Toys and Test Tubes Are Tools of the Trade for Pediatric Ophthalmologist and Vision-Scientist

Eric Pierce, M.D., Ph.D., enjoys the best of two careers, one as a physician taking care of children with eye problems in the Division of Ophthalmology at the Children’s Hospital of Philadelphia, and a second as a vision scientist searching for treatments for inherited retinal degenerations. In his laboratory at the F.M. Kirby Center for Molecular Ophthalmology, the primary focus of Pierce’s research is investigation of the pathogenesis of retinitis pigmentosa (RP), the most common form of inherited retinal degeneration. Pierce is interested in delineating the specific biochemical steps by which mutations in RP genes lead to death of the light sensitive rod and cone photoreceptor cells of the retina and the ensuing loss of vision. He is hopeful that if we can understand in a detailed way how mutations lead to vision loss, we may be able to develop therapies to prevent vision loss from RP and other forms of inherited blindness as well.

In his clinical practice at Children’s Hospital of Philadelphia, he is challenged with the difficult task of getting and keeping the attention span of his sometimes “wiggly” patients. His doctor’s bag is filled with his most valuable clinical tools: simple toys and games that are often supplied by his own children, ages 5 and 7. Even with toys available, there are days when a child is so distracted or cranky that Pierce’s work in the laboratory solving the mysteries of retinal degeneration appears to be easier to accomplish!

Pierce received his Ph.D. from the University of Wisconsin-Madison, and then his M.D. from the joint Harvard Medical School - M.I.T. Division of Health Sciences and Technology. He completed a residency in ophthalmology at the Massachusetts Eye and Ear Infirmary followed by a combined research-clinical

Dr. Pierce is hopeful that if we understand how mutations lead to vision loss then we can develop therapies to prevent vision loss from retinitis pigmentosa (RP) and other forms of inherited blindness.
Mutations in the *RP1* gene are a common cause of retinitis pigmentosa (RP). Pierce and his team are now trying to determine the function of the RP1 protein in vision, and how mutations in RP1 lead to death of the photoreceptor cells. They have discovered that the RP1 protein is part of the axoneme (a small tube made of protein polymers called microtubules) of the connecting cilium and of the outer segment of photoreceptor cells. The connecting cilium is a slender structure that connects the outer segments and inner segments of photoreceptor cells. The inner segment is the factory of the cell, where proteins necessary for vision are made. These proteins are then transported through the connecting cilium to the outer segment, which contains stacks of membrane discs where light is converted into a neurological signal and vision begins (Figure 1). The axoneme passes through the connecting cilium and continues into the outer segment. RP1 binds most to the portion of the axoneme that is in the photoreceptor outer segment. This is interesting because the membrane discs that make up the outer segment form next to the axoneme where RP1 is located. This means that RP1 could be involved in helping outer segment discs to form. Consistent with this idea, mice engineered with techniques called gene targeting to produce a mutant RP1 protein, undergo a rapid retinal degeneration characterized by incorrectly oriented outer segment discs that fail to properly stack up into outer segments. Given the location of RP1 in the axoneme, and the abnormal disc orientation observed in the mutant RP1 mice, it is attractive to hypothesize that RP1 functions as a connection between newly formed discs and the axoneme, and that this interaction helps discs form in the correct orientation and to stack up into outer segments. Mutations in RP1 may cause blindness by disrupting the connection between new discs and the axoneme, leading to incorrectly formed outer segments. Dr. Pierce and his group are hopeful that if they can define how RP1 controls disc orientation they will be able to use this knowledge to develop rational therapies to prevent vision loss from RP1 and potentially other retinal degenerations.

Figure 1. Left: Localization of the RP1 protein in the axoneme of human photoreceptor cells. Rods (slender cells) and a cone cell are indicated. The nuclei of the photoreceptor cells are shown in blue. Middle: Drawing of rod photoreceptor, with different portions of the cell indicated. Right: Enlargement of the junction between the inner and outer segments, showing the axoneme passing through the connecting cilium into the outer segment. The location of RP1 in the outer segment portion of the axoneme is indicated in red.
While searching for other genes that might be involved in retinal vascular disease, Pierce discovered the RP1 gene, which he later found to harbor mutations that cause inherited blindness.

