Could Resveratrol, an Ingredient in Red Wine, Prevent Skin Cancer?

As far back as 6,000 B.C., our ancestors realized that red grapes had at least one special property — namely, that they could be fermented into delicious wines. Now, it appears that these grapes have even more to offer: a molecule called resveratrol. Numerous medical studies suggest that resveratrol, which some plants produce to ward off fungal infections, may help combat heart disease, cancer, Alzheimer's disease, and other illnesses.

Researchers at Columbia's Department of Dermatology are studying this molecule as a possible preventive treatment for basal cell and squamous cell skin cancers.

“W e got interested in resveratrol because it is very effective at blocking DNA damage induced by ultraviolet-B (UVB) light, which is the most important risk factor for skin cancer,” explains lead investigator Arianna Kim, Ph.D., the Herbert Irving Assistant Professor of Dermatology. “When UVB light hits skin cells, it can damage the DNA. If there’s enough damage over time, the cells can become cancerous. So, we wanted to find out if resveratrol could prevent or reverse adverse effects resulting from those genetic changes.”

Thus far, the results are promising. In one experiment, mice were given regular doses of an oral solution of resveratrol and chronically exposed to UVB light. “We saw a 70-percent reduction in non-melanoma skin tumors in the treated mice, compared to a control group that didn’t get any resveratrol,” Dr. Kim reports.

Banner Year for Columbia Dermatology Research Funding

Columbia Dermatology’s remarkable 2009/2010 funding totaled $3.8 million and included:

- Dr. David R. Bickers was awarded a $1 million grant from the NIH for studying skin stem cells. This P30 Core Center Grant, the only one in the US awarded to a department of dermatology by NIAMS, was funded under the 2009 American Recovery and Reinvestment Act (ARRA) and allows the Department to recruit two new basic science researchers.
- Dr. Angela Christiano was awarded a $326,000 ARRA grant to study the genetic basis of inherited hair diseases, especially alopecia areata, and a $1 million New York State stem cell (NYSTEM) research grant.
- Dr. David Owens and Dr. Srikala Raghavan received NYSTEM grants totalling $720,000.
- Dr. Julide Tok Celebi was awarded a $1.7 million NIH grant, funded under ARRA, to investigate the role of GAB2 in metastatic melanoma.
- The Department’s NIH Postdoctoral Training Grant was renewed in 2009 with three training slots for a total award of $352,214.
- New faculty member Dr. Bin Zheng, jointly recruited by Dermatology and the Institute for Cancer Genetics, is a K99 recipient of $750,000 over 3 years.

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Chairman’s Message

Because medical science has become so complex, interdisciplinary collaboration is now essential for fostering discoveries and developing new ways of treating or preventing disease. Clearly, no single department can do it all. This goes double for a small department like ours, which can flourish only by building bridges with other, larger departments within the university.

A perfect example of the importance of collaboration can be found in this issue’s cover story which describes a study of resveratrol, an ingredient in red wine that holds promise as a treatment for skin cancer. This work would not be possible without the insights of a skin cancer biologist and the skills of a synthetic chemist.

Our emphasis on collaboration is also exemplified in our newest recruit — Ellen Lumpkin, Ph.D., who will hold joint appointments in the Departments of Dermatology, and Physiology and Cellular Biophysics. Dr. Lumpkin is an outstanding investigator in the neurophysiology of skin and touch sensation. Her arrival will mark the beginning of an innovative new research program within our Department, focusing on links between the skin and the brain — a little explored frontier of both dermatology and neuroscience.

We look forward to building more bridges at Columbia in the days ahead.

David R. Bickers, M.D.
Carl Truman Nelson Professor and Chairman

Irving Gift Supports New Dermatology Research Space

Manhattan-based philanthropists Herbert and Florence Irving have made a $1 million gift to the Department of Dermatology to support the renovation of laboratory space in the Russ Berrie Medical Science Pavilion at Columbia University Medical Center.

“This is an important gift, as it allows us to expand our facilities for basic research,” says David R. Bickers, M.D., the Carl Truman Professor and Chairman of Dermatology. “Moreover, it brings all of our basic scientists together under one roof, which is critical for promoting collaboration.”

