

Microtechnological Solutions for Ocular Diseases:

Bioelectronic Implants,
Minimally Invasive Surgery,
and Drug Delivery Platforms

A Doheny Vision Research Symposium
January 9–10, 2004

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Dear Colleagues,

We were once again honored to have an exceptional group of speakers with us at the Doheny Eye Institute for the fourth annual symposium conducted by our organization. Microtechnological advances are truly yielding some exciting solutions to ocular disease that will benefit doctors and patients worldwide. We firmly believe that the knowledge shared will impact the quality of our lives on a scale that we cannot yet comprehend.

Our sincere thanks to everyone who helped make the symposium possible. To those who came, we thoroughly enjoyed your participation and fellowship. For you and everyone else who will benefit from it, we provide this summary of the information presented at our event.

We would like to thank those of our speakers who traveled the distance necessary to enrich our learning experience: Dr. Gerald Chader, of the Foundation for Fighting Blindness; Dr. Mark Blumenkranz, of Stanford University; Dr. Yasuo Tano, of Osaka University, Japan; Dr. Robert Greenberg, of Second Sight, LLC; Dr. Rosa Braga-Mele, of the University of Toronto, Canada; Dr. Timothy Olsen, of the University of Minnesota; Dr. Weng Tao, of Neurotech, USA; and Michael O'Rourke and John Saharek of Bausch & Lomb. Dr. Chader's keynote address put the research in a perspective and context that set the tone for the symposium, and the insights shared by each of our guest speakers added greater depth and meaning to the experience for all of us.

We are tremendously grateful for the support of our collaborative leadership team, including Dr. Stephen Ryan, honorary symposium chairman, and Dr. Eugene de Juan, Jr., symposium co-director. Your efforts and expertise made an inestimable contribution to our event and our institution as well as to the many other colleagues and patients we work with.

It must be said that our achievements would not be possible without the assistance of our generous benefactors, patrons, donors and friends. Every one of you has supported our work with true generosity of spirit. With your continued support, the Doheny Eye Institute will carry on its legacy of preeminent patient care, vision research and physician education. Thank you once again for the contributions that prove your appreciation for the work we do and events like our symposium that share our discoveries so that more may benefit.

Sincerely,

Ronald E. Smith, M.D.

Chairman, Department of Ophthalmology

Keck School of Medicine of USC

Charles Stewart and Hildegard Warren Professor

Doheny Eye Institute

Mark Humayun, M.D., Ph.D.

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Los Angeles, California

Minimally Invasive Surgery Offers New Opportunities for Surgeons and Patients

The surgeon's hands are amazingly steady as he punctures the white conjunctiva of the patient's eye in three places. With a few short twists of his pick, he injects tiny, tunnel-like devices called cannulas to hold open each hole. The holes are so small and clean, that they will heal without any sutures. Through these holes, the surgeon inserts a light pipe, forceps and a cutter to operate in the confines of the posterior segment of the patient's eye while the patient remains fully awake. This is what Doheny doctors mean when they talk about minimally invasive surgery.

The patient in this operation sought help for vision loss and distortion caused by macular pucker, a common problem among older people. It occurs when a thin layer of scar tissue develops on the surface of the central portion of the retina, called the macula, causing it to wrinkle and distort. After a 45-minute operation using the TSV25, the latest minimally invasive surgical system, this patient will enjoy significant visual improvement and typically will feel very little pain during recovery.

The TSV25 surgical system used in the above operation is one of the first microtechnological solutions developed as a result of research by Doheny's MADLAB and sponsorship and manufacturing expertise by Bausch & Lomb. With its miniaturized 25-gauge tools—about half the size of previous instruments—the system allows ophthalmic surgeons to perform vitreoretinal surgery through small punctures and to operate on the retina without actually cutting into the eye.

"It's a great feeling to perform an intricate procedure, then realize that you don't have to close [the wound]. You can just remove the cannulas and check the eye," said Doheny's Dr. Eugene de Juan, Jr., who performed the surgeries as the symposium attendees observed via remote video. "With such a small wound, the surgery is much less traumatic to the ocular tissues. As a result, patients enjoy better comfort, more rapid healing and faster postoperative visual recovery."

The next generation of the TSV25 system is already being planned at the Doheny MADLAB in collaboration with Bausch & Lomb, the manufacturer of the first system of this kind. By combining the clinical experience of Doheny doctors in product design and industry involvement in production and marketing, the MADLAB is well on its way toward designing the next generation TSV25, which may include wireless, voice-activated control, advanced fluidics to improve the safety of infusion/aspiration, and a smaller cutter hand piece.

