Madeleine Duvic dominates field of CTCL discovery

Her answer was an astounding, “Yes, that sounds great! I had just gone through the match, my mom had just died of cancer, and just to know what I would be doing in one or two years was wonderful.”

Solving the T-cell puzzle

Duvic says she has always had an interest in T-cells in general, how they work and how they do their jobs. As a medical student and intern, she took care of people with CTCL, those with Sezary Syndrome in particular, and she was fascinated with the disease.

But when she came to MD Anderson in the early 1980s, right in the middle of the acquired immunodeficiency syndrome (AIDS) epidemic, it was the lack of T-cells that caught her attention. Duvic ran one of the first AIDS dermatology clinics in the country, working with people who had low levels of T-cells.

“I published quite a few articles on discoveries of cutaneous manifestations of HIV infection in AIDS.” Among her findings was that psoriasis, which is a T-cell mediated disease, was worsened by AIDS. “It didn’t make sense,” Duvic says. “As a clinician-scientist, when you find something that’s totally paradoxical, you know there is something to learn about it.”

So why would people who had no T-cells get bad psoriasis?

“It turns out they have some CD8 cells that are doing it,” Duvic explains, “not the C4s (T-cell helpers) that the virus kills.” She also saw patients with psoriasis heal fairly quickly once they were treated with azidothymidine (AZT), a drug used to delay development of AIDS. That led to a patent and a study of AZT in non-HIV infected psoriasis patients.

“A clinician-scientist keeps his or her eyes open and they make these remarkable discoveries based simply by talking to patients. I’ve learned to listen to my patients a lot.”

A designing woman

Over the years, her attentiveness has paid off.

Twenty years ago, CTCL patients would be treated with total body beam radiation in a radiation oncology clinic or face radical surgery. Duvic decided to take an immunologic approach and is among the key players,

Madeleine Duvic, M.D., professor, Dermatology, is among MD Anderson’s pioneers.

- In 1987, she created the first photopheresis center in Texas.
- She established one of the institution’s first multidisciplinary centers which provided integrated care with total body electron beam radiation, dermatology and oncology.
- Duvic is the principal investigator of the largest Alopecia Areata Registry in the world. (Alopecia Areata is a common autoimmune skin disease resulting in the loss of hair on the scalp and elsewhere on the body.)

But among her greatest accomplishments is the study of cutaneous T-cell lymphoma (CTCL). And to think this physician-scientist, trained at Duke Medical School, wasn’t sure in which sub-specialty she would land until a twist of fate cleared the pathway for her.

“I was studying immunology, so I didn’t know where that was going to lead,” recalls Duvic, “maybe infectious diseases, maybe pulmonology, or maybe rheumatology.” She took a rotation in dermatology at the beginning of her senior year and liked it. That same year, one of the residents who had been chosen for the program dropped it, so Duvic was approached to fill the role.

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either as a designer or consultant, in the development for the last four drugs approved for the treatment of CTCL. Among them, bexarotene, was her idea, and ultimately produced by the pharmaceutical company, Ligand, in both an oral and gel form.

Today, patients with Sezary Syndrome are still at the forefront of her clinical practice and her research. Duvic says she has been waiting for years to sequence the Sezary genome. Now, she is working to attract a collaborator who can afford it. “Every patient deserves to have their cancer genome sequenced,” she says.

For her efforts, Division Head Robert Gagel, M.D., recently selected Duvic as one of two faculty to receive the Clinical Leadership Award. Steven Waguespack, M.D., professor, Endocrine Neoplasia and Hormonal Disorders, also received the honor. Duvic says research and helping people are what drive her to discovery.

“When you improve a patient who is full of tumors and miserable, that’s what it’s all about.”

Dermatology research involves cutting edge studies

Michael Migden, M.D., associate professor, Dermatology, is an expert in the study of Hedgehog signaling inhibitors. In recent years, he has participated in multiple protocols in search of treatment that could effectively treat advanced basal cell carcinoma.

Advanced basal cell carcinoma patients were delivered some hope with the development of the drug vismodegib, approved by the FDA in 2012, which showed promising results.

“Prior to the approval of vismodegib, there was no reliably effective systemic treatment for advanced basal cell carcinoma. These cases were commonly sent for extensive surgery and postoperative radiation to attempt disease control,” Migden says.