Mr. Irving is co-founder and former vice chairman of SYSCO Corp, a worldwide company that evolved from Global Frozen Foods, which he and his brother-in-law began in the 1940s. He joined the company after serving in the Army during World II, and subsequently built the small company into the largest food distributorship in the country.

Mr. Irving is a long-standing friend of the Department of Dermatology, stemming from his experience as a patient at the Medical Center. Since then, the Irvings have donated tens of millions of dollars to the institution, supporting research, education and patient care. One of those gifts made possible the Herbert Irving Center for Dermatology and Skin Cancer, which houses the Department’s clinical and administrative offices.

“Herb and Florence have been uncommonly generous to us,” says Dr. Bickers. “As much as I value their gifts, I treasure their friendship and advice over the years. They are truly remarkable people.”

Left: Herbert and Florence Irving
Still, much more work needs to be done. The problem is that resveratrol is very unstable and is quickly broken down by the body, so little of it reaches the cells that need it. You would have to drink cases of wine a day to reach therapeutic blood levels. And, concentrating resveratrol in a supplement or putting it in a cream doesn’t make it more “bioavailable,” scientists say.

However, a solution may be close at hand. Around the same time Dr. Kim began her research, Scott A. Snyder, Ph.D., an Assistant Professor of Chemistry, whose lab is located on Columbia University’s Morningside Heights campus, started his own resveratrol studies, seeking to create more stable forms of the molecule. A lover of red wine, Dr. Snyder began this research on a lark. “People had been trying to make these structures for 30 years, with no success,” he explains. “I thought it would be a nice challenge.”

His work soon caught the attention of Dr. Kim and her colleagues in Dermatology, who proposed a cross-campus collaboration. It’s been a good match of expertise. Dr. Kim has demonstrated that Dr. Snyder’s molecules retain the same anti-skin cancer properties of natural resveratrol, yet persist much longer. Now, she’s studying how these molecules affect the complicated series of steps involved in DNA damage and the development of cancer. In the process, the researchers hope to learn exactly which processes need to be targeted in order to prevent or arrest skin cancer, and which resveratrol formulations are most effective in accomplishing this.

If a resveratrol-based treatment for skin cancer can be developed, it’s probably still years away. In the meantime, Dr. Kim advises, cover up and reduce your sun exposure. And drinking a glass of Pinot Noir certainly can’t hurt!

Molecular structure of resveratrol and one of its dimers (formed from two identical resveratrol molecules).
When a particularly challenging dermatology case arises, doctors around Columbia University Medical Center (CUMC) know to call on Marc E. Grossman, M.D., Professor of Clinical Dermatology at CUMC and Director of the Dermatology Consultation Service at New York-Presbyterian Hospital at Columbia. Dr. Grossman created this inpatient service in 1978, when he was a CUMC third-year dermatology resident. The service was the first of its kind and continues to set the standard of care in consultative dermatology.

Q: What led you to create the Dermatology Consultation Service?
A: Back in 1978, if an inpatient had a skin disorder, it fell on the attending physician to reach a diagnosis. Sometimes, the attendings were stretched too thin. So, I felt that patients would be better served by having a dermatologist doing hospital consultations full time, someone who could quickly evaluate the problem. This not only improves care, but it can also save lives — some skin conditions can be life-threatening if not diagnosed and treated immediately.

Q: What kinds of cases do you see?
A: I see patients all over the hospital. Almost every inpatient has a rash of one type or another. Often, it’s a primary skin condition like psoriasis or dermatitis. But in many instances, the rash is a result of treatment for another disease, like chemotherapy for cancer or immunosuppressant therapy after an organ transplant. Also, a rash may be a symptom of an underlying disease. Occasionally, that symptom is the key to figuring out what is wrong with a patient.

Q: Can you cite an example?
A: Once, based on a skin finding — itchy, red bumps — my residents and I made a diagnosis of Fabry’s disease, a rare genetic disorder that interferes with the metabolism of fats and can lead to heart failure. Another time, we were called in to see an air force general from the Dominican Republic who was unable to eat or swallow. Nobody could figure out what was causing his symptoms. Based on signs in his upper airway, we diagnosed pemphigus vulgaris, an autoimmune disorder.