What are the Benefits?

On the first day of the two-day symposium, the discussion focused on new surgical procedures made possible or just plain made easier by the TSV25. The system is quickly catching on with ophthalmic surgeons, who are always looking for better ways to operate on the small and delicate human eye, including everything from repairing hemorrhages, macular puckers, and macular holes in adults, to performing tricky procedures on the tiny eyes of children with various forms of retinopathy.

The system includes a cutter that, when introduced through the tiny cannula inserted into the eye, can remove the underlying vitreal fluid (vitrectomy) along with diseased tissues from the back of the eye. This has greatly simplified many surgeries that require vitrectomies. However, the vitrectomy is not without side effects.

What are the Risks?

“Nuclear sclerosis [cataracts] inevitably develops after successful vitrectomy [removal of the jelly-like vitreous fluid in the back of the eye] in elderly patients,” said Dr. Yasuo Tano, Chairman, Department of Ophthalmology, Osaka University. “We have been performing non-vitrectomizing vitreous surgery in patients with macular degeneration to prevent postoperative nuclear sclerosis. This prevented the development of nuclear sclerosis for more than three years after surgery.”

Dr. Tano believes that vitrectomies result in hyperoxygenation, which leads to the eventual development of cataracts in adult patients. Pediatric patients appear to avoid this result. In looking for a solution to this side effect in adult patients, Dr. Tano has found that if the vitreous sheath is left intact and carefully peeled back as one solid mass, no cataract develops. If a vitrectomy is required, Dr. Tano recommends replacing the lens to prevent the cataract from forming.

Dr. Mark Humayun of Doheny has also found advantages in treating branch retinal vein occlusion, a condition that commonly diminishes the vision of patients with hypertension or diabetes, without vitrectomy. He presented a study at the symposium showing that limited manipulation of the vitreal sheath, without vitrectomy, could achieve comparable outcomes to a sheathotomy with vitrectomy when treating complicated branch retinal vein occlusions. A clinical trial is being proposed to test this finding.

Challenges and Rewards

As doctors fine-tune the application of microtechnological solutions to vitreoretinal surgery, they face significant challenges in confirming their hypotheses through clinical trials. Patients must often be monitored over periods of many years to test the benefits of certain procedures. The practicality of long-term studies is often questionable given the limited time and resources of most doctors and institutions. Researchers are discovering that some advances may need to be shelved indefinitely as regulatory requirements that address issues of patient safety slow the microtechnological revolution.

Representatives from Bausch & Lomb at the symposium presented discouraging statistics about the hurdles they face as they try to bring new microtechnological solutions to market. “We have calculated that new pharmaceuticals have an average 1.9% chance of making it to market without failing one or more regulatory requirements,” said VP of Global Strategy for Bausch & Lomb Michael O’Rourke.

To survive the regulatory gauntlet, doctors and industry are being forced to make hard choices early in the process about which projects they will pursue. Nevertheless, the rewards can be significant. Bausch & Lomb estimates that the market for posterior eye disease solutions will eventually reach \$3 billion per year. The more than 69 million people served will realize significant improvements in their quality of life as a result.

Preserving and Restoring Sight Through Microtechnology— What Should Researchers Pursue?

“Next to cancer, most Americans fear blindness. Our goal is to find new retinal treatments. Our subject is, of course, the human eye,...and particularly in our aging population, we have a real problem in the back of the eye.” With this straightforward preamble, Dr. Gerald Chader set the tone for an illuminating overview of the needs and opportunities that exist for preserving and restoring sight with microtechnology.

As the Chief Scientific Officer of the Foundation Fighting Blindness (FFB), a nonprofit foundation funding worldwide research of retinal diseases, Dr. Chader received the rapt attention of the audience during his keynote address. This was not surprising, since FFB interacts closely with Congress to influence funding for the National Eye Institute, the main source of federal funding relied on so heavily by most of the doctors in attendance.

Dr. Chader is a 26-year veteran of the National Eye Institute, who served as Chief of its Laboratory of Retinal Cell and Molecular Biology and trained over 40 postdoctoral fellows. He has won several research awards and authored more than 300 scientific publications. He recently finished a term as editor of *Investigative Ophthalmology and Visual Science* and is co-editor of the review series *Progress in Retinal and Eye Research*.

In his keynote address, Dr. Chader made a strong case for emphasizing research on new solutions for diabetic retinopathy, glaucoma, age-related macular degeneration (AMD) and retinitis pigmentosa (RP). Because of the rapid increase in patient populations and the inadequacy of current treatments, degenerative diseases of the retina-vitreous-choroid complex (posterior segment) should be the major focus of future studies and funding, he stated.

