



foresight

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SCHOOL OF MEDICINE
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A Partnership in Care

the patient/physician relationship

When Rockford resident Carmella Propst realized she might have glaucoma, she knew she had to find more than just a personable physician. She had to find a knowledgeable, experienced specialist she could trust to help her be able to see. She found that in UW Health ophthalmologist Todd Perkins, MD.

"I believe driving 75 miles to Madison to get the best eye care in the area is well worth it," Propst says. "I know that I may not have my vision if not for Dr. Perkins and his team."

Propst made her first trip north on the referral of a Rockford retina specialist who noticed that her eye pressure was increasing. Being a patient was nothing new to Carmella Propst – she had been in numerous clinics and hospitals during treatment of thyroid cancer and a retinal detachment. But with a diagnosis of fairly advanced glaucoma, she was initially concerned about what might lie ahead for her vision and was hesitant about starting treatment in an unfamiliar office. Those fears were quickly put to rest.



Patient Carmella Propst after glaucoma surgery.

"I have had my fair share of negative experiences at clinics, but the minute I walk in the front door of the UW Health clinic, I feel relaxed," Propst says. "Everyone from the receptionist that checks me in to the residents studying under Dr. Perkins knows how important it is to make a patient feel comfortable."

A glaucoma specialist, Dr. Perkins determined that Propst had pigmentary glaucoma. Glaucoma is a complex group of disorders in which the optic nerve in the back of the eye sustains a characteristic type of progressive damage. The major risk factor for causing the damage is the intraocular pressure. There is a gland in the front of the eye that produces a fluid (known as the aqueous humor) that provides nutrients to the cells on the back of the cornea. The aqueous humor

Continued on page 2



Grape Expectations

researching resveratrol

Could a non-toxic plant compound found in food sources such as the skins of grapes, some berries, and peanuts, ward off cancer or assist in its treatment? That is a question that Arthur Polans, PhD, a professor in the UW Department of Ophthalmology and Visual Sciences, has been investigating.

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from the chair

by Paul L. Kaufman, MD

In this issue of *foresight*, you'll learn about three significant contributions toward our missions of patient care and community service, research, and teaching. The physicians and scientist in these stories are improving the lives of individual patients and students of medicine, as well as the Wisconsin community and beyond, in their routine work, day-in and day-out.

In the patient care story, you'll meet Carmella Propst, a Rockford patient with advanced glaucoma who developed a strong partnership with UW faculty ophthalmologist Todd Perkins, MD. Together, Carmella and Dr. Perkins made decisions that helped Carmella retain her vision and cope with frightening aspects of her disease and treatment.

The research story highlights the work of department faculty scientist Arthur Polans, PhD, who is studying resveratrol, a non-toxic plant compound that could possibly ward off cancer or assist in its treatment. Dr. Polans believes resveratrol and related natural products hold great promise for the future in treating cancer more effectively, likely in combination with other cancer-fighting drugs, and with fewer side effects.

In our education story, you'll learn about the significant contributions of UW neuro-ophthalmologist Richard Appen, MD, who will retire after 34 years of service to the ophthalmology profession. Dr. Appen's steadfast commitment to patients, medical students, ophthalmology residents and fellows, as well as to his faculty colleagues, establishes an enduring legacy for this physician.

I hope you enjoy the new design elements of this issue of *foresight* which focuses on the day-in and day-out contributions of our dedicated faculty. As always, I'm interested in your comments and feedback about our publication.



A Partnership in Care

continued

is produced and then must exit the eye through outflow channels located where the iris and the cornea meet (the "angle"). If the outflow channels do not drain properly, the aqueous humor is not able to exit the eye sufficiently, causing the eye pressure to rise. The eye pressure acts as the resistance to the arterial blood supply to the optic nerve tissue, and if the eye pressure is too high, optic nerve damage results. If eyedrops that facilitate the drainage of the aqueous humor or reduce its production are not sufficient, a surgical procedure to increase the drainage of the aqueous humor may be required. Pigmentary glaucoma is the type of glaucoma in which pigment granules from the iris clog up the outflow channel and cause the eye pressure to rise.

