

DISCOVERY

The Discovery Fund for Eye Research

FROM THE MEDICAL DIRECTOR

Dear Friends,



I thank you in advance for your ongoing support, which is sorely needed! As we move into the year 2005, our research programs have picked up considerable momentum. With your help, we can keep that momentum going and fully accomplish the goals of our research, delivering effective new treatments to those who currently have little hope.

We are very excited to describe here on page one the work being done by Drs. Ron Kurtz and Tibor Juhasz, two of the world's leading authorities on the use of the femtosecond laser. Never before has the term "cutting edge" been more appropriate to describe studies in the areas of corneal transplantation and glaucoma research. In the second article, Dr. Henry Klassen's work in retinal stem cell transplantation also describes an avant garde approach to treatment which could potentially help thousands of people both blind and visually impaired.

Our Macular Degeneration Partnership and National Keratoconus Foundation continue to enlist the support of generous individuals and organizations. This time, such support has enabled the creation of some very practical tools and events.

Due to the innovative ideas and hard work of the scientists and other staff at UCI and The Discovery Fund, we have secured three new multi-year grants that will enable us to fund some of our best research concepts: 1) a research challenge grant from Research to Prevent Blindness (RPB) to support expansion of our current projects; 2) a grant from The Skirball Foundation to support molecular ophthalmology research and 3) an NIH grant to help us develop a topical (eye drop) vaccine to prevent eye infections like herpes.

Kind regards,

Anthony B. Nesburn

Anthony B. Nesburn, M. D.
Medical Director

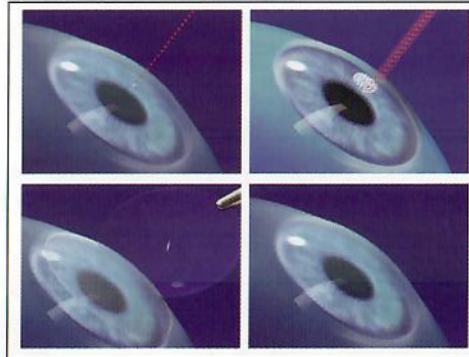
UCI RESEARCH: ULTRAFAST LASER

New Approaches for Corneal Transplant and Glaucoma Surgery

UC Irvine researchers are now working to make possible exciting new approaches to eye surgery using the ultrafast femtosecond laser. Two renowned researchers who developed the femtosecond laser technology for use in LASIK eye surgery, Drs. Ron Kurtz and Tibor Juhasz, are now leading a team whose work promises to vastly improve cornea transplant and glaucoma surgery. Kurtz is now an associate clinical professor and Juhasz is professor of ophthalmology and bioengineering at UCI.

"When I was a resident, the femtosecond laser was still in the testing phase for industrial use," said Kurtz. "As I learned more about the laser, it became clear that it could be a powerful tool for eye surgery. Now that we have successfully applied it to LASIK surgery, we plan to work with the UCI team to leverage its non-invasive precision to create other innovative techniques in ophthalmic surgery."

In addition to Kurtz and Juhasz,



The femtosecond laser cuts a flap in the cornea at the molecular level

the UCI research team includes corneal surgeons Roger Steinert, Ron Gaster, Lawrence Chao, and Ramin Pirnizar, as well as basic research faculty Cristina Kenney, Tony Nesburn, James Jester, Steven Wechsler, Don Brown and Oscar Perng. A separate team focusing on glaucoma applications includes George Baerveldt and Richard Hill.

IntraLase, Inc., the company that Drs. Kurtz and Juhasz co-founded in 1997, is also located in Irvine. Their FDA approved machine has been used for over 150,000 IntraLase LASIK surgeries since their product was introduced in 2002. In LASIK

surgery, the femtosecond laser is used in place of a microkeratome blade to make a flap in the cornea. It creates an incision using extremely rapid, highly focused pulses of laser energy. In fact, the laser spots are only 3 microns (about half the thickness of a human cell) and are created in femtoseconds or about one quadrillionth of a second.

Many patients and eye doctors now prefer the IntraLase option because of its potential for improved precision and reduced complications. Although the equipment does increase costs for ophthalmologists and their patients, surgeons expect the laser will eventually become the standard of care.