“Fifty-five percent of all major eye diseases occur in the back of the eye. Yet in 2001, less than 5% of ophthalmic pharmaceutical sales came from drugs designed to treat such diseases,” Dr. Chader said.

The impact of posterior segment disorders is profound. Age-related macular degeneration is the leading cause of blindness for people 55 or older in industrialized countries. It is estimated to affect more than 15 million people in the U.S. and a similar number in Europe and elsewhere. Retinitis pigmentosa and juvenile macular degeneration affect more than 200,000 people in the US and a similar number elsewhere, often striking early in life and leaving victims visually impaired for the rest of their lives. No effective treatments now exist for RP and its allied diseases or for the more serious dry form of AMD.

Any advances that microtechnology can facilitate for age-related posterior segment disorders will have a dramatic impact on the quality of life of older people. The percentage of the US population over age 55, and particularly over age 85, is predicted to grow exponentially over the next 45 years. As a result, an epidemic of AMD is predicted in the next 25 years as 76 million baby boomers approach age 55.

The cost savings involved in delivering new treatments for the blind is also dramatic. If only 20,000 people are helped, the government will save an estimated \$4 billion over a 20-year period. In human terms, of course, there is no adequate way to account for the value of enabling sight-impaired senior citizens to maintain their independence and dignity. Nor can a price tag be placed on restoring sight to blind children so they can live more normal and productive lives.

Dr. Chader went on to discuss the most promising research now underway to help treat diabetic retinopathy, glaucoma, AMD and RP. He placed special emphasis on the need to expedite development of the retinal implant, a project spearheaded by the Doheny Retina Institute.

Eye surgery offers major opportunities for treating posterior segment diseases through gene therapy, pharmaceutical therapy and transplantation. Dr. Chader believes that novel methods of intraocular and transscleral delivery of antineovascular agents will help treat wet AMD. Transplantation of photoreceptor cells has shown progress in animal models. His excitement peaked, however, when he discussed the potential of retinal implant technology.

“The chip may be the best overall solution for sight restoration in retinal degenerations. This is especially true for cases in which the disease has advanced to a point where more conventional therapies are not applicable.... The success of the limited 16-pixel electrode retinal implant points to the ability of the brain to receive, synthesize and make sense out of even relatively crude inputs.... If it reaches its potential, chip technology could supplant many of the orthodox treatments now in the testing stage.”

Dr. Chader also emphasized the need for researching better drug delivery systems. “Our main problem is that the eye is small and fairly impenetrable. It is even more difficult to get drugs to target the retina. Our success in solving this problem will impact our success in almost every other area of treatment. One of the most promising areas of research addressing this unmet need is encapsulated cell technology (ECT). This should be the first technique to apply microtechnology to the problem of retinal degenerative disease.”

For drug delivery with ECT, a capsule the size of a pencil tip is inserted into the back of the eye. The device is well tolerated by the eye over many weeks as it slowly secretes a controlled and continuous stream of protein pharmaceuticals to protect photoreceptor cells.

In conclusion, Dr. Chader said, “The future of ocular microtechnology looks bright. It now looks very possible that we may eventually help the seriously impaired AMD patient see a spouse or a grandchild—even enable him or her to do a *New York Times* crossword puzzle. In the final analysis, the cost for new microtechnological development is and will continue to be substantial—but who can put a price tag on restoring a person’s sight?”

Advances in Vitreoretinal Solutions

Just how far has microtechnology advanced the practice of ophthalmology? To the point that many treatments for the back of the eye may soon become outpatient procedures, commonly performed in the ophthalmologist's office rather than the operating room.

Suffering from complications of age-related macular degeneration? Need medication delivered directly to the disease in the back of the eye? Although more complicated procedures will continue to be performed in the operating room for the foreseeable future, many simpler procedures will soon require only a mild anesthetic, the latest minimally invasive tools, and the calm hand of an experienced doctor.

Vitreoretinal Surgery

While doctors have learned that vitreous manipulations should be limited to avoid complications, the minimally-invasive TSV25 surgical system makes many procedures, including vitrectomies, a breeze compared to procedures of the past that commonly employed sutured incisions. Dr. Eugene de Juan, Jr. offered a detailed demonstration and explanation of the advantages of the TSV25. "With only 35 minutes required from open to close for a vitrectomy, there's no reason why operations cannot be performed in a doctor's office. If your schedule for the day is already full, you could even add in a procedure during your lunch hour," he said.