Q: What’s the secret to your success?
A: Over the years, I’ve built up a wealth of visual experience. Very often, I can walk in the room, take one look at the patient and make a diagnosis. It also helps that we have smart, well-trained residents who are in the hospital day and night. They’re my eyes and ears, so to speak.

Q: Do you ever fail to make a diagnosis?
A: Rarely. But some cases we never figure out. They sit on my desk like cold-case files, until we solve them one way or another. By doing a little detective work and staying on top of the medical literature, we can usually determine if the skin symptom is a rare manifestation of a common disease, a rare disease, or even a new disease.

Q: What’s the Grand Rounds “Best of Grossman” conference?
A: That’s the Department’s annual conference that provides our residents with the opportunity to present the best consult cases of the year. We’ve been doing it for 25 years. It’s an invaluable teaching tool for our residents and faculty. There’s nothing else quite like it in the country.

Dr. Grossman lectures the residents with colleague Dr. Paul Schneiderman, as Chief Resident Dr. Nicole LeBoeuf looks on.
mohs surgery: Saving Faces

Dr. Désirée Ratner’s best work is never noticed. But she wouldn’t have it any other way.

Dr. Ratner, Professor of Clinical Dermatology and Director of Dermatologic Surgery at Columbia, specializes in Mohs micrographic surgery, an exacting procedure for removing high-risk basal cell and squamous cell skin cancers, layer by layer, while minimizing damage to healthy surrounding tissue. After the cancer is removed, reconstruction begins.

“My goal,” says Dr. Ratner, “is to put patients back together so that once they’ve healed, no one would know they’ve had surgery.” Since these cancers typically occur on the face, ear, neck, lips, and the back of the hands, this is no small accomplishment.

The first step in Mohs surgery (invented by Dr. Frederic Mohs in the 1930s) is to remove all of the visible skin tumor. Next, while the patient waits, the surgeon examines the tissue microscopically to determine whether its edges and underside are surrounded by normal skin cells — a sure sign that no cancer remains. The tissue sample and the surgical wound are carefully mapped so that if more tissue does need to be excised, the surgeon will know the precise location.

An experienced surgeon like Dr. Ratner, who performs hundreds of these procedures a year, can often remove all of the cancer on the first try.

Most Mohs surgeons also perform same-day reconstructive surgery, which speeds healing and improves cosmetic results. The entire process — surgery and reconstruction — is performed under local anesthesia, so a hospital stay is not necessary.

One of approximately 30 Mohs surgeons in New York City, Dr. Ratner is known for tackling the most difficult cases — those requiring extensive tissue removal and thus extensive reconstruction. Such cases may require the involvement of other surgical specialists, such as oculoplastic surgeons or head and neck surgeons.

Facial reconstructions are particularly challenging. To achieve optimal results, the surgeon must hide incisions in the skin’s natural folds and preserve the natural symmetry of the face — tasks that require artistic as well as technical skills. “It’s a behind-the-scenes craftsmanship,” she says. “I take it as a compliment when you cannot tell, for example, that someone’s entire nose has been reconstructed.”

Ironically, Dr. Ratner wasn’t especially good with her hands as a child. “My mother likes to tell people that I couldn’t use scissors in kindergarten,” she admits. Evidently, her dexterity has improved, enough so that she has been listed as one of Castle Connolly/New York Magazine’s “Top Doctors.”

The 99 Percent Solution

“Mohs surgery is largely reserved for high-risk basal or squamous cell cancers,” says Monica L. Halem, M.D., Assistant Clinical Professor of Dermatology, the newest member of the Mohs surgery team at Columbia and a highly skilled reconstructive and cosmetic surgeon. “By ‘high risk,’ we mean tumors that are likely to grow back, so you want to get it all out the first time.”

Mohs surgery is the most effective treatment for these forms of cancer, she adds. “The five-year cure rate is about 99 percent for new cancers, and 95 percent for recurrent cancers.”

A variation of the technique can be used for small, localized melanomas, but not for large, advanced melanomas, which tend to form discontinuous tumors.
fellowship profile:
Hillary Johnson, M.D., Ph.D.