Femtosecond laser technology provided the basis of femtochemistry research that won the 1999 Nobel Prize in Chemistry. The use of the laser in ophthalmology was developed by a team of physicists, biomedical engineers and ophthalmologists at the University of Michigan, Center for Ultrafast Optical Sciences, where both Kurtz and Juhasz worked previously.

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RETINAL CELL TRANSPLANTATION

Very few treatments have been discovered that can restore vision after the retina has been damaged. To the surprise of many researchers, however, it has been proven that transplanted retinal tissue can survive and develop to replace damaged photoreceptors – the key eye cells responsible for vision. That's why researchers at UC Irvine are participating in an effort to find a successful method for retinal transplantation.

Dr. Henry Klassen, who holds a researcher appointment in the department of Ophthalmology at UCI, is one of the lead scientists searching for the keys to successful retinal cell transplantation. Over the past five years, he has played a key role in building a multi-disciplinary team ranging from molecular immunologists and neurobiologists to ophthalmic surgeons skilled in microsurgery. If successful, the team's studies will lead directly to clinical trials in human subjects applying treatments designed to overcome blinding retinal diseases such as retinitis pigmentosa (RP).

"Retinal stem cells offer great promise in helping us overcome many of the obstacles to successful transplantation," says Klassen. "Studies have shown that stem or progenitor cells have the capacity to integrate into the



Henry Klassen, M.D., Ph.D., stem cell expert

diseased retina and differentiate into photoreceptors. We have also found that stem cells from the retina and the brain generally survive transplantation from one species or strain to another without rejection. The capacity of these cells to integrate themselves into the retina, combined with a high degree of immune tolerance – particularly in the eye, indicates that we have favorable conditions for successful retinal transplantation."

One of the greatest challenges researchers face in achieving successful retinal transplantation is the development of a large useable supply of retinal progenitor cells. Perhaps the best cells for transplant

are stem cells from fetal tissue, but controversy over the use of fetal tissue has forced scientists to look elsewhere. Recently, researchers have been able to identify non-fetal stem cells right in the retina of adults and neonates, thereby offering a solution that could avoid the politics of using fetal tissue. Scientists reason that when research moves to clinical trials involving humans, retinal stem cells may be able to be collected from these donors as a possible source of unlimited tissue samples.

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DISCOVERY



A patient education program, dedicated to providing accurate, timely and unbiased information about age-related macular degeneration (AMD) to patients and families. Created by the non-profit Discovery Fund for Eye Research in 1998, the Macular Degeneration Partnership is a coalition of patients, families, physicians, low vision specialists and leaders in the field of aging.

AMD Toolkit Now Available in California

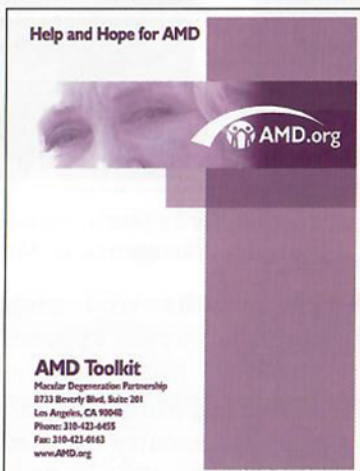
It's hard enough for people to hear they have age-related macular degeneration (AMD) and will lose their central vision. What's worse is not getting the message quickly that much can be done in daily life to improve the chances for vision rehabilitation. To get this vital information out to thousands of patients, the Macular Degeneration Partnership (MDP) has organized the development of a new AMD Toolkit.

"I wish I had learned about macular degeneration sooner!" is one common exclamation by people who first contact the MDP. With the AMD Toolkit, they will have that wish granted. The Toolkit contains a wealth of information, tools and resources, packed into a sturdy vinyl envelope. It is being distributed to eye doctors throughout California, who will then hand them out to AMD patients.

"Give them something besides the bad news," is what the MDP is telling physicians as part of this

awareness program. And the response among ophthalmologists has been universally positive. One doctor commented, "This is exactly what I need for my patients. I would love to spend an hour with each one and with their families, but I just don't have the time. The AMD Toolkit will be a tremendous help."

The AMD Toolkit includes information about the disease, vision rehabilitation, nutrition and supplements, protecting the eyes, and available resources. It's packed with educational brochures from local and national agencies plus tips about assistive devices, ultraviolet sunlight protection, healthy foods and vitamins. A magnetic Amsler Grid to attach to the refrigerator to make daily vision testing easier, coupons and samples



complete the package. Now, patients will be able to learn the facts, develop important skills and find useful resources - early!