In challenging surgeries involving the shallow anterior segment of the eye, such as cataract removal, partial vitrectomy to decompress the eye has proven very helpful. Dr. Rosa Braga-Mele of the University of Toronto presented just such a case, demonstrating the effectiveness of the TSV25 in helping the surgeon work in tight spaces.

Anterior segment surgery in the still smaller eyes of pediatric patients can prove particularly challenging. Dr. Jonathan Song of Doheny/USC demonstrated a simple method for operating on young children with cataracts. Cataracts can cause a condition called amblyopia, which prevents the brain from forming clear images from the affected eye. To avoid the resulting negative impact on vision development, this condition should be corrected early. Dr. Song recommends using the TSV25 to perform a primary capsulotomy, with intra-ocular lens placement during pediatric cataract extraction.

Dr. Khaled Tawansy of Doheny/USC demonstrated the advantages of using the TSV25 in the even smaller eyes of neonatal patients suffering from retinopathy of prematurity (ROP). Lens-sparing vitrectomy is becoming increasingly popular in the management of dry retinal detachment in well-ablated eyes of such patients. He observed that the small 25-gauge instruments of the TSV25 provide distinct advantages in treating retinal detachment, facilitating lens-sparing vitrectomy in some eyes that would otherwise require lens removal.

In the definitive study of the advantages of minimally-invasive surgery, Dr. Lawrence Chong of Doheny/USC presented the outcomes of 130 consecutive surgeries using the TSV25 on eyes that had never before experienced vitrectomy. He found that 25-gauge vitrectomy hastens postoperative recovery by decreasing surgical time and minimizing post-operative astigmatism and inflammation.

Ocular Drug Delivery

Better methods for drug delivery could improve the majority of posterior segment treatments now under study. Localized and controlled drug delivery to targeted areas of the eye is more effective than pills or eye drops that send drugs through many body tissues and significantly dilute their benefits. On the second day of the symposium, several speakers presented innovative methods of drug delivery designed to improve the accuracy and efficiency of such treatments by the least invasive means possible.

Dr. Chong presented a new non-biodegradable, sustained drug delivery insert called Retisert™. It releases controlled amounts of fluocinolone acetonide over a period of up to three years to help manage posterior eye disease. The system, which is well-tolerated by the eye, minimizes the toxic side effects common with large systemic doses of the drug. Additionally, this system demonstrates statistically significant benefits in the treatment of posterior uveitis and diabetic macular edema. Pilot studies of its effectiveness in treating uveitis and classic and occult AMD are underway.

A bioerodable implant that releases sustained amounts of dexamethasone to the back of the eye to treat macular edema has been devised by Posurdex. Ninety days after implantation, visual acuity in patients was improved by two lines or more, and statistically significant decreases in both retinal thickness and fluorescein leakage were also measured.

“The significant improvement in vision demonstrated by Posurdex is very encouraging,” said Dr. Mark Blumenkranz, Professor and Chairman of the Department of Ophthalmology, Stanford University School of Medicine. “When considering that this study enrolled patients with only the most serious, persistent cases of macular edema, these results appear even more compelling.”

Dr. Signe Varner of Doheny/USC presented a study that tested the feasibility of a helical (corkscrew-shaped) drug-delivery implant for the eye. In vitro data indicated this device can deliver triamcinolone acetonide over a period of one year. Implantation in rabbit eyes was quick and simple, and long-term follow-up revealed excellent biocompatibility without surgical complications.

For site-specific delivery of low doses of protein drugs over a period of up to one year, Dr. Weng Tao of Neurotech USA presented the application of ECT. Ciliary neurotrophic factor (CNTF), a neuroprotective gene, was delivered consistently and continuously by the device directly into the vitreous of dogs for either seven weeks or 14 weeks. The device was well tolerated and proved its ability to significantly protect photoreceptors. Tests are planned to evaluate the effectiveness of ECT in treating RP, AMD and glaucoma.

It has already been proven that drugs can diffuse through the sclera, the tough, white, outer tissue of the eye that serves as the eye's protective coat. Dr. Timothy Olsen of the University of Minnesota presented the advantages of trans-scleral drug diffusion in treating chronic, subacute posterior segment disease. It offers a safe, non-invasive means of delivering drugs, although diffusion is limited and decreases with the increased molecular size of the drug being administered.

Dr. Jennifer Lim of Doheny/USC presented clinical experience with the subretinal injection of triamcinolone to treat choroidal neovascularization (CNV) in patients with AMD. The studies showed the treatment may be useful for occult subfoveal CNV, but further research of this mode of drug delivery is necessary.