Migden, a Mohs surgeon, is one of the researchers in a multi-center study, intended to evaluate the potential of this targeted therapy for neoadjuvant use, in which patients will receive the drug or a placebo followed by Mohs surgery (see additional story on page three).

“Our radiation oncologists prefer to have surgery followed by adjuvant radiation. There are times when surgery just can’t get it all, or the patient could possibly get disfigured along the way in an attempt to get it all,” Migden says.

Patients enrolled in the study will receive the drug or placebo for three months. After that, their tumors will be measured to determine whether they have decreased in size. Those assessments will be followed by 100% margin controlled resection with immediate pathology performed by the Mohs surgeon, the process by which Mohs surgery is defined. Migden says the study will answer important questions:

• Can neoadjuvant use of this targeted therapy shrink the tumor and allow for a smaller surgery and perhaps a smaller scar or high cure rate?
• Does this targeted therapy provide contiguous resolution of tumor or does it leave skip lesions of tumor behind as the clinical lesion appears to shrink?

These are questions that need to be answered for hedgehog pathway inhibitors, he says. Migden also believes these agents should be studied for use after extensive surgery with positive margins. He suggests that studies might be performed in such patients to investigate activity of these targeted therapies to dissolve potential residual tumor burden when there is concern a portion of it may remain beyond the reach of surgery.

INNOVATOR study maps skin cancer progression

Migden is among a team of MD Anderson dermatologists who are contributing to a study that received a two-year $100,000 award from the Landon Foundation last spring. Kenneth Tsai, M.D., Ph.D., assistant professor, Dermatology Research, received the INNOVATOR Award from the American Association for Cancer Research (AACR) for his proposal to examine how normal skin progresses to squamous cell carcinoma.

According to Tsai, squamous cell carcinoma and its precancerous lesions are relatively common and well-defined clinically and histologically. “We don’t have a good understanding of the genetic events that occur along the way.”

In less than one year after receiving the award, Tsai says he and his team have discovered some interesting findings.

“First, we have identified several microRNAs that seem to be important in driving the transition from normal skin to precancerous actinic keratosis to invasive squamous cell carcinoma.” They are currently testing to see how the microRNAs affect cell death and responses to UV radiation.

In addition, we have found that precancerous lesions have at least as many mutations as the actual cancers. “We are not sure what this means, but suspect that all of the genetic seeds for cancer are present in the pre-neoplastic lesion,” Tsai says.

The project represents the efforts of many individuals in the lab, principally Vida Chitsazzadeh, an M.D., Ph.D. student with extensive bioinformatics and resource support from Preethi Gunaratne, Ph.D., University of Houston; Cristian Coarfa, Ph.D., Baylor; Xiaoping Su, Ph.D., Hui Yao, Ph.D., Li Shen, Ph.D., Elsa Flores, Ph.D., and Ernest Hawk, M.D., MD Anderson.

Ultimately, Tsai says the team hopes to identify targets for chemoprevention at all stages and to develop therapies for them.
Why is Dermatology important for the cancer center?

During my medical training, I had the good fortune to work with a dermatologist whose specialty was dermatologic manifestations of medical disease. He taught me that the skin integument was a window into the body’s organ systems, and that if one looked carefully, a high percentage of internal medicine disorders had unique dermatologic manifestations. Cancer is one such example. Many sporadic and genetic cancer syndromes can help in the diagnosis of malignancy and provide insight into the nature or type of cancer.

In addition, primary cancers of the skin, or other cancers that metastasize to the skin, are growing in number. The graying and aging of the population has further increased the number of skin cancers that can impact or threaten human life.

In this issue of the DoIM News, we feature clinical and research efforts of our dermatology faculty. Ron Rapini, M.D., professor and chair, has worked with his faculty to develop important programs for the institution. There is a substantial effort performed in collaboration with the Division of Cancer Prevention and Populations Sciences to identify and treat skin cancers early in their development and to provide curative therapy. In addition, Deborah MacFarlane, M.D., professor and director of the Mohs Unit, leads a talented group of Mohs surgeons who tackle some of the most challenging skin cancer cases in the State of Texas.