Pierce's current research projects in his laboratory at the F.M. Kirby Center include:

- Investigation of the role of RP1 in retinal degenerations
- Investigation of how mutations in the ubiquitously expressed RNA splicing factor proteins PRPF3 and PRPF8 lead to retinitis pigmentosa 18 and 13, respectively
- Development of new techniques to produce animals with targeted single base mutations in photoreceptor genes
- Identification and characterization of genes involved in retinal neovascularization

Pierce's laboratory is funded by grants from the Rosanne H. Silbermann Foundation, Inc., the F.M. Kirby Foundation, Inc., the National Eye Institute, the National Cancer Institute, the Foundation Fighting Blindness, Research to Prevent Blindness, and the E. Matilda Zeigler Foundation for the Blind.

The Rosanne H. Silbermann Foundation, Inc. Supports Dr. Pierce’s Research

Dr. Eric Pierce’s work has been funded for the past four years by the Rosanne H. Silbermann Foundation. The foundation does not accept applications and supports medical research in areas of particular interest to the Silbermann family. Pierce says, “I am very pleased to have received funding from the Rosanne H. Silbermann Foundation. This support has enabled our laboratory to pursue multiple projects directed toward understanding the causes of inherited retinal degenerations. For each of these projects, we are positioned to make important progress toward this goal.”

Scheie physicians and scientists are making great progress towards developing and evaluating treatments to reduce vision loss in age-related macular degeneration and other inherited retinal degenerations.

To find out how you can make a difference by contributing to Scheie, call Ann Sacks at (215) 662-8774, e-mail ann.sacks@uphs.upenn.edu or visit our website www.penneye.com.
The annual alumni meeting was held on May 30 and 31 and featured guest speakers Dr. Michael X. Repka, Professor of Ophthalmology and Pediatrics at Johns Hopkins University and Dr. Michael S. Ip, Assistant Professor of Ophthalmology and Co-Director of the Fundus Photograph Reading Center at University of Wisconsin. Following the scientific meeting, a dinner dance was held at the Four Seasons on May 31 in honor of faculty who have been at Scheie for 20 years or more. Dr. Stuart Fine and Dr. Nick Volpe introduced and listed the many accomplishments of each honoree, whose names are listed below.

Bruce K. Brownstein, M.D.
Alexander J. Brucker, M.D.
Edward A. Deglin, M.D.
William C. Frayer, M.D.
Juan E. Grunwald, M.D.
James A. Katowitz, M.D.
David M. Kozart, M.D.
Alan M. Laties, M.D.
Charles W. Nichols, M.D.
Stephen E. Orlin, M.D.
Graham E. Quinn, M.D.
Dwight E. Stambolian, M.D., Ph.D.
Richard A. Stone, M.D.
T. Ramsey Thorp, M.D.
130th Anniversary Meeting to Honor Scheie Alumni

The 130th anniversary meeting will be held May 21-22, 2004. The guest speakers for the scientific meeting will be Donald Budenz, M.D., from Bascom Palmer Eye Institute and Daniel Martin, M.D., from Emory University. All Scheie alumni are encouraged to participate by attending or presenting. At the 130th anniversary dinner dance, to be held on May 21, 2004, Scheie will honor alumni from the classes of 1964, 1974, 1984 and 1994. The faculty are looking forward to renewing old acquaintances and learning what our alumni/ae have been doing since graduation from Scheie. Dr. Harvey Brown, an alumnus from the class of 1974, will work with Dr. Steve Orlin, Cornea Service Director, and Ann Sacks, Director of Alumni Relations, to plan a special reunion for the alumni honorees.
Microscopic Details Matter in Clinician-Scientist’s Research on Retinitis Pigmentosa

Dr. Aleman interprets computerized images of a patient’s retina.