"Although Carmella's eye pressures weren't that high compared to most people with glaucoma, they were becoming higher and higher each time she was seen at the eye clinic," Dr. Perkins comments. Unfortunately, the glaucoma eyedrop medications usually used to treat glaucoma failed to control Propst's pressure.

Dr. Perkins performed surgery to treat Propst's glaucoma in the right eye in March of 2005 and in the left eye in January of 2007. She was awake for the surgery, with surgical drapes covering most of her face and her arms held by her sides. Her history of claustrophobia caused some apprehension, and again Dr. Perkins put her fears at ease. "I followed all of Dr. Perkins' suggestions on how to prepare for the surgery, and his advice removed many of my concerns. Also, he played soothing music during the procedure and had an anesthesiologist available in case I was unable to relax," Propst explains.



Todd Perkins, MD

Since her final surgery, Propst no longer needs any glaucoma eyedrops, and aside from a slight sensitivity to light, she sees very well. "Surgery was definitely the correct option for me. I've had great results and Dr. Perkins helped me feel extremely comfortable with the entire process," she says.

Propst attributes much of the success to the strong partnership she felt with her physician and his team. "I found it extremely comforting to know that Dr. Perkins would offer many care options to me, and we made the final decision together," she says.

The trust in that partnership reaped a rich reward. "I have come to appreciate my eye sight immensely over the past 10 years," Propst says. "It is definitely a case of not appreciating what you have until you might lose it."

education & events

EDUCATION

The biennial **UW Orbital Anatomy Dissection Course** was held on March 1, 2007 for more than 30 medical students, ophthalmology residents and fellows, and community physicians. UW oculoplastics specialists Cat Burkat, MD, and Mark



Cat Burkat, MD, demonstrates the pertinent anatomy of the tear drainage system from an intranasal approach.

Lucarelli, MD, along with UW ophthalmic facial plastic surgery fellow Alon Kahana, MD, PhD, directed the course. Guest lecturers included Seth Dailey, MD, from otolaryngology and Lindell Gentry, MD, of neuroradiology. In addition to the lectures, the course included an opportunity for orbital and facial dissections by participants.



David Wilson, MD

The **Wisconsin Eye MD Spring Symposium** for Wisconsin ophthalmologists was held on May 11-12, 2007 in Kohler, Wis. Our guest speakers included the McPherson lecturer, David Wilson, MD, Chair of the ophthalmology department at Oregon Health Sciences University in Portland. Dr. Wilson discussed "A Clinicopathologic Study of Cataract, Glaucoma, Corneal, and Retinal Surgery." The Kambara lecturer was Alfred Sommer, MD, professor and dean emeritus of Johns Hopkins Bloomberg School of Public Health in Baltimore, Md. Dr. Sommer presented "A Primer on Global Health."



Alfred Sommer, MD

The **Third Annual Harvard Medical School Intensive Cataract Surgical Training Conference** was held June 2-3, 2007 in Boston, Mass., with UW comprehensive ophthalmologists Stephen Sauer, MD, and Andrew Thliveris, PhD, MD, serving as faculty trainers for second-year ophthalmology residents throughout the United States. The UW Department of Ophthalmology and Visual Sciences was one of 44 eye care institutions represented by faculty cataract surgeons at this nationwide training conference.

The UW Department of Ophthalmology and Visual Sciences will host its 11th **Biennial Clinical Neuro-Ophthalmology Symposium** on September 7-8, 2007 at the Edgewater Hotel in Madison. Special guest speakers include Valerie Biousse, MD, Cyrus H. Stoner Professor of Ophthalmology and of Neurology at Emory University in Atlanta, and Andrew Lee, MD, Professor of Ophthalmology, Neurology, and Neurosurgery at the University of Iowa in Iowa City.