Others in the department are focused on dermatologic manifestations associated with cancer or its treatment. For example, there are dermatologic manifestations of graft vs. host disease and skin cancer associated with the use of targeted cancer therapies, and specific types of cutaneous malignancies such as lymphoma.

We are very proud of the growth and development of this department and look forward to great things from them in the future.
A “rendezvous” improves quality of life

Patients regain ability to swallow

Lopa Mishra, M.D., professor and chair of Gastroenterology, Hepatology and Nutrition, says Alexander Dekovich, M.D., has improved the quality of life for many patients who had little or no hope of relief from esophageal obstruction.

Joseph Lillard enjoyed a small serving of mashed potatoes and gravy over the holidays. While that may sound like a light-weight meal to most of us, to Lillard it was a delectable treat. For eight months after receiving radiation for his head and neck cancer, he could not swallow anything because of a complete occlusion of his cervical esophagus, a side effect of the treatment. His only form of nourishment was through a gastrostomy tube (PEG).

Lillard wasn’t sure he would ever regain the ability to eat and drink until he learned about a procedure which would be performed by gastroenterologist Alexander Dekovich, M.D., who had also inserted his PEG. “I was happy to hear about the rendezvous procedure that would allow me to at least try to swallow,” Lillard says.

Dekovich and his colleague Patrick Lynch, J.D., M.D., performed the rendezvous procedure by entering Lillard’s esophagus in retrograde fashion through the gastrostomy site. They then tunneled through the occlusive membrane in the cervical esophagus and met with the antegrade placed endoscope in the pharynx. Once this was accomplished, a guide wire was passed into the stomach and a series of dilators was then passed over the guide wire to dilate the stricture and re-establish continuity of the esophagus. Lillard learned, after the fact, that the work had been performed by a master of his trade.

“I didn’t know this procedure wasn’t available everywhere. I’m so grateful to be a patient of MD Anderson and of Dr. Dekovich.”

According to Division Head Robert Gagel, M.D., “Dr. Dekovich has a deft touch to push a dilator through narrow passages that would stop lesser skilled physicians. So instead of patients living a PEG or some other bypass or procedure, they have the ability to eat solid food or at least liquid food.”

Sixty-nine-year-old Claudia Baraldi had a similar experience. Before her first rendezvous procedure three years ago, Baraldi would sip tea, coffee or wine, and then have to spit it out. She was warned the stricture could return. She received her third treatment last summer.

“I will probably need another treatment in the future and I will certainly make sure that Dr. Dekovich performs it again,” Baraldi says. “His patient care attitude is as outstanding as his surgical skills.”

and Nutrition, received Lifetime Achievement Awards. According to Gagel, Rolston is responsible for the “development of our current approach to treatment of neutropenia in the cancer patient.” Dekovich, he said, “has tackled a difficult problem in the cancer population—esophageal strictures caused by cancer and its treatment with radiation and chemotherapy.”

(See accompanying story)

**Recipient of other leadership awards:**

**Innovations in Business:**
Margaret Row, M.D., associate professor, Emergency Medicine

**Clinical Leadership:**
Madeleine Duvic, M.D., professor, Dermatology, and
Steven Waguespack, M.D., professor, Endocrine Neoplasia and Hormonal Disorders

**Researcher of the Year:**
Gilbert Cote, Ph.D., professor, Endocrine Neoplasia and Hormonal Disorders

**Rookie Researcher of the Year:**
Jichao Chen, Ph.D., assistant professor, Pulmonary Medicine Research

**Innovations in Clinical Care:**
Jerry Henderson, M.D., assistant professor, Emergency Medicine

Saamir Hassan, M.D., assistant professor, Cardiology, was also recognized for receiving the highest number of votes during the division's Quality Improvement projects last September. Hassan's presentation, “Improving Left Ventricular Ejection Fraction Assessment,” proved that the quantitative method implemented over a 10-month period decreased the variability among participating inter-observers.

Other faculty had an opportunity to deliver updates about their programs. Franklin Herlong, M.D., professor, Gastroenterology, Hepatology and Nutrition, addressed developments in the Hepatology Program and Clinic, while geriatricians Beatrice Edwards, M.D., professor, and Holly Holmes, M.D., associate professor, General Internal Medicine, spoke about their program, which is now called the Healthy Aging Clinic.