This project was funded by grants to The Discovery Fund from the UniHealth Foundation, AMD Alliance International and Alcon Labs. If you would like to receive the Toolkit, just visit the MDP website at www.AMD.org or call the toll-free number at 888-430-9898, request the AMD Toolkit and mention this newsletter.

New Vision Pavilion Attracts AARP Conventioners

The annual AARP convention has always been a wonderful chance for the MDP team to meet thousands of people who are at risk for macular degeneration. AARP members from around the country talked with us at this year's three day event, called Life @ 50+.

After several years of success with the AARP, the MDP decided to form a coalition of vision organizations to provide an even more comprehensive resource to retired people. As a result, this year's convention featured a brand new Vision Pavilion packed with information, tools and fun.

To make the Pavilion possible, the Macular Degeneration Partnership joined with the American Optometric Association, assistive

device companies, manufacturers of sunglasses and lighting companies, among others. MDP partner Ready Pac Produce provided delicious sautéed spinach (high in antioxidants) to satisfy the appetites of visitors, while Kemin Foods distributed vitamins samples.

A raffle was held that proved very popular, giving away magnifiers, sunglasses, task lighting and other goodies. Attendees received over 5,000 information packets from the MDP and were directed to the National Eye Institute's EyeSite exhibit for further assistance (MDP hosted EyeSite in Los Angeles two years ago). On the adjacent stage, lectures on vision, nutrition and prevention were presented. Look for the MDP at next year's event too, which will be held in New Orleans, September 29 - October 1, 2005. ■

Free AMD Educational Seminar & Vision Fair

November 30, 2004
Beckman Conference Center
University of California, Irvine
9 a.m. - noon

Visit the Vision Fair from 9 to 10 a.m. to try out assistive devices and find helpful resources. From 10 to noon, hear experts speak and answer your questions about AMD research and new treatments, vision rehabilitation and coping with vision loss. Reservations required - 714-261-6888

GOING ONCE, GOING TWICE...SOLD!

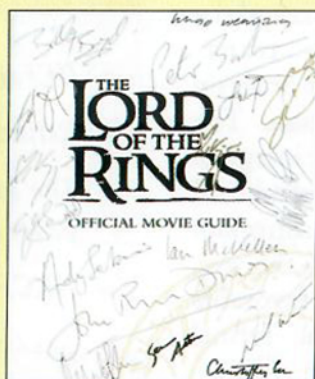
This year's *Seeing the Stars* eBay Internet auction was a resounding success, raising nearly \$29,000. Excitement ran high as bidders from all over the world went into heated "cyber-battle" over the 207 donations of celebrity eyewear and memorabilia. The highest bid of **\$4,174.96** went for the cast-autographed *The Lord of the Rings* official movie guide, donated by its phenomenal director, Peter Jackson. There were many other wonderful and fun items on the block from supporting luminaries such as Cher, Sean Astin, Sir Ian McKellen, Richard Chamberlain, cast members

of the Survivor TV series, Melissa Gilbert, Laurence Fishburne, the family of Gene Roddenberry, Robin Williams, Kate Winslet and Jackie Chan. Mr. Chan also served as an active member of our *Seeing the Stars* auction committee.

The Discovery Fund for Eye Research would like to take this opportunity to give special thanks to Linda and Jerry Bruckheimer for their invaluable contributions as chairpersons. We dedicate our success to them and all of the wonderful celebrities who were involved. We hope to see you in 2005 for our next *Seeing the Stars* auction! ■



Gene Roddenberry



Autographed "The Lord of the Rings" Official Movie Guide



Richard Chamberlain

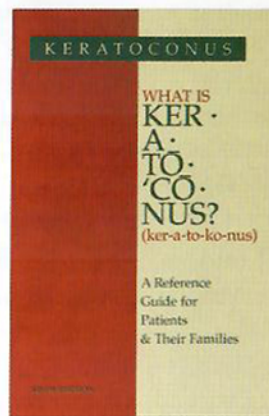
NKCF

NATIONAL KERATOCONUS FOUNDATION

5th Edition of *What is Keratoconus?* Now Available

Polymer Technology, a Bausch & Lomb company, has once again provided support to the National Keratoconus Foundation (NKCF) by underwriting the printing costs of 10,000 copies of the booklet, *What is Keratoconus? A Reference Guide for Patients & Their Families*, 5th Edition. The funding allows the NKCF to continue to offer the newest edition of this valuable educational booklet free to KC patients worldwide.