Diagnosis in ophthalmology always has been limited by the magnification and resolution of the examining instruments available to physicians at the time. Today, technology has advanced so that a clinician can see microscopic details of a patient’s retina, the light-sensing lining inside of the eye. But interpreting what is seen requires a knowledgeable and discerning eye. Tomas S. Aleman, M.D., a clinician-scientist at Scheie’s Center for Hereditary Retinal Degenerations, is pursuing the underlying mechanisms and treatments for retinitis pigmentosa (RP), a group of serious and incurable forms of inherited retinal blindness. Aleman uses a sophisticated scanning method, optical coherence tomography (OCT), to study the fine details of the layers of the retina, seeking the anatomical basis of the patient’s vision loss. The aim of his work is to determine which retinal layers (and the cells or connections therein) are being affected most by the genetic disease. Quantifying the OCT computer images makes them valuable for monitoring changes in patients’ vision. Aleman’s ultimate plan is to use these retinal images to evaluate with greater precision the effects of future therapies to slow the progression or even restore vision in RP.

Aleman received his M.D. degree from Havana University School of Medicine where he later completed his residency in ophthalmology. He came to Scheie’s Center for Hereditary Retinal Degenerations in 1997 as a post-doctoral fellow with Samuel G. Jacobson, M.D., Ph.D. During his fellowship, he became an integral part of the Center, taking on extensive clinical-research responsibilities. Aleman’s knowledge and expertise are in constant demand by Scheie scientists and physicians, who seek his collaboration and his valued opinion about the basis of an electrophysiological abnormality, interpretation of an OCT image, or a question about an unknown disease mechanism.

Same Gene May Cause Cataracts in Mice and Men

Why do cataracts form? Kristen Huang Ph.D., a research assistant professor at the F.M. Kirby Center for Molecular Ophthalmology has been investigating the genetic basis of congenital cataracts for the past three years in collaboration with Dwight Stambolian M.D., Ph.D., Associate Professor of Ophthalmology and senior scientist at the F.M. Kirby Center for Molecular Ophthalmology. The aim of Huang’s current research is to identify the X-linked gene that causes mice to be born with cataracts in the X-linked cataract mouse (Xcat mouse). This mouse is a model for a rare human congenital cataract disease, the Nance-Horan Syndrome. According to Huang, “There is good evidence that the same gene is affected in both Xcat mice and Nance-Horan patients, but we won’t know for sure until we clone the Xcat gene. This research will reveal important information about the genes required for proper lens development.” Once the Xcat mutation is identified, Huang and her colleagues will examine this same region of the X chromosome in DNA isolated from Nance-Horan patients to determine if they carry a similar mutation.

Huang received her Ph.D. in biochemistry from Case Western Reserve University where she then completed a postdoctoral fellowship in the Department of Molecular Biology and Microbiology. Huang considers herself primarily a cell biologist and geneticist. But like most scientists, she has had to tackle the constantly changing task of genomic analysis. “Because new data are being deposited daily, you have to stay up to the minute.” She adds, “The amount of genomic information available is enormous and can be intimidating. You have to focus or you waste a lot of time wading through all the different genomic databases and resources.”

Dr. Huang identifies a gene sequence.
Corneal Surgeons...

Stephen Orlin, M.D., began his life in America in 1982 when on 24-hours notice he flew from his native South Africa for a one-hour interview for a residency position at Scheie. Although he spent more time in the air than on the ground, it was a trip well worth his while. Orlin completed his residency in 1985 and his fellowship in cornea and external diseases in 1987, after which he joined the full-time faculty at Penn. Orlin is now Chief of the Cornea Service and Co-Director of Refractive Surgery. His major interests include challenging reconstructive surgery of the anterior segment and corneal transplantation. Orlin has been listed in Philadelphia Magazine’s “Top Docs” and in Best Doctors in America for his expertise as a corneal specialist. He has an international reputation as an exquisitely talented surgeon and as an inspiring teacher. Orlin has lectured to ophthalmologists from all over Russia and performed surgery in St. Petersburg, bringing with him corneas donated by the Lions’ Club Eye Bank of Philadelphia. Orlin enjoys teaching residents and medical students and has been recognized as one of the most outstanding teachers at Scheie, having received the Golden Apple Award three times. Third-year resident Dr. Michael Tracy offered the following: “There is no finer mentor, both personally and professionally, than Steve Orlin. His dry wit makes him a delight to work with and his clinical and surgical acumen is matched only by his unsurpassed ethical standards.”