For pinpoint accuracy in pharmaceutical treatment of the back of the eye, subretinal sustained release could be the “perfect” drug delivery system, according to Dr. Eugene de Juan, Jr. Polymeric matrix drug-loaded filaments offer one such system that could ultimately bypass the side effects and diffusional limits of intravitreal delivery. Based upon initial investigations in rabbits, this approach appears to be well tolerated by the retina.

“I believe that subretinal sustained release represents ‘the future’ of drug delivery systems aimed at treating posterior segment diseases,” said Dr. de Juan. “It scores a direct hit to the target with a potent drug dosage, it is suitable for large molecules, and it offers greater safety through decreased drug exposure to anterior structures.”

How No Eye Has Seen Before: Progress With the Retinal Prosthesis

After more than fifty years of blindness, Harold Churchey recognized two lines of light at the end of a tunnel of darkness he had lived with for most of his life. "I can see a line going up and down, and I see a line going across," he told Doheny researchers as he scanned a large white L placed against a black background. For the benefit of the attendees at Doheny's symposium, Dr. Mark Humayun replayed many of the historic recordings that chronicle the development of the retinal prosthesis at the Doheny Retina Institute.

"He couldn't tell it was the letter L," Dr. Humayun noted when describing the videotaped scene. "We were sitting on the edge of our chairs, waiting for him to say it was the letter L, but he couldn't figure out the image.... At that moment, we realized that for the device to be of any use, people's brains had to be retrained." So that's exactly what they did. As part of the study, the Doheny team trained the subjects to recognize common objects.

Mr. Churchey, who in February 2002 became the first person in the world to test the device, continues to use the system as part of an ongoing clinical trial. A second patient received the implant in July of the same year, and a third patient received a more refined version in March 2003. Although the device is still rudimentary, patients have been able to "see" large shapes, movement, and even color.

Doheny's retinal prosthesis is a microelectronic system that includes a small camera mounted in a pair of eyeglasses, a receiver implanted behind the patient's ear, and a transformer connected via a threadlike cable to a miniature electrode-studded silicone implant affixed to the retinal lining. Electronic signals carried to the brain by the device are interpreted—normally—as sight.

To further test the system, the Doheny Retina Institute has just obtained FDA approval to allow subjects to take the entire system home for prolonged use. Two questions need to be answered: How much can patients improve their artificial vision after continued use of the prosthesis? What adjustments in design will need to be made to improve it and enable everyday usage?

Dr. James Weiland is Director of the Intraocular Retinal Prosthesis Laboratory at the Doheny Retina Institute and an Assistant Professor of Ophthalmology at the Keck School of Medicine of USC. He said, "The next step is to enhance the vision of our patients to the point that it significantly improves how they can function in their daily lives. We are confident that if we continue at our current rate of progress, patients will learn to recognize a wide variety of objects and interact much better with their surroundings and other people. In fact, I am 99 percent certain that we will eventually create a device that will enable someone totally blind to recognize a human face."

Doctors at the symposium representing Osaka University and Stanford University presented their own retinal chip projects. In July of 2001, Japan began its artificial vision project. The goal was to enable previously blind subjects to count the fingers on a hand. Dr. Yasuo Tano acknowledged that Japan's project is 15 years behind the US, but he underscored the advantages of his country's less invasive, transretinal intrascleral chip design. Time will tell the success of this approach.

Dr. Mark Blumenkranz described retinal chip research at Stanford University that seeks to further blur the line between man and machine. Researchers there have discovered a way to get existing photoreceptor cells to grow toward the retinal chip, thereby shrinking the space between the electrodes and the cells they need to talk to. This is significant since the closer the chip is to the photoreceptor cells, the more efficiently it can communicate images to them.

The audience was visibly impressed by the studies now in progress to develop the world's first artificial vision systems. Thanks to advances in microtechnology, we are close to the time when many blind people who currently have no other treatment options for diseases such as macular degeneration and retinitis pigmentosa will have a chance to regain working eyesight.

Symposium Faculty

We are grateful to the following faculty for their participation in the symposium.

Mark Blumenkranz, M.D.

Dr. Blumenkranz is Chair of the Department of Ophthalmology at Stanford University. He is a graduate of Brown University, where he completed his undergraduate studies, a Master of Medical Studies in biochemical pharmacology, and his M.D. He served a residency in ophthalmology at Stanford University and a fellowship in vitreoretinal diseases at the Bascom Palmer Eye Institute, where he subsequently joined the faculty. Dr. Blumenkranz founded the Vitreoretinal Fellowship Programs at the Kresge Eye Institute and William Beaumont Hospital, where he was also Director of Vitreoretinal Surgery prior to returning to Stanford University. His areas of expertise include the medical and surgical treatment of complex forms of retinal detachment and of macular diseases, including diabetic retinopathy, AMD and vitreomacular tractional syndromes.