Deputy Division Heads Ellen Manzullo, M.D., and Dimitrios Kontoyiannis, M.D., also delivered Leadership Reports. Manzullo gave an update on the House Staff Training Program, while Kontoyiannis cited key research developments for Fiscal Year 2013.
Acute Graft-versus-Host Disease (GVHD) develops as a result of a stem cell transplant and is a significant cause of problems after the procedure. Immune cells in the tissue (graft) identify tissues of the patient (host) as foreign or different, and selectively damage the skin, gut, liver or lungs.

Sharon Hymes, M.D., first became intrigued with this complication first, during her medical training, and then during her residency at Johns Hopkins Hospital. It is now her area of expertise.

“When I came to Houston as a faculty member at The University of Texas Medical School, I spent one day a week at MD Anderson seeing a variety of problems, including cutaneous GVHD,” says Hymes, professor, Dermatology. Once she joined the MD Anderson faculty, she sought out Richard Champlin, M.D., chair, Stem Cell Transplantation and Cellular Therapy, who was receptive to the idea of a joint oncology-dermatology clinic designed to diagnose and treat GVHD.

Acute GVHD can be one of the most serious complications following allogeneic stem cell transplantation when the donor and the recipient of the stem cells are not genetically identical. “When we see a patient who has this problem, especially acutely,” Hymes says, “we look at their skin to make sure there isn’t a rash. If the patient does have a rash, we document how widespread it is, and exactly what it looks like.”

According to Hymes, “The pathogenesis of chronic GVHD is less understood, but it appears to be a disorder of immune regulation. The skin, both clinically and pathologically, can show a multitude of changes that aid in the diagnosis of the disease.” She says blisters typically are indicative of a more serious disease and prompt physicians to use systemic therapy. Patients with a milder form of GVHD may be treated with topical medications.

Hymes says there are currently a multitude of trials for both acute and chronic GVHD that are not only trying to determine the optimal additional treatment of GVHD, but that also are working to regulate the anti-tumor effect that can occur in the GVHD setting.

“There is the dilemma,” Hymes says. “Patients with GVHD may also be experiencing an anti-tumor effect that decreases their chance of relapse. The goal is to learn more about this and harness the powerful immunologic reactions that take place in order to induce and maintain remissions.” Hymes also says active research is under way to minimize GVHD without losing the graft-versus-tumor effect.
Milestones and achievements

CARDIOLOGY
For the fourth year in a row, 100% of the fellows who attended the Echo Board Review taught by Jose Banchs, M.D., assistant professor, passed their boards.

Allison Fee, advanced practice nurse, and Joy Wu and Anthony Barajas, cardiac ultrasound technicians, were named specifically by patients for providing outstanding service and care during the October Leader Rounds.


Dr. Lopez-Mattei also has been elected a fellow of the American Society of Echocardiography. The fellow designation recognizes members who have fulfilled both the training and performance requirements necessary for certification through the National Board of Echocardiography.

Myrshia Woods, physician assistant, received an Apple Award in recognition of her exceptional service to our patients. She was honored during the annual Health Education Week awards ceremony, Monday, Oct. 21.

Edward T.H. Yeh, M.D., professor and chair, spoke on the topic, “SUMO, Seizure and Sudden Death,” at the University of Pittsburgh, School of Medicine, Pittsburgh, Tuesday, Oct. 1.

Dr. Yeh was also invited to present at the AHA Scientific Sessions 2013, Sunday, Nov. 17. The title of his talk was “Molecular Basis for Chemotherapy-emerging Evidence and Evolving Perspectives.”

ENDOCRINE NEOPLASIA AND HORMONAL DISORDERS
Debra Nichols, research nurse; Shamim Ejaz, clinical investigational technician; Jassmyn Carr, coordinator, clinical studies; and Charles Stava, program manager; recently passed the Society of Clinical Research Associates (SOCRA) examination and are now Certified Clinical Research Professionals. The certification evaluates a practitioner’s knowledge, understanding and application of the conduct of clinical investigations involving humans in accordance with specific international guidelines and the United States Code of Federal Regulations and ethics that guide clinical research.