Orlin is married to Dr. Glenda Rabie, a primary care physician. Their son, Anton, is a second-year medical student at Penn, and daughter, Lindi, is a senior at Emory. An avid runner, Orlin has participated in national and international marathons, most recently in Prague, Czech Republic.

Michael E. Sulewski, M.D., came to Scheie in 1991 after completing a two-year cornea fellowship at Johns Hopkins. He joined the Cornea Service at Scheie and assumed the role of Chief of Ophthalmology at the Philadelphia VA Medical Center. An expert in corneal transplantation, refractive surgery, and cataract surgery, Sulewski’s research interests include new treatments for dry eyes and corneal infections. He served as a co-investigator in the NIH-supported Herpes Eye Disease Study.

Sulewski devotes most of his time to patient care and enjoys tackling the most challenging cases. He teaches residents and medical students in the classroom and clinic, as well as in the operating room. Sulewski is a recipient of Scheie’s Golden Apple resident teaching award and has been listed in Philadelphia Magazine’s “Top Docs” issue because of his expertise in corneal and refractive (LASIK) surgery. According to patient Cathy Amerling, “I had struggled with extreme nearsightedness all my life. When I heard about the LASIK procedure I thought I would probably be turned down as a candidate since I had such a high prescription. I found Dr. Sulewski, who was extremely well versed in the latest advances in refractive (LASIK) surgery. He told me he could help and was very optimistic. The procedure went perfectly and I can now see 20/20 on my own, without the need for glasses. I am so happy and constantly amazed as I look around me, seeing with such clarity as I’ve never known before.”

Sulewski is married to Pamela and they have two children. Michael is 14 and going into the 9th grade and Melanie is 9, going into the 4th grade. In his spare time, Sulewski is an avid player of golf, tennis and squash.
Scheie Welcomes New Residents and Fellows

Residents

Gil Binenbaum, M.D.
Gil is a 1989 graduate of Wharton and a 2002 graduate of the School of Medicine. After six exciting years on Wall Street as a foreign currency trader, Gil decided to follow his true passion of medicine. He completed the Presbyterian Transitional Program where he helped revamp the application and admissions process. Gil enjoys spending spare time with wife Andrea, and their two children, Emi and Nate.

Jennifer K. Hall, M.D.
Jenny earned her undergraduate and medical degrees from Penn, as well as a master’s degree from Yale University. Most recently, Jenny worked with Nicholas J. Volpe, M.D. to research the role of unilateral temporal artery biopsy and presented the results at ARVO and NANOS. In addition to spending time with husband David and their three children, Jenny enjoys hiking, gardening and textile arts.

Newman Sund, M.D., Ph.D.
Newman hails from New York. He received his undergraduate degree from Columbia University and his M.D./Ph.D. from Penn in 2001. Newman’s research interest led him to the lab of Michael Tolentino, M.D., where he worked to help identify mediators of angiogenesis in the eye. A frequent traveler to East Asia, Newman and wife Vivian enjoy snowboarding at Lake Tahoe, rollerblading and hiking.

B. Michael Walker, M.D.
Mike’s path to Scheie includes training in aerospace engineering at the U.S. Naval Academy, a degree in mechanical engineering from the University of Colorado, four years of full-time employment as an engineer and a finally a medical degree from Penn. During medical school, Mike worked in the lab of Grant Liu, M.D. performing visual cortex mapping using functional MRI. In his spare time, Mike plays the guitar and enjoys golfing, mountain biking and canoeing with wife Lisa.

Wayne Wu, M.D., Ph.D.
Born in Fuling, China, Wayne received his undergraduate degree from Peking University. Wayne came to the U.S. in 1990 and received his Ph.D. in biochemistry from the University of Wisconsin and his medical degree from the University of Michigan where he performed clinical research on nanophthalmos (small eyes). In his free time, he enjoys spending time with his wife, Charlene, and playing chess with their son, James.