As might be expected of someone with not one but two advanced degrees, Dr. Hillary Johnson has a hand in many activities. Most of her day is spent learning surgical skills as a fellow in Procedural Dermatology at Columbia under the tutelage of Désirée Ratner, M.D., who directs the Procedural Dermatology fellowship program. But Dr. Johnson is also involved in research, and an unusual kind of research at that.

In collaboration with the American Academy of Dermatology, Dr. Johnson studies ways to improve patient safety. “While our field is one of the safest, there are ways to make it even safer,” she explains. “For example, there are 18 clear steps involved in taking a biopsy specimen and making a diagnosis. A step can be missed anywhere along the way. The challenge in this case is to standardize and streamline these steps so that human error plays less of a role. In a way, this is an engineering challenge. It’s a different way of looking at medicine, but an important way of improving the outcomes of care.”

Dr. Johnson also studies ways to improve the efficacy of Mohs surgery, a treatment for non-melanoma skin cancer and subsequent facial reconstruction surgery (see p. 5).

Super Wednesday: keeping current in dermatology

Thousands of scholarly articles related to skin diseases are published each year, far too many for any one dermatologist to read. Fortunately, there’s another — and arguably more effective — way for skin-care specialists at Columbia University Medical Center to stay up to date: Super Wednesday.

Super Wednesday is the Department of Dermatology’s monthly fully-accredited continuing education conference for faculty, fellows, residents, and medical students who have an interest in skin disease.

The half-day conference begins with case presentations by the Department’s residents. At this time, attendees learn about particularly interesting or difficult cases, such as a recent patient with Degos disease, a rare blood vessel disease that causes small, red skin lesions, or a patient with progressive multifocal leukoencephalopathy, a potentially devastating side effect of a new treatment for psoriasis.

Super Wednesday also features a Tumor Conference, where attending physicians or fellows in Dermatology present cases involving malignancies, again with a focus on the new, difficult, and unusual.

All members of the hundred-plus full-time and voluntary Dermatology faculty are invited to present at either of the sessions. “This is one of the benefits of being a member of our faculty,” says Elizabeth Knobler, M.D., Associate Clinical Professor of Dermatology, who is the organizer of Super Wednesday. “It’s a unique opportunity to discuss challenging cases with their peers and avail themselves of the expertise at Columbia.”

For many attendees, the highlight of Super Wednesday is our visiting professor, who discusses the latest findings, treatments, and trends in dermatology. Recent topics have included the changing nature of skin disease in HIV patients, skin infestations such as scabies and bed bugs, and methicillin-resistant Staphylococcus aureus (MRSA), an increasingly common and potentially deadly skin infection. Afterwards, the guest speaker meets in a conference with residents, rounding out a superlative educational session.

Residents Dr. Andrew Avarbock and Dr. Samantha Herman, with faculty members Dr. Eric Herman and Dr. Elizabeth Knobler.
Events

Comedian Jackie Mason Hosts Friends of Columbia Dermatology

Columbia Dermatology’s diverse circle of supporters includes such well-known personalities as the extraordinarily entertaining comedian, Jackie Mason. As a way of expressing his continued support for the Department, Jackie extended an invitation to a select group of our contributors to two of his shows in the Tri-State area and offered to greet them backstage.

His performance did not disappoint! After a hilarious routine that included his biting political satire and side-splitting observations on the folly of modern life, our guests, pictured below, left for home knowing why Jackie Mason is regarded as one of the greatest stand-up comics of all time.

Cosmetic Dermatology Educational Event

On October 13, 2009, Columbia Dermatology’s Skin and Laser Center held the first in a series of lectures open to the public on new treatments and therapies in the field of cosmetic dermatology. Before a group of invited guests, Columbia faculty members Dr. Robyn Gmyrek, Assistant Clinical Professor of Dermatology and Division Chief, Cosmetic Surgery, and Dr. Monica L. Halem, Assistant Clinical Professor of Dermatology, conducted a presentation focusing on minimally invasive cosmetic procedures. Guests learned about the latest in laser treatments, Botox and Restylane injections, as well as the procedure of tumescent liposuction now available at Columbia Dermatology. A small reception followed.

The Skin and Laser Center will be holding additional educational lectures this year. For information about future dates and topics, please contact Michele Nunez by phone on (212) 305-0010, or by Email at mn2112@columbia.edu.