This booklet about keratoconus is especially helpful to patients who have recently been diagnosed, giving them and their families a basic understanding of the disease. It contains an overview of signs, symptoms and treatment options for keratoconus. The new edition of the booklet has been updated with the latest information about KC, and also includes information on the NKCF resources available for patients and their families. NKCF's programs are underwritten in part by grants from the Discovery Fund for EyeResearch.



KC Patient Education Seminars

Presenting new developments in treating Keratoconus is one of the many ways that the NKCF helps those with KC. On October 2, 2004, an NKCF sponsored Patient Education Seminar was held in Teaneck, New Jersey, with several of the area's leading experts in the field providing their insights on KC.

Kristen Fry, O.D., M.S., presented an "Introduction to Keratoconus." David Chu, M.D., discussed the latest answers to the question "What Causes Keratoconus?" Dr. Donald Hersh presented "Contact Lenses for Keratoconus," while William Constad, M.D., provided in-depth information on "Corneal Transplant Surgery." Finally, Dr. Peter Hersh updated the seminar attendees on "Lasik, PRK, Intacs and CK for Keratoconus."

The next Patient Education seminar sponsored by the NKCF is scheduled for early 2005 in Orange County, California. ■

Translational Research Update

EXPANDING EYE SURGERY OPTIONS

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Ronald M. Kurtz, M.D., UCI associate clinical professor

Corneal Transplants Simplified

Corneal transplants currently restore vision for some 40,000 individuals each year. The UCI team will be investigating the femtosecond laser for a type of cornea transplant that surgeons consider to be extremely difficult. In this procedure, the laser is used to replace the back (posterior) part of the cornea in a procedure known as posterior lamellar keratoplasty (PLK).

"In the standard corneal transplant, surgeons remove the entire cornea in 'cookie cutter' fashion and replace it with a similarly shaped cornea from a donor. The problem with this method is obvious," says Dr. Roger Steinert, UCI professor of ophthalmology and bioengineering. "Why replace the full-thickness cornea in cases where the disease affects just the innermost layer?"

In 1997, an ophthalmologist from the Netherlands devised a method for PLK surgery using traditional

instruments for replacing just the back portion of the cornea. Despite several advantages, the procedure was complex and few cornea surgeons opted to perform it. Dr. Steinert believes the femtosecond laser can offer a simpler and safer means of performing PLK surgery. With it, the surgeon will make side cuts of a remarkably precise depth (about 300 microns) and split the cornea's thickness. The surgeon will then be able to pull the posterior portion of the cornea through the side slit and insert the new donor tissue.

One of the main advantages of PLK surgery is that the laser process leaves the top layer of the cornea intact. Sutures are not needed because the top layer holds the new posterior layer in place. Dr. Steinert says, "I'm very impressed by the abilities of this laser. Achieving this level of precision with a blade is practically impossible."

Another benefit of PLK is the resulting strength of the cornea after surgery. "If you are hit in the eye, the graft-junction is more likely to hold," says Dr. Steinert, who has treated a number of patients who ended up with damaged corneas even years after full-thickness transplants. Dr. Steinert also expects that vision for patients may improve faster after laser surgery, as compared to 6-12 months for full-

thickness cornea transplants.

Advantages in Glaucoma Surgery

The femtosecond laser is also being studied as a tool for treating glaucoma by creating channels beneath the eye's surface to allow fluid inside the eye to drain more easily. This lowers the pressure inside the eye, which is the objective in treating glaucoma with either eye drops or surgery.

After conventional glaucoma surgery to create a new drainage site, the body's normal healing response quite often results in scarring and closure of the drainage channel. In contrast, the very short and powerful energy of the femtosecond laser may allow the surgeon to make channels beneath the surface of the eye while leaving overlying tissues intact. This approach aims to avoid the healing process associated with conventional glaucoma surgery, thus preserving the flow of the eye's fluid through the newly created channel.