Rosa Braga-Mele, M.D., M.Ed., FRCSC

Dr. Rosa Braga-Mele is Assistant Professor, Department of Ophthalmology, Faculty of Medicine at the University of Toronto, Canada. She is also Director of the Cataract Unit and Surgical Teaching at Mount Sinai Hospital, Toronto, and sits on the Faculty of Medicine's Education Council for undergraduate and postgraduate training. A cataract specialist, Dr. Braga-Mele speaks frequently at national and international conferences on surgical techniques and innovations in the area of cataract surgery and complicated cataract cases.

Gerald Chader, M.D., Ph.D., hc

Dr. Gerald Chader is Chief Scientific Officer for the Foundation Fighting Blindness, a nonprofit organization that funds worldwide research on inherited retinal degenerations and interacts with Congress to promote increased funding for the National Eye Institute. Dr. Chader received his Ph.D. in biochemistry and molecular biology from the University of Louisville Medical School. Following an appointment as Andelot Fellow in the Department of Biological Chemistry at Harvard Medical School, he served as professor at the Harvard Medical School in the Howe Laboratory of the Massachusetts Eye & Ear Infirmary and tutor of biochemical sciences at Prince House, Harvard College. Dr. Chader subsequently joined the intramural staff of the National Eye Institute of the National Institutes of Health, where he served in the Senior Executive Service as Chief of the Laboratory of Retinal Cell and Molecular Biology and Director of the Intramural Research Program. He joined the Foundation Fighting Blindness in 1996. His main research interest is in retinal degenerations.

Lawrence Chong, M.D.

Dr. Lawrence Chong is Chief of Clinical Operations at the Doheny Retina Institute and Associate Professor of Ophthalmology at the Doheny Eye Institute and the Keck School of Medicine of USC. Dr. Chong earned his M.D. from Harvard University. He completed his residency at Doheny/USC and a retina-vitreous fellowship at Duke University Eye Center. He returned to Doheny to serve as Chief Resident before joining the faculty at the Institute. Dr. Chong's research interests include AIDs retinopathy, macular degeneration, retinal pigment epithelial selective lasers and dye-enhanced laser treatment of ocular tumors. His clinical interests include retinal detachment, diabetic retinopathy and age-related macular degeneration.

Eugene de Juan, Jr., M.D.

Dr. Eugene de Juan, Jr., is a co-founder and CEO of the Doheny Retina Institute and Professor of Ophthalmology at Doheny Eye Institute and the Keck School of Medicine of USC. Dr. de Juan served as a member of the medical staff of the Duke University Eye Center, holding joint teaching appointments with the Department of Ophthalmology and Department of Cell Biology. He subsequently joined the faculty of the Wilmer Ophthalmologic Institute at Johns Hopkins University School of Medicine, where he was the Joseph E. Green Professor of Ophthalmology. He also served as a co-director of Vitreoretinal Service and Director of the Microsurgery Advanced Design Laboratory (MADLAB). A pioneer of macular translocation surgery, Dr. de Juan also designs and develops microsurgical instruments. Dr. de Juan completed his medical degree and internship training at the University of South Alabama College of Medicine. He served an internship at the University of South Alabama Medical Center followed by a residency at the Wilmer Ophthalmologic Institute in Baltimore, MD, and a fellowship in vitreoretinal surgery at Duke University.

Robert Greenberg, M.D., Ph.D.

Dr. Robert Greenberg is President and CEO of Second Sight, LLC. He holds an adjunct faculty position at the University of California, Los Angeles, and sits on the board of directors of the Southern California Biomedical Council. Previously co-manager of the Alfred E. Mann Foundation, Dr. Greenberg has also served as a medical officer and lead reviewer for IDEs and 510(k)s at the Office of Device Evaluation in the Neurological Devices Division of the U.S. Food and Drug Administration. He holds a medical degree from the Johns Hopkins School of Medicine and a Ph.D. in biomedical engineering from the Biomedical Engineering Department of Johns Hopkins University.

Mark Humayun, M.D., Ph.D.

Dr. Mark Humayun is Director of the Biomimetic MicroElectronic Systems Center and Associate Director of Research at the Doheny Retina Institute. He holds faculty appointments at the University of Southern California in Ophthalmology, Biomedical Engineering and Cell and Neurobiology. Following completion of his medical degree at Duke University Medical School, Dr. Humayun served a residency in ophthalmology at Duke Eye Center and fellowships at the Retinovascular Center at Johns Hopkins Hospital and at the Johns Hopkins Medical Institution in vitreoretinal surgery. He completed a Ph.D. in biomedical engineering at the University of North Carolina, Chapel Hill. He served as Assistant Professor of Ophthalmology at the Johns Hopkins Wilmer Eye Institute prior to joining Doheny/USC to co-found the Doheny Retina Institute. Dr. Humayun's research focuses on microelectronic solutions for the most challenging of eye diseases, including macular degeneration, retinitis pigmentosa and diabetic retinopathy.

