

PROMOTION RECOMMENDATION
THE UNIVERSITY OF MICHIGAN
MEDICAL SCHOOL
DEPARTMENT OF OPHTHALMOLOGY AND VISUAL SCIENCES

Cagri G. Besirli, M.D., Ph.D., assistant professor of ophthalmology and visual sciences, Department of Ophthalmology and Visual Sciences, Medical School, is recommended for promotion to associate professor of ophthalmology and visual sciences, with tenure, Department of Ophthalmology and Visual Sciences, Medical School.

Academic Degrees

2006	M.D.	Washington University School of Medicine
2006	Ph.D.	Washington University School of Medicine
1998	B.S.	University of Michigan

Professional Record

2018-present	Skillman Career Development Professor of Pediatric Ophthalmology, University of Michigan
2013-present	Assistant Professor, Ophthalmology and Visual Sciences, University of Michigan
2010-2012	Clinical Lecturer of Ophthalmology and Visual Sciences, University of Michigan

Summary of Evaluation:

Teaching: Dr. Besirli teaches all levels of trainees; undergraduate students, residents, fellows, allied health providers, and health care providers throughout the region, as well as nationally, through lectures and invited presentations. He is routinely invited to major conferences to give lectures for various national and international organizations, including the Retina Society, Macula Society, and Association for Research in Vision and Ophthalmology (ARVO). Dr. Besirli has trained nine undergraduate students, one graduate student, 16 fellows, and seven medical students. He is a major contributor in the Ophthalmology and Visual Sciences International Fellows program. Dr. Besirli trains visiting scholars in the clinic and operating room on medical and surgical retina, specifically in the area of pediatric retina and retinopathy of prematurity. He routinely assists in the training of allied health personnel both within the department and regionally. His endeavors reach beyond ophthalmology as he has participated in educational activities for Mott Children's Hospital operating room nurses, perioperative nurses, and neonatal intensive care unit staff, providing routine updates on pediatric retina, vitreoretinal surgery, and the screening and treatment of retinopathy of prematurity. His clinical and surgical practice offers ophthalmology residents a unique opportunity to learn first-hand about performing complex retinopathy of prematurity surgery.

Research: Since being appointed as an assistant professor, Dr. Besirli's basic science and clinical research programs aim to identify molecular targets to develop neuroprotective strategies for retinal degeneration. The primary purpose of his research is to identify the factors and intracellular checkpoints that regulate retinal cell death or survival, with the ultimate goal of developing new

therapeutic agents for retinal detachment, macular degeneration and inherited retinal degenerations. Photoreceptor death is the root cause of vision loss in many retinal diseases. Numerous interventions have failed to stop photoreceptor cell death and prevent vision loss. A key gap remains in the ability to develop successful neuroprotective strategies and prevent photoreceptor loss. Dr. Besirli is focused on novel strategies to reprogram metabolism and boost photoreceptor survival to address this gap. His laboratory research has focused on investigating critical roles of HK2 and PKM2 in linking photoreceptor function to survival, developing the next generation of PKM2 activators with improved potency and solubility for intraocular delivery, which will lay the foundation for future translational pharmaceutical efforts. Dr. Besirli continues to perform studies to understand the HK2-dependent molecular pathways that link metabolism to photoreceptor survival, evaluation of ocular toxicity of a novel bifunctional P13K-MEK inhibitor being developed as an anti-cancer agent, the discovery of a novel, injectable biodegradable drug delivery platform to replace postoperative medication used in patients undergoing ocular surgery. He has been well funded through clinical trials, the National Institutes of Health, industry and foundation grants. Dr. Besirli has published more than 75 peer-reviewed articles, and has been invited to present his research on 18 occasions regionally, nationally and internationally. He holds four patents.

Recent and Significant Publications:

Padhi TR, Anderson BJ, Abbey AM, Yonekawa Y, Stem M, Alam D, Modi RR, Savla LP, Trese MT, Capone A, Drenser KA, Besirli CG: Choroidal neovascular membrane in paediatric patients: clinical characteristics and outcomes. *Br J Ophthalmol* 102(9): 1232-1237, 2018.

Dedania VS, Ozgonul C, Zacks DN, Besirli CG: Novel Classification System For Combined Hamartoma Of The Retina And Retinal Pigment Epithelium. *Retina* 38(1):12-19, 2018.

Smith A, Pawar M, Van Dort ME, Galbán S, Welton AR, Thurber GM, Ross BD, Besirli CG: Ocular Toxicity Profile of ST-162 and ST-168 as Novel Bifunctional MEK/PI3K Inhibitors. *J Ocul Pharmacol Ther* 34(6): 477-485, 2018.