Fellows

Stefanie Davidson, M.D.
Fellow in Pediatric Ophthalmology
Stefanie was graduated from UNC-Chapel Hill, earned her medical degree from UMDNJ Medical School and completed an internship at UMDNJ-Robert Wood Johnson. She recently completed her residency at Tufts University/New England Eye Center. Stefanie, a newlywed, enjoys spending free time with her husband, Joseph, a fellow in Dermatology at HUP.

Jennifer Focht, M.D.
Fellow in Glaucoma
A graduate of Bucknell University, Heather attended Jefferson Medical College prior to completing her ophthalmology residency at SUNY Upstate Medical University in Syracuse. Heather and fiancé, E.J., are busy planning an October wedding. We welcome Heather back to the Philadelphia area.

Carolyn Glazer-Hockstein, M.D.
Fellow in Medical Retina
Carolyn is no stranger to Scheie having recently completed her residency here. She will function as a part time medical retina fellow and a part time attending physician on the Comprehensive Ophthalmology Service. Carolyn spends free time with her husband, Neil, and their 10-month old daughter, Leia.

George Mayo, M.D.
Fellow in Vitreoretinal Surgery
George served 4 years as a Lt. Commander in the Medical Corps of the US Navy after graduating from University of Pennsylvania School of Medicine. He completed an ophthalmology residency at University of Texas Health Science Center in San Antonio. George and wife, Kathy, a second year resident in Obstetrics and Gynecology at Philadelphia College of Osteopathic Medicine, are excited about their return to Philadelphia.

Kenneth Shindler, M.D., Ph.D.
Fellow in Neuro-Ophthalmology
Ken, a graduate of Washington University in St. Louis, was awarded the Society of Heed Fellows Fellowship to support his Neuro-Ophthalmology fellowship at Penn. Ken plans to join the Scheie/Penn faculty in July 2004 as a physician-scientist working on neuroprotection in patients with optic nerve disorders. Ken and wife, Christine, are actively involved in the Philadelphia Sport and Social Club.
Russell Van Gelder to Deliver Inaugural Berger Lectureship

The world of ophthalmology and vision science suffered a tremendous loss with the untimely passing in 2001 of one of Scheie Eye Institute’s young physician-scientists, Jeffrey W. Berger, M.D., Ph.D. On October 16, 2003, Scheie will honor his vision, leadership, research acumen and legacy with the Inaugural Jeffrey W. Berger Lectureship. Russell N. Van Gelder, M.D., Ph.D., Assistant Professor, Department of Ophthalmology and Visual Sciences and Assistant Professor, Department of Molecular Biology and Pharmacology at Washington University School of Medicine in St. Louis, will present the inaugural lecture, entitled “Sensing Light Without Sight: Basic Science and Clinical Application.” It is particularly appropriate for Dr. Van Gelder to be the inaugural Berger lecturer since he and Dr. Berger not only were acquainted but also shared many interests in the visual system, the retina, and a commitment to medical student and resident education. In addition, both were considered among the most promising young physician-scientists in the field of ophthalmology and eye and vision research. The department is proud to include this annual lectureship among the other Jeffrey Berger memorials: the Jeffrey W. Berger Clinician-Scientist Award to support young faculty who are conducting research, the Jeffrey W. Berger Student Research Scholarship to support medical students conducting ophthalmic research, and the Jeffrey W. Berger Golden Apple Award for Excellence in Resident Teaching. For more information on the Jeffrey W. Berger Lectureship, please contact Priscilla Stein at 215-662-8020 or priscilla.stein@uphs.upenn.edu.

New Faculty

Robert A. Stoltz, M.D., Ph.D.
Robert A. Stoltz, M.D., Ph.D., a recent graduate of the ophthalmology residency and vitreoretinal surgery fellowship at Scheie, joined the Retina Service as an Assistant Professor of Ophthalmology in July. In addition to his clinical duties at Scheie and the VA Medical Center, Rob will continue to pursue his research interest as Principal Investigator of the Reading Center for the Complications of AMD Prevention Trial (CAPT). The CAPT is a large, multi-center clinical trial, supported by the National Eye Institute, which is evaluating a preventive intervention for patients with early AMD. Rob also will be an invaluable resource for residents and medical students in the clinic and the operating room. Rob enjoys spending his spare time with his wife Christine and daughter Gillian.