Jennifer I. Lim, M.D.

Dr. Jennifer Lim is Associate Professor of Ophthalmology at the Doheny Eye Institute and the Keck School of Medicine of USC. A retinal specialist, she also serves as Medical Director of the Clinical Trials Unit at the Doheny Eye Institute. Dr. Lim earned her undergraduate and medical degrees from Northwestern University. She completed her residency at the University of Illinois Eye and Ear Infirmary in Chicago and two fellowships at the Wilmer Ophthalmologic Institute at Johns Hopkins Hospital in Baltimore, MD. She was an Assistant Professor of Ophthalmology at Emory Eye Center of Emory University and a Clinical Assistant Professor at the University of California, San Francisco, prior to joining Doheny/USC. Dr. Lim's research and clinical interests encompass retinal and vitreous diseases, including age-related macular degeneration, diabetic retinopathy and retinal detachment.

Timothy W. Olsen, M.D.

Dr. Timothy Olsen is Director of Retina at the University of Minnesota, where he holds the William H. Knobloch Chair. He is also founder of the Minnesota Lions Macular Degeneration Center. Dr. Olsen attended the University of Kansas through medical school, completing an ophthalmology residency at the University of Minnesota, and a vitreoretinal fellowship at Emory University in Atlanta, GA. Dr. Olsen served on the faculty of the University of Wisconsin before joining the University of Minnesota. His research focuses on macular degeneration, including the study of proteomics and functional genomics, drug delivery systems and surgical devices.

Michael O'Rourke

Michael O'Rourke is Global Vice President of Strategy for Bausch & Lomb, with responsibility for pharmaceutical and vitreoretinal products. He served with 3M Pharmaceuticals, Howmedica and Alza before joining Chiron Vision as Marketing Director responsible for all aspects of the European surgical business. When Bausch & Lomb acquired Chiron Vision, Mr. O'Rourke was named Manager of worldwide vitreoretinal surgical and cataract products. In his present position he focuses on posterior segment strategies within pharmaceuticals and drug delivery systems.

John Saharek, MBA

John Saharek is Director of Marketing for Bausch & Lomb's cataract and vitreoretinal surgical business. He holds an MBA with a concentration in finance from the University of Hartford. Mr. Saharek served as a regional business manager with Roche Diagnostics, as Chemistry Marketing Manager for Point of Care Diagnostics, and Director of Global Strategy for Instrumentation Laboratory before joining Bausch & Lomb.

Jonathan Song, M.D.

Dr. Jonathan Song is Medical Director of the Doheny/USC Refractive Laser Medical Center and Assistant Professor of Clinical Ophthalmology at the Doheny Eye Institute and the Keck School of Medicine of USC. Dr. Song earned his M.D. from University of California, San Francisco. He completed his residency at Doheny/USC, where he served as Chief Resident. He completed fellowships in pediatric ophthalmology at Childrens Hospital Los Angeles and in cornea/refractive surgery at Doheny Eye Institute.

Yasuo Tano, M.D.

Dr. Yasuo Tano is Chairman of the Department of Ophthalmology at Osaka University Medical School and Vice President of Osaka University Hospital, Osaka, Japan. He is the immediate past president of the Japanese Ophthalmological Society and Executive Editor of the Japanese Journal of Ophthalmology. Dr. Tano is also a member of the Advisory Committee for the International Council of Ophthalmology and a charter member of the ICO Foundation. He received his M.D. from Osaka University Medical School. After completing his residency in Japan, he served vitreoretinal research fellowships at Bascom Palmer Eye Institute, Miami, FL, and at Duke Eye Center, Durham, NC. He has authored and co-authored more than 500 English and Japanese publications in various fields of ophthalmology and has written more than 50 books and

chapters on related topics. Among the first to perform vitrectomy in Japan, Dr. Tano is a pioneer in non-vitrectomised macular surgery and a leading surgeon in macular translocation. He has invented several vitreoretinal medical instruments.

Weng Tao, M.D., Ph.D.