Current Concepts in Eye Care, an all-day continuing education program for optometrists, will be held Saturday, September 8, 2007 at the UW Health Sciences Learning Center in Madison. The program will feature Grand Rounds style presentations by 12 UW ophthalmologists covering topic areas in cornea, glaucoma, neuro-ophthalmology, oculoplastics, pediatric ophthalmology, and retina.

The annual **Phacoemulsification Course**, coordinated by Andrew Thliveris, PhD, MD, will be held at the UW School of Veterinary Medicine on October 12-13, 2007. Collaborating faculty from UW-Madison, the Medical College of Wisconsin, and the University of Iowa will provide lectures and "wet lab" training sessions for residents of the three institutions.

EVENTS

The "**Macular Degeneration: Progress in Sight VI**" Symposium, sponsored by the UW Department of Ophthalmology and Visual Sciences and the Wisconsin Council of the Blind and Visually Impaired, was held on April 18, 2007 at the Alliant Energy Center in Madison. This free educational event is one of the largest macular degeneration symposiums in the country, with about 750 attendees this year. The 2007 symposium featured information on recent advances in macular degeneration prevention, treatment, and research. Exhibitors displayed the latest video magnifiers, computer aids, and other useful tools for persons with impaired vision.

ANNOUNCEMENTS

The **UW Health Deming Way Eye Clinic** at 2349 Deming Way in Middleton opens September 10, 2007. Services will include cataract and comprehensive eye care, refractive surgery evaluations, and an optical shop. To schedule appointments, please call (608) 824-3937.

research update

Grape Expectations researching resveratrol

Could a non-toxic plant compound found in food sources such as the skins of grapes, some berries, and peanuts, ward off cancer or assist in its treatment? That is a question that Arthur Polans, PhD, a professor in the UW Department of Ophthalmology and Visual Sciences, has been investigating.

Dr. Polans explains that resveratrol was first used as an herbal medicine thousands of years ago. In the plants in which it is found, resveratrol works as a natural antibiotic to protect the plant against disease. In 1992, resveratrol took center stage as a possible explanation of the so-called "French paradox" in which the French, who eat diets high in saturated fat, nonetheless have a low occurrence of heart disease. Some studies have suggested that the key to this paradox is resveratrol – in the form of red wine consumed in larger quantities by the French.



Arthur Polans, PhD, and Lalita Subramanian, PhD, review results from the high performance liquid chromatography (HPLC) analysis of serum samples from tumor-bearing mice treated with resveratrol. They are determining the appropriate amount of resveratrol and its metabolites in order to correlate the drug treatment with tumor inhibition in the same mice.

For Dr. Polans, who came to Madison in 1995 to study eye and related tumors, an interest in resveratrol was sparked by reports of the natural plant product's limited toxicity at levels that potentially could treat cancers. "The current treatment of many cancers has been less than adequate," Dr. Polans says. "For example, the treatment of neuroblastoma, an aggressive childhood disease of the sympathetic nervous system, is often ineffective and has serious side effects, leading to death in about half of the children with advanced disease."

The toxicity of current cancer drugs has made scientists like Dr. Polans especially eager to investigate a non-toxic natural product that has clinical potential in the prevention and treatment of cancer. Although his interest is primarily in research to find effective treatments for eye cancer, Dr. Polans notes that certain mechanisms of drug action are common between different types of cancer. When scientists study one type of cancer, they often learn about basic biochemical pathways in cells that are then relevant to other cancers. For this reason, Dr. Polans' laboratory studies several cancer models in addition to those that originate in the eye.

Dr. Polans explains that a drug goes through specific stages before it is approved by the federal Food & Drug Administration (FDA). Investigators must: 1) identify the drug's mechanism of action, 2) prove pre-clinical success with animals, and 3) test the drug's toxicity and efficacy in humans.

In 2004, Dr. Polans and his laboratory collaborated with Daniel Albert, MD, MS, a close colleague in the Department of Ophthalmology and Visual Sciences, as well as members of the UW Paul P. Carbone Comprehensive Cancer Center and the UW Departments of Pharmaceutical Sciences and Biostatistics, to decipher the biochemical pathways affected by resveratrol (stage 1 in drug development) and to investigate the efficacy of resveratrol in the treatment of neuroblastoma, retinoblastoma, and ocular and skin melanoma in animal models (stage 2).