With the femtosecond laser, UCI's team of clinicians, bioengineers and basic scientists hopes to increase the number of surgical treatment options available to sufferers of eye disease. This work at UC Irvine is supported by two grants awarded to Dr. Juhász from the National Eye Institute. ■

Foresight to give Eyesight

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RETINAL CELL TRANSPLANTATION

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However, retinal cells have proven to be among the most difficult central nervous system (CNS) progenitor cells to amplify or grow in larger quantities for scientific usage. Therefore, an effective method of obtaining and banking larger number of cells must be devised in order to have an adequate supply on-hand for research. Dr. Klassen's team will work on this and other important challenges on the road ahead.

"In addition to building a sufficient supply of progenitor cells, we need to devise a method of locating and identifying them following transplantation to the retina," says Klassen. "We also need to understand the mechanisms controlling their development into mature retinal cells. This will allow us to create a sufficient supply and ensure that they stop dividing and generate functional photoreceptors following transplantation."

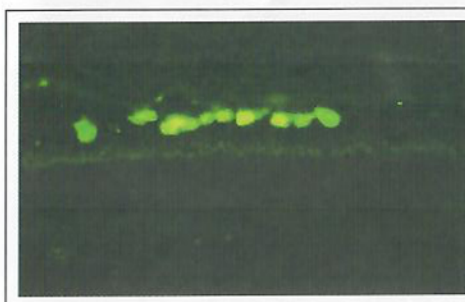
Dr. Klassen is a full-time neural stem cell biologist who is also trained as an ophthalmologist with specialization in retinal degenerative disease. He received his B.A. in neurobiology from UC Berkeley, an M.S. from UC Santa Cruz, and a Ph.D. in neurobiology from the University of Pittsburgh. After a medical internship at The Cambridge Hospital (affiliate of Harvard Medical School), and a residency in ophthalmology at Yale

Eye Center, he completed a fellowship at Moorfields Eye Hospital in London before becoming the director of stem cell research at Children's Hospital of Orange County/UC Irvine. He continues to work at Children's Hospital and maintains an active collaboration with Dr. Michael Young at the Harvard Medical School. Dr. Young's renowned work also focuses on repair of the diseased retina and the immunobiology and cell biology of CNS stem cells.

Klassen has won many competitive grants for his research, including a Career Development Award from the Foundation Fighting Blindness and an NRSA Fellowship from the National Eye Institute. His research findings have been widely published in such journals as the Proceedings of the National Academy of Sciences, the Journal of Neuroscience, and Molecular and Cellular Neuroscience.

The transplantation team working with Dr. Klassen has moved from rodents to large animal models and hopes this translates to human subjects once an effective cell-based strategy for retinal repair is established. For the past two years, the team has been transplanting retinal progenitor cells to the eye of the pig. This has shown evidence of integration of the progenitor cells into the damaged retina and

differentiation of the grafted cells into photoreceptors.



Green retinal cells after grafting

For transplantations to be successful, photoreceptors must survive, develop, function normally and connect with the remaining retinal cells that conduct images to the brain. Doctors believe that with further study of the connections between transplant and natural tissue, they will be able to help these tissues work together as they do after common organ transplantation procedures.

"We were immensely encouraged when we discovered that retinal stem cell transplantation into animals resulted in the cells morphing into functioning photoreceptors with rod and cone markers," says Klassen. "Now we need to take this to the next level and show sustained restoration of vision in the transplanted animals."

To develop into photoreceptor cells, the retinal stem cells must be coaxed. Years of research in the field

of developmental biology is making this type of work possible. Using a complex series of stages, scientists are now able to convince undifferentiated stem cells to become a variety of mature cell types throughout the body. Among the challenges that scientists face, however, is how to get the cells to grow into photoreceptor cells, and then prevent the newly formed photoreceptor cells from dying just like the original diseased cells.

Once effective methods for retinal cell transplantation are discovered, transplantation procedures could help 20,000 people left totally blind by retinal degenerations and another 500,000 people in the US who are visually impaired due to retinal diseases.

"Our team is working in one of the most exciting fields of study in ophthalmology," Klassen commented. "With further support and research, we will soon be able to help thousands of people who have lost their eyesight to retinal disease."