Wubben TJ, Pawar M, Smith A, Toolan K, Hager H, Besirli CG: Photoreceptor metabolic reprogramming provides survival advantage in acute stress while causing chronic degeneration. *Sci Rep* 7(1): 17863, 2017.

Pawar M, Busov B, Chandrasekhar A, Yao J, Zacks DN, Besirli CG: FAS apoptotic inhibitory molecule 2 is a stress-induced intrinsic neuroprotective factor in the retina. *Cell Death Differ* 24(10): 1799-1810, 2017.

Service: Dr. Besirli provides exceptional clinical care to his patients on the Retina and Uveitis services at the Kellogg Eye Center. He is an expert in the diagnosis, management and surgical treatment of the retina and vitreous as well as management of acquired and inherited pediatric retinal disorders. He co-directed the annual meeting of the Michigan Society of Eye Physicians and Surgeons. Nationally, he serves on the ARVO Commercial Relations committee and is a study section member for the congressionally directed Medical Research Program Vision Research Program for the Department of Defense. Dr. Besirli serves as a grant reviewer for the PSI Foundation in Canada, the Academy of Medical Sciences in the United Kingdom, and the Icelandic

Research fund. His research excellence is evidenced by the obtention of numerous awards, including, the American Society of Retina Specialists Honor Award, Best Poster Award at the All India Ophthalmic Conference, and being named to the Top 40 under 40 Power List by the *Ophthalmologist*.

External Reviewers:

Reviewer A: “He is a well-funded investigator, with over \$9 million in grants looking at models of neuroprotection of photoreceptors as well as gene therapy. His research and publications in these areas are notable in the literature and extremely important contributions to our knowledge especially of photoreceptor degeneration...I believe that his accomplishments have certainly exceeded most of the physicians at his level of experience and may in fact exceed the work of many senior professors of ophthalmology.”

Reviewer B: “It is my informed judgment following this evaluation that Dr. Besirli is an exceptional candidate to be promoted to the rank of Assistant Professor. Dr. Besirli’s wide-ranging experience in vitreoretinal disorders and retinal degeneration put him in a[n] outstanding position to take on this role...The research conducted throughout his career on these topics is highly rigorous, and has meaningful impact on the field.”

Reviewer C: “He is the consummate clinician scientist because juggling all the research that he is doing and also being busy clinically is very demanding. ...He has developed a respect by the community of retinal specialists that is usually only given to those who are much older...Dr. Besirli is not a future star. He is a star and the University of Michigan is lucky to have such an accomplished yet humble person.”

Reviewer D: “He has distinguished himself as a ..., humble, intelligent clinician scientist in the field of retina who came to my attention after winning the Ronald G. Michels fellowship award in 2011, given only to a handful of the best retina fellows in the country. Dr. Besirli has a special ‘niche’ interest in pediatric retinal diseases and surgery, of which there are probably only a few dozen specialists in the country. He has distinguished himself by being a young leader in the field of pediatric retina, giving multiple lectures on this topic at his own institutional as well as nationally. As a surgeon, he was able to bridge the translational gap to bench research by making several discoveries in his [junior] career.”

Reviewer E: “...Cagri has become an internationally respected clinician scientist. He is an excellent example of a physician who can manage to integrate clinical practice, teaching and research...He has successfully competed for grants from a wide variety of organizations, including the NIH.”

Reviewer F: “His contributions have been significant, and provide fundamental core knowledge in the field. Dr. Besirli has gained national prominence and is recognized as a leader in the field of retinal metabolism and neuroprotection... He puts the interest of the patient first and has been at the forefront of the effort to build knowledge and find new treatments for patients with retinal disease. He has been doing pioneering work in the area of gene therapy and provides cutting-edge treatment for patients with inherited retinal degenerations. Besides providing clinical care, Dr. Besirli’s laboratory research is focusing on advancing the field by identifying potential therapeutic targets to prevent retinal degeneration.”

Summary of Recommendations:

Dr. Besirli is an ophthalmologist and scientist who specializes in pediatric retinal disorders. He is an active clinician, who teaches medical students, residents, and fellows, with outstanding evidence for teaching excellence. He is strong in research, teaching and service. I am pleased, therefore, to recommend Cagri G. Besirli, M.D., Ph.D. for promotion to associate professor of ophthalmology and visual sciences, with tenure, Department of Ophthalmology and Visual Sciences, Medical School.



Marschall S. Runge, M.D., Ph.D.
Executive Vice President for Medical Affairs
Dean, Medical School

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