Dr. Polans and his collaborators determined that the underlying mechanism of action of resveratrol "involves the direct activation of the mitochondrial intrinsic apoptotic pathway and a general perturbation of calcium

homeostasis in the cell." Resveratrol directly interacts with the mitochondria, organelles in the cell normally responsible for energy production, causing the release of small proteins from the mitochondria. In this manner mitochondria activate a cascade of enzymes that degrade the cell through a process of programmed cell death. Simultaneously, resveratrol causes the release of calcium from intracellular stores, including the mitochondria, leading to the activation of another set of degradative enzymes that result in cancer cell death.

Resveratrol was then tested in mouse models of human cancer. In these studies, human tumor cells were injected directly below the skin of mice with a deficient immune system, thus allowing human tumors to develop. Different dosages of resveratrol were then administered orally to the mice. "Results showed that resveratrol inhibited the growth of tumors by as much as 80 percent," Dr. Polans notes. Resveratrol was effective against the growth of multiple models of cancer, including neuroblastoma, ocular and skin melanoma, retinoblastoma, and breast cancer. "Elevated levels of resveratrol attained by injecting the compound in close proximity to the tumor enhanced its potency, leading to complete tumor regression," added Dr. Polans. Amazingly, nearby normal cells were unaffected by even the higher doses of resveratrol; there were no signs of toxicity in any of the animal studies.

In stage 3 of drug development, Drs. Polans and Albert have initiated collaborations with Memorial Sloan-Kettering Cancer Center in New York and M.D. Anderson Cancer Center in Houston to conduct clinical trials that use resveratrol and other natural products in the treatment of neuroblastoma, retinoblastoma, and ocular



Scientists in Dr. Polans' laboratory use a common technique referred to as Western blotting to demonstrate that resveratrol treatment of cancer cells is altering the levels of specific proteins. They then study the role of those proteins in biochemical pathways contributing to the proliferation and survival of cancer cells and how resveratrol alters those pathways leading to tumor cell death.

education update

A Committed Teacher leaving his mark

He's a humble ophthalmologist with a strong commitment to his immediate family and to his extended ophthalmology family of patients and medical students, as well as faculty colleagues, residents, and fellows in the UW Department of Ophthalmology and Visual Sciences. For more than 30 years, Richard Appen, MD, has provided excellent neuro-ophthalmology care to his patients as he has shared his clinical expertise and professional guidance with the many students he has taught throughout his career.

"As we all go through our daily chores, we tend to wonder whether what we do really makes a difference," admits Dr. Appen, who will retire in August 2007. "I hope I have made a difference in the lives of the students I've taught."

He has, according to several of Dr. Appen's former students who attest to the difference he's made in their approach to patient care and teaching. "Rich taught me to look twice and order tests once," recalls former UW resident and fellow Gregg Heatley, MD. A glaucoma specialist at UW for the past 15 years, Dr. Heatley says his former teacher cautioned him "to be sure that any patient tests ordered would provide information that would fundamentally change the care of that patient."

Dr. Heatley says he also learned how to be a better teacher by watching Dr. Appen. "If you think you have taught your student something well, teach it two more times. It is amazing how often we have to hear the same information in order to place it in memory where we can retrieve it from a different situation or perspective later," Dr. Heatley says.

Dr. Appen's teaching style also greatly impacted UW retina specialist Ronald Danis, MD, who met Dr. Appen prior to his ophthalmology residency at UW from 1985 through 1988. "As a medical student at Northwestern, I arranged to participate in a one-month elective with Rich," remembers Dr. Danis. "This experience strengthened my resolve to come to UW as a resident. Rich was truly inspirational. It was clear that he considered teaching and patient care as equal to each other in terms of importance. He was amazingly helpful and tolerant of me as I learned the skills I needed to become an ophthalmologist. I have subsequently used Rich as the sort of ideal model of how I should be interacting with students and residents as a teacher."