GASTROENTEROLOGY, HEPATOLOGY AND NUTRITION
Gottumukkala Raju, M.D., professor, will receive an American Society of Gastrointestinal Endoscopy (ASGE) Distinguished Service Award at the Digestive Diseases Week in May. Raju is being recognized for his long-term contributions to GI Endoscopy in the areas of equipment research and development. He is also receiving the award for his support of the educational and research mission of the society.

John Stroehlein, M.D., professor, was elected to a three-year term as the at-large member of the Executive Committee of the Medical Staff. Committee members, selected by their peers, exemplify outstanding leadership abilities and a solid knowledge base of the institution’s strategic planning efforts.

GENERAL INTERNAL MEDICINE
Geriatricians Beatrice Edwards, M.D., professor, and Holly Holmes, M.D., associate professor, were named specifically by patients for providing outstanding patient service and care during the October Leader Rounds.

Carmen Escalante, M.D., professor and chair, and Wenli Liu, M.D., associate professor, were named recipients of the 2013 General Internal Medicine Statewide Preceptorship Program Decade of Service Award at the Texas chapter’s annual meeting, Saturday, Nov. 16-Sunday, Nov. 17, in San Antonio. Both Escalante and Liu were recognized for their mentorship of medical students since 2003.

Jessica Hwang, M.D., associate professor, has been named co-chair of the American Society of Clinical Oncology (ASCO) Provisional Clinical Opinion Committee on Hepatitis B Testing. Hwang was extended the invitation because of her expertise in the field of Hepatitis B.

INFECTIOUS DISEASES, INFECTION CONTROL AND EMPLOYEE HEALTH
Javier Adachi, M.D., associate professor, has been elected to the 2013 Class of Fellows in Clinical Safety and Effectiveness for The University of Texas System. Dr. Adachi was recognized for his role in health care delivery improvement, and his contribution to patient safety.

Deputy Division Head Research Dimitrios Kontoyiannis, M.D., professor, has been nominated for the 2014 Robert M. Chamberlain Distinguished Mentor Award. The Postdoctoral Association Executive Committee recognized him for devoting a significant portion of his career toward the development of trainees. Kontoyiannis was honored at a ceremony on Tuesday, Feb. 4.

He has also been invited to serve on the Scientific Committee for the 6th Advances against Aspergillosis in Madrid, Spain, Thursday, Feb. 27-Saturday, Mar. 1.

Lisa Marsh, research nurse supervisor, was recognized among the four finalists for the 2013 Rogers Award during a ceremony, Friday, Sept. 27. Lisa is photographed with Regina Rogers, a senior member of the MD Anderson Cancer Center Board of Visitors, who established the award in 1987 to honor her parents, Julie and Ben Rogers. The award is also in appreciation for the treatment Rogers’ brother and mother received at our institution. George Calin, M.D., Ph.D., professor, Experimental Therapeutics, was named the 2013 recipient of the 2013 Julie and Ben Rogers Award for excellence in research.
Aparna Ingleshwar, postdoctoral fellow, received first place in the patient-centered care category at The Kelsey Research Foundations’ 14th Annual Health Services and Outcomes Research Conference, Tuesday, Dec. 10, in Houston. She was recognized for her work, “A Pilot Study to Evaluate a Multi-media Patient Decision Aid (MM-PtDa) for Osteoarthritis (OA), Osteoporosis (OP) and Rheumatoid Arthritis (RA) Patients.”


Josiah Halm, M.D., assistant professor, has been invited to present a poster at the International Forum on Quality and Safety in Healthcare in Paris. He will showcase the hospitalist section with his abstract, “Cancer Hospitalists” – Improving Cancer Outcomes and Contributing to Making Cancer History®.”

Robert Volk, Ph.D., professor, and a team of MD Anderson researchers, have been notified that they have been approved for a funding award by the Patient-centered Outcomes Research Organization (PCORI) to study, “Promoting Informed Decisions about Lung Cancer Screening.” The study is one of 82 proposals approved for PCORI funding to advance the field of patient-centered comparative effectiveness research, and to provide patients with information that will lead them to make better-informed decisions about their care.

Jichao Chen, Ph.D., assistant professor, was the recipient of the Distinguished Paper Award for July through September 2013 for the article, “Lung Epithelial Branching Program Antagonizes Alveolar Differentiation,” which was published in Proceedings of the National Academy of Sciences (PNAS).

