of Medical Sciences, Tehran, Iran
- Specialized and Technical Manager of Central Eye Bank of Iran, Tehran, Iran.

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Applications of ImageJ in Cytological and Histological Investigations

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Fatemeh Suri, PhD

Ophthalmic Research Center, Research Institute for Ophthalmology and Vision Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

Biography

I have Ph.D. in Cell and Molecular Biology and have spent a postdoctoral fellowship in the field of genetics of ocular diseases. Now, I am Assistant Professor and head of Genetic and Gene therapy Unit at Research Institute for Ophthalmology and Vision Science of Shahid Beheshti University of Medical Sciences. I am interested and working on genetics factors underlying human inherited ocular diseases, especially glaucoma and inherited retinal dystrophies, investigating molecular mechanisms of eye diseases, and developing novel therapeutics approaches.

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Choroidal parameters analysis in OCT images

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