Top: Dr. Monica L. Halem discusses tumescent liposuction.

Columbia Dermatology Receives $100,000 from Kiehl’s

At the Kiehl’s Worldwide Skincare Symposium held at Columbia University on February 3rd, Kiehl’s, the New York City-based company, announced that it has made a commitment of $100,000 to support Columbia Dermatology basic research and education, relevant to skin biology and skin barrier function. Kiehl’s is hopeful that these findings will assist them in their development of new, innovative skincare products. Department faculty members Dr. David R. Bickers, Dr. Robyn Gmyrek and Dr. Adam Geyer gave presentations at the event.

Top: Dr. Robyn Gmyrek discusses the benefits of antioxidants. Below, Guest Dr. Sarah Dolder, Dr. Adam Geyer, Patrick Kullenberg, GM, Kiehl’s Worldwide, and Dr. David R. Bickers.

Save the Date

Grand Rounds: Super Wednesdays
March 24, April 28, and May 19, 2010
Fulltime Clinical Faculty
David R. Bickers, MD
Carl Truman Nelson Professor and Chairman
Robert R. Walther, MD
Clinical Professor of Dermatology and Vice Chair
Danielle Engler, MD
Associate Clinical Professor of Dermatology and Director, Dermatology Clinic
Maria Garzon, MD
Professor of Clinical Dermatology and Clinical Pediatrics, and Division Chief, Pediatric Dermatology
Robyn Gmyrek, MD
Assistant Clinical Professor of Dermatology; Director, Faculty Practice; Division Chief, Cosmetic Dermatology; and Director, Skin and Laser Center
Marc E. Grossman, MD*
Professor of Clinical Dermatology
Director, Dermatology Consultation Service, NYPH/CUMC
Monica L. Halem, MD
Assistant Clinical Professor of Dermatology
N. Michelle Hanjani, MD
Assistant Professor of Clinical Dermatology
Cheryl Hutt, MD
Assistant Clinical Professor of Dermatology and Director, Residency Program
Elizabeth Knobler, MD
Associate Clinical Professor of Dermatology
Julian Mackay-Wiggan, MD
Assistant Clinical Professor of Dermatology and Director, Clinical Research Unit
Kimberly Morel, MD
Assistant Professor of Clinical Dermatology and Clinical Pediatrics
Jessica Newman, MD*
Assistant Professor of Dermatology and Division Chief, Bronx VA Section of Dermatology
Huyen Nguyen, MD
Assistant Professor of Clinical Dermatology
Désirée Ratner, MD
Professor of Clinical Dermatology and Division Chief, Dermatologic Surgery
Julide Tok Celebi, MD
Associate Professor of Clinical Dermatology
Dermatopathology Laboratory
David N. Silvers, MD
Clinical Professor of Dermatology and Pathology and Division Chief, Dermatopathology
Basil A. Horst, MD
Assistant Clinical Professor of Dermatology
Sameera Husain, MD
Assistant Professor of Clinical Pathology in Dermatology
George Niedt, MD
Assistant Clinical Professor of Dermatology
Asher Rabinowitz, MD
Associate Clinical Professor of Dermatology
Angela Christiano, PhD
Richard and Mildred Rhodebeck Professor of Dermatology and Professor of Genetics & Development; Vice Chair, Research Department of Dermatology; and Director, Center for Human Genetics
David R. Bickers, MD
Carl Truman Nelson Professor and Chairman
Karima Djabali, PhD
Herbert Irving Assistant Professor of Epithelial Cell Biology
Andrew Engelhard, PhD
Assistant Professor of Dermatology
Arianna Kim, PhD
J. Lowery Miller & Herbert Irving Assistant Professor of Dermatology
David Owens, PhD
George Henry Fox Assistant Professor in Dermatology and Assistant Professor of Pathology
Srikala Raghavan, PhD
Assistant Professor of Epithelial Cell Biology of Dentistry and Dermatology
Julide Tok Celebi, MD
Associate Professor of Clinical Dermatology

* Affiliated physician

If you would prefer not to receive publications from Columbia’s Department of Dermatology, or if you would like to be added to our mailing list, please email kdb2126@columbia.edu.