Paul J. Tapino, M.D.
Paul J. Tapino, M.D., a 2003 graduate of the Scheie residency, joined the faculty in July as a comprehensive ophthalmologist at HUP, Scheie and the VA Medical Center. His clinical activities include patient care, consultations, and attending residents in the outpatient clinic and the operating room. Because of his keen interest in resident education, Paul has been appointed Assistant Chief of Service. In that capacity, he will assist Nicholas J. Volpe, M.D., Residency Program Director, with developing a resident curriculum and method of assessment which comply with the ACGME’s new competency requirements for housestaff. Paul and wife Erika eagerly await the arrival of their first child who is due in November!
Specialties & Services

Applied Ophthalmic Neurobiology Laboratory
Alan M. Laties, M.D.
Richard A. Stone, M.D.

Center for Preventive Ophthalmology and Biostatistics
Judy Alexander, B.A.
Mary Brightwell-Arnold, B.A.
Stuart L. Fine, M.D.
Bojidar Madjarov, M.D.
Maureen G. Maguire, Ph.D.
Ellen Peskin, M.A.
Robert A. Stoltz, M.D., Ph.D.

Pediatric Oculoplastic Surgery
James A. Katowitz, M.D.

Low Vision Research and Rehabilitation Center
Janet DeBerry Steinberg, O.D.
Ranjoo Prasad, O.D.
Dawn Ciccarone, M.S., OTR/L

Medical Retina
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Joshua L. Duniaef, M.D., Ph.D.
Stuart L. Fine, M.D.
Juan E. Grunwald, M.D.
Albert M. Maguire, M.D.
Robert A. Stoltz, M.D., Ph.D.
Michael J. Tolentino, M.D.

Medical Therapies Initiative
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Rong Wen, M.D., Ph.D.

Neuro-Ophthalmology
Laura J. Balcer, M.D.
Steven L. Galetta, M.D.
Grant T. Liu, M.D.
Nicholas J. Volpe, M.D.

Neuroprotection Laboratory
Alan M. Laties, M.D.

Vivian Simkins Lasko
Retinal Vascular Research Laboratory
Joan DuPont
Juan E. Grunwald, M.D.
Jody R. Piltz-Seymour, M.D.

Oculoplastics & Orbital Disease & Surgery
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James A. Katowitz, M.D.

Ophthalmic Technicians, Director
Michele Sheehan, COMT

Genetics
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Glucoma
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Jody R. Piltz-Seymour, M.D.
Prithvi S. Sankar, M.D.
Richard A. Stone, M.D.

Pathology
William C. Frayer, M.D. (Emeritus)
Franz Fogt, M.D. (Interim)
Robert L. Peiffer, DVM, PhD, DIP, ACVO (Adjunct)

Pediatric Oculoplastic Surgery
James A. Katowitz, M.D.

Photography
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Cheryl Devine
William Nyberg
Laurel Weeney

Retinal Degeneration Histopathology Laboratory
Ann H. Milam, Ph.D. (Adjunct)

Strabismus-Adult
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Contact Lens Service
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Cynthia Silvestri, COA, NCLC

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Michael Tracy, M.D.
B. Michael Walker, M.D.
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Wayne Wu, M.D., Ph.D.

Fellows
Stefanie Davidson, M.D./Pediatric Ophthalmology
Heather L. Focht, M.D. / Glaucoma
Carolyn Glazer-Hockstein, M.D. / Medical Retina
Femida Kherani, M.D. / Oculoplastics
George L. Mayo, M.D. /Vitreoretinal Surgery
Kenneth S. Shindler, M.D., Ph.D. /Neuro-Ophthalmology

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1501 Lansdowne Avenue, #208, Darby, PA

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Visiting Professor Lectures are on Thursdays:
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Noon-1:00 PM (Thayer Conference Room, SEI 5th Floor)

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