Department Chair Paul Kaufman acknowledges that caring for patients and teaching residents and medical students can be challenging tasks to balance in an academic ophthalmology setting. "Rich was adept at finding a synergy between these two missions and making it work," Dr. Kaufman notes. "His patients and his students were the beneficiaries. Over my 35 years in academic ophthalmology, with wide exposure to stellar teachers worldwide, he is one of the two or three best I have ever seen."



Richard Appen, MD, (at the head of the table) discusses various clinical scenarios with UW medical students to help them identify patients' symptoms and diagnoses based on eye examination findings. Medical students from left: Mark Been, Christopher Bermant, Ryan Sydnor.

Grape Expectations

melanoma. Results from these preliminary studies will determine whether these drugs should be tested in larger, randomized clinical trials and eventually recommended for the treatment of these cancers. Dr. Polans estimates that testing the drug in randomized human trials is about two to five years away. The scientist explains that more financial resources are needed in order to speed up the time it takes to develop a drug for testing in humans. "It's very costly to prepare resveratrol or a modified form of resveratrol that meets FDA standards for application in humans," explains Dr. Polans. "Until these manufacturing standards are met, resveratrol can't be given to human beings to treat specific diseases including cancer."

In Dr. Polans' laboratory, which receives about \$350,000 per year in grants from public and private institutions, research continues to identify resveratrol compounds with improved efficacy and enhanced delivery in humans. Eventually these compounds will be manufactured to meet FDA requirements. "Resveratrol and related natural products hold great promise for the future," Dr. Polans says. "Our goal with these compounds is not necessarily to "cure" cancer – but to treat it more effectively, with fewer side effects and likely in combination with other cancer-fighting drugs. We can then learn to live with cancer."



Arthur Polans, PhD, pictured with his laboratory staff. Front row: Arthur Polans, PhD; second row (left to right): Leslie Fabian; Saswati Bhattacharya, PhD; Katia Klenschina; third row (left to right): Brittany Radke; Lalita Subramanian, PhD; Soesiawati Darjatmoko; fourth row (left to right): Teresa Walker, PhD; Dhruv Sareen; Paul van Ginkel, PhD; back row: Jason Kenealey.

A Committed Teacher

continued

Looking back on his own career and contemplating his impact on future ophthalmologists and physicians, Dr. Appen is quick to point out that his own teachers including ophthalmologists Matthew Davis, MD; Peter Duehr, MD; Rodney Sturm, MD; and Richard Dortzbach, MD, greatly influenced how he practiced ophthalmology. "When I am seeing patients, I still find myself thinking, 'What if Dr. Davis were watching – would he approve?'" Dr. Appen says. "My teachers were conscientious and thorough – and they always put patients first."

According to Chair Emeritus Daniel Albert, MD, MS, Dr. Appen has left his own mark as a teacher and mentor. "Rich's judgment and advice are sought after by colleagues, students, and friends," comments Dr. Albert. "As vice-chair for education, he has done a tremendous job teaching medical students, selecting residents, mentoring and guiding them, and remaining a friend after they have left the program."

Editor's Note: Dr. Appen says he will continue on a limited basis to assist in training UW medical students, as well as ophthalmology residents, after his formal retirement. He also looks forward to having more time for birding and bicycling with his wife Alice, for playing tennis with his daughter, and for participating in the lives of his grandchildren.



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visiting professors

The UW visiting professor program features expert ophthalmologists invited to lecture at the department's weekly Grand Rounds conference to an audience of UW, community, and regional doctors. The visiting professors also spend an afternoon teaching UW residents. The Grand Rounds program is held at:

7:30 a.m. on Fridays at UW Hospital and Clinics in the G5/113 auditorium.

September 21, 2007 – **Richard F. Spaide, MD**
Assistant Clinical Professor
New York Medical College
Retina Vitreous Surgery

October 26, 2007 – **D. Rex Hamilton, MD, MS**
Director, UCLA Laser Refractive Center
Jules Stein Eye Institute
Cornea and Refractive Surgery

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