Dr. Weng Tao is Vice President, Research and Development in the Pre-Clinical Department at Neurotech, USA. Dr. Tao received her M.D. from the Capital Institute of Medicine in Beijing, China, and her Ph.D. in cell physiology and biophysics from the University of Connecticut Health Center at Farmington, CN. She completed post-doctoral training at Yale Medical School. Dr. Tao's research presently focuses on development of encapsulated cell technology (ECT). Before joining Neurotech USA, Dr. Tao was Director of Cell Research and Team Leader responsible for the development of ECT at CytoTherapeutics, Inc. She held managerial and research positions in the area of immunological diseases, including inflammation, infectious diseases and cancer, at American Cyanimid, M6 Pharmaceuticals and Regeneron.

Khaled Tawansy, M.D.

Dr. Khaled Tawansy is Clinical Director of the Pediatric Vitreoretinal and Uveitis Service at Childrens Hospital Los Angeles, Research Director of the van Wyck-Dalany Children's Retina Center, and Associate Professor of Ophthalmology at the Doheny Eye Institute and the Keck School of Medicine of USC. Dr. Tawansy completed a Bachelor of Biomedical Engineering at Johns Hopkins University and his M.D. at the University of Michigan. He served residencies in internal medicine at the University of California, Irvine, and in ophthalmology at Henry Ford Hospital before completing fellowships in vitreoretinal surgery at University of British Columbia and in medical retina at Vanderbilt University. His interest in childhood diseases led to additional fellowship training in pediatric retina and uveitis at the Massachusetts Eye & Ear Infirmary and the Schepens Retina Foundation at Harvard University and in pediatric vitreoretinal surgery at William Beaumont Hospital. Dr. Tawansy's research and clinical efforts are devoted to the

unique problems of retinal diseases in children, including retinopathy of prematurity and allied retinal vascular diseases, hereditary vitreoretinopathies, retinal detachment, penetrating trauma and posterior uveitis.

Signe Varner, Ph.D.

Dr. Signe Varner is Director of Ocular Drug Delivery for the Doheny Retina Institute and Assistant Professor of Research Ophthalmology at the Doheny Eye Institute and Keck School of Medicine of USC. Dr. Varner received her Ph.D. in bioengineering from Georgia Institute of Technology in Athens, GA. She studied cellular physiology at Woods Hole Marine Biological Laboratory, participated in the Summer Institute in Health Policy and Management at Johns Hopkins University School of Public Health, and completed a post-doctoral fellowship at the Microsurgery Advanced Design Laboratory (MADLAB) at the Wilmer Eye Institute, Johns Hopkins University. Dr. Varner has served as a Senior Scientist at AtheroGenics, Inc., and as a graduate research assistant, Division of Cardiology, at Emory University School of Medicine and Cellular Biomechanics Laboratory, Georgia Institute of Technology. She is currently completing studies in the Master of Regulatory Science Program at the University of Southern California School of Pharmacy.

James Weiland, Ph.D.

Dr. James Weiland is Director of the Intraocular Retinal Prosthesis Laboratory at the Doheny Retina Institute, Assistant Professor of Ophthalmology at the Doheny Eye Institute and the Keck School of Medicine of USC and Assistant Professor of Biomedical Engineering at USC. Dr. Weiland served with Pratt & Whitney Aircraft Engines before earning an M.S. in electrical engineering and an M.S. and Ph.D in biomedical engineering from the University of Michigan. He joined the Wilmer Ophthalmologic Institute at Johns Hopkins University as a postdoctoral fellow before being appointed Assistant Professor of Ophthalmology at that institution. He joined the Doheny Eye Institute in 2001 as part of a larger group of faculty that collectively founded the Doheny Retina Institute. Dr. Weiland's research interests include retinal prostheses, neural prostheses, electrode technology, visual evoked responses and implantable electrical systems.

The Doheny Eye Institute

The Doheny Eye Institute was established in 1947 by Carrie Estelle Doheny, wife of Los Angeles oilman Edward L. Doheny. The Institute is affiliated with the Keck School of Medicine of the University of Southern California.

The Doheny Eye Institute has been dedicated to the “restoration, preservation, and improvement of human eyesight,” since it was established in two small rooms at St. Vincent Hospital in Los Angeles. Today, Doheny at USC has emerged as a world-renowned center for vision research, education, and patient care.

The Doheny Retina Institute

The Doheny Retina Institute is committed to relieving the suffering of patients with severe retinal diseases. The Institute fulfills its mission through an unprecedented combination of clinical research, patient care and telemedicine.

Breakthroughs are achieved through an entrepreneurial environment that encourages rapid development of effective and safe new products, treatments and procedures that benefit from early and ongoing focus on patient care and from collaboration with industry to ensure that products reach the patients they are intended to serve.

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