Jose Banchs, M.D., was awarded a $200,000 grant from Astellas, Inc. for the study, “Use of Regadenoson for a Stress Echocardiogram Protocol Using Speckle Tracing Imaging.”

Tasneem Bawa-Khalfe, Ph.D., assistant professor, received a one-year, $50,000 Innovative Pilot Proposal Award from the Center of Cancer Epigenetics for her work, “SUMO-mediated Regulatory Control of Active Chromatin Sites.”

Dermatology

Rotating resident Lotika Singh, M.D., won first place for her poster at the Texas Dermatological Society Meeting in Galveston, Friday, Oct. 4-Saturday, Oct. 5, in Galveston. She was first author of the work, “Development of New Melanomas and Atypia in Pre-existing Nevi in Patients Undergoing BRAF-Inhibitor Therapy.” Sharon Hymes, M.D., professor, was final author.

At the same meeting, Whitney LaPolla, M.D., rotating fellow, received a third place poster award, while Rachel Gordon, M.D., rotating resident, received a third place for her podium presentation.

Emergency Medicine

Monica Wattana, M.D., instructor, is the recipient of a one-year, $22,000 Emergency Medicine Foundation/NIDA Award for her work, “Pilot Validation of an Opioid Misuse Risk Measure for Emergency Department Patients with Cancer.”

Jayne Viets-Upchurch, M.D., assistant professor, has been invited to present a poster on cord compression at the International Forum on Quality and Safety in Healthcare, April 8-11, in Paris.

The Kreg Anderson Workshop Prevention of Chemotherapy-induced Cardiotoxicity, Friday, Nov. 15, was a resounding success, according to organizers, with talks from national experts in the fields of breast cancer, leukemia, lymphoma, pediatric cancers, and sarcoma. The format was live and live-streamed to over 425 participants from 26 countries.

The Department of Cardiology, under the leadership of Edward T.H. Yeh, M.D., professor and chair, is the world leader in a new field called Onco-cardiology. With new insight from Yeh’s research, “Topoisomerase 2β: A Promising Molecular Target for Primary Prevention of Anthracycline-induced Cardiotoxicity,” Yeh says that “the time is ripe to develop strategies to protect cancer patients from chemotherapy-induced cardiotoxicity.”

In addition to primary and secondary prevention, survivorship issues were also discussed by a panel of experts. The workshop has been taped and can be viewed at www.cancerandtheheart.org.
Going Green in 2014

Stop! before you grab the Styrofoam cup in the break room or run your report to get a clearer view of it. The Division of Internal Medicine Team Anderson Award is Going Green this fiscal year by cutting back on the use of paper products.

“Specifically, the goal will be measured through a 5% reduction in copier paper and disposable cups,” says Kelly McDermott, project director, Internal Medicine administration, “and it also includes 75% compliance in the number of recycled toner cartridges throughout the fiscal year.”

McDermott says the conservation approach was an ideal choice when the institution announced that divisions and their departments would need to meet or reduce the operating expense budget.

“The Fiscal Year 2014 Incentive Plan goals are changing to be more relevant to an employee’s role at the MD Anderson. They’re also meant to be more attainable and meaningful to employees, promote collaboration throughout the division and focus on quality of service, level of accountability and operational efficiencies,” she says.

Targets, triggers change, too

This year, the award will shift from an institutional financial trigger to achievement of division financial and performance targets. For instance, there is a payout trigger once the division’s annual operating expense budget is met. McDermott says the payout expectations were established by the institution and all divisions are expected to meet or beat this effort. Employees are eligible to receive the payout if one or both of the payout goals have been met:

1. The department meets or reduces the operating expense budget, and
2. It achieves a non-financial, mission-driven goal that focuses on achieving operational efficiencies that is quality or productivity-based.

Another major difference is the level of payout,” McDermott says. “Employees can be left in the dark and get nothing or earn up to $600. If the division does not meet the operating expense budget, then no one will receive anything. If we meet our operating expense budget and your department meets one of its goals, then you will receive $200,” she explains. Finally, departments can receive different amounts, depending on the goals that each department achieves.

“We recognize that this may require a shift in the way that some employees go about their daily routine. It does take a conscious effort to use less paper and to refrain from grabbing that disposable cup.”