"The work being done by Dr. Klassen and his team shows tremendous promise," Dr. Anthony Nesburn, vice chair for eye research at UCI, commented. "To help it reach its ultimate potential to transform lives, we continue to search for private and government support." ■

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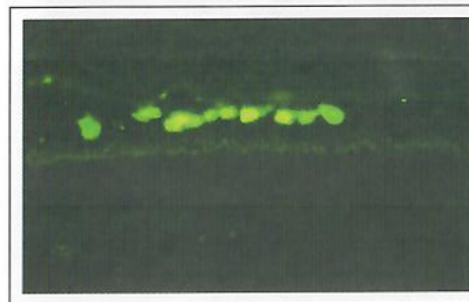
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DISCOVERY

2ND GOLF TOURNEY SCORES FOR EYE RESEARCH

There's nothing quite like a good round of golf followed by good food to reward those who work hard to help others. The Discovery Fund for Eye Research's second annual golf tournament and awards dinner gave doctors and eyecare companies a chance to enjoy just such an opportunity at an event that generated over \$25,000 for eye disease research. This year's tournament was held on August 16 at the Dove Canyon Country Club in Dove Canyon (near Irvine), California.

Among the long list of generous companies supporting the tourney were presenting sponsor Allergan, co-sponsors Alcon, Advanced Medical Optics and Visx, and fairway sponsors IntraLase, John Markley and Refractec. Over 100 golfers participated, joining in a friendly four-person scramble that made everyone look good by playing only the best ball landed by each group on each shot.

"Thank you for making this event such a great time and a terrific success for eye research," said James Salz, M.D., long-time Discovery Board member and chairman of the event. Dr. Salz helped everyone get into the true spirit of the game by bravely sporting traditional golf attire – including the knickers!

Radio funnyman Rick Dees joined Dr. Salz to support the eye research fundraiser and ended up helping their foursome win the award for "Low Gross Score." An avid golfer, Dees also scored "Closest to the Pin" in the tourney. That didn't keep Dees from taking a shot at Dr. Salz' attire, however, or from joking with the audience at the event. "I don't want to alarm anyone, but we have a message from the kitchen telling us all to 'stay away from the turkey!'" Dees kidded as he helped Salz make announcements during the feast.

The winners of "Low Net Score" and the Allergan Cup were Bill Locanto, Adam Karon and Jason Zeller. The longest drives were hit by Dan Tran and

Marty Firestone.

The highlight of the evening was the live auction by Rick Dees of two nights lodging, candlelight dinner, massage, and a picnic basket lunch for two at the beautiful Stonepine Resort in the Carmel Valley (www.stonepinecalifornia.com). Words of thanks were given to Stonepine owner Gordon Hentschel for making the special weekend available to benefit The Discovery Fund and to Jonathan Davidorf, M.D. for the winning bid. Other ideas for auction items are always welcome. Resort weekends, fine dining at local restaurants, and golf items are still needed for next year's auction. If any readers can help, please contact Donna Posner at 949-366-0234 or email her at awesmDNA@aol.com. ■



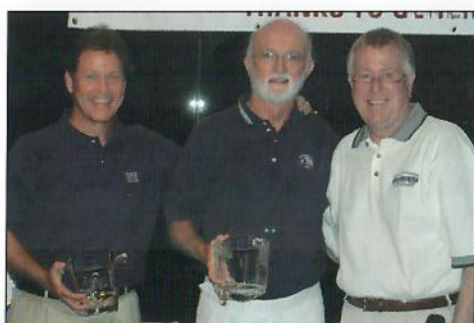
Marty Firestone was the woman with the Longest Drive



The Allergan Cup and Low Net Score went to Bill Locanto (accepted by his wife), Adam Karon and Jason Zeller



Anthony B. Nesburn, M.D. thanks the sponsors



Rick Dees and Dr. Jim Salz accept the Low Gross Score award from Tom Hebert



DISCOVERY is published two times a year to provide news and information about the non-profit Discovery Fund to donors, patients and friends.

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DON'T MISS THE FUN NEXT YEAR!

Please join us again for the 3rd Annual Golf Tournament to raise funds for the Morris S. Pynoos Eye Research Laboratories at the University of California, Irvine. For a great day of golf and friendship in support of eye research, mark your calendar for Monday, August 15, 2005, the date of our next event.



Monarch Bay Golf Course in Dana Point

This tournament will be played within view of the Pacific Ocean at Dana Point on the beautiful Monarch Bay Course. Many from the Los Angeles area are already planning on staying nearby at the luxurious St. Regis Hotel on Sunday evening to avoid the Monday am drive.

THE DISCOVERY FUND FOR EYE RESEARCH

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