n ew Insights Into Lethal Melanomas

Zebrafish model of human tumor reveals genetics, promising drugs

Researchers at Children’s Hospital Boston and collaborators from several other institutions have used a zebrafish model of melanoma to identify two important mechanisms that promote the growth of this aggressive human skin cancer, which begins in pigment-producing melanocytes.

In the first of two papers featured on the cover of the March 24 issue of *Nature*, the scientists established a new oncogene in melanoma: SETDB1, the first identified using a zebrafish model of the disease. In the second paper, the same Children’s researchers used the model to determine that the combination of an existing arthritis drug and a new drug under study for late-stage melanomas with mutations in the gene BRAF may hold promise for treating some types of melanoma.

The zebrafish melanoma model was developed about six years ago, said Leonard Zon, the Grousbeck Professor of Pediatrics and director of the hospital’s Stem Cell Program and senior author of both papers, “to find new genes that caused human melanoma and support the development of new drugs against a disease for which there are very few treatment options.”

Target Identified for Aggressive Breast Cancer

Given current early detection methods for breast cancer, many people can be treated successfully. But for the 20 percent of patients with so-called triple negative breast cancer, the outcome is bleak.

Now, however, researchers from Harvard Medical School and Baylor College of Medicine have identified a critical molecular component to the disease. Additional experiments in mice suggest potential therapies involving combinations of FDA-approved, readily available drugs.

“Whereas many basic discoveries have the potential to impact patients’ lives within ten, 20 or 30 years, this has the potential to impact patients’ lives within one year,” said Thomas Westbrook, formerly a postdoctoral fellow at HMS and an assistant professor of biochemistry and molecular biology at Baylor College of Medicine since 2007.

The Wisdom of Crowds

Contest yields innovative strategies for conquering Type 1 diabetes

Seven research teams with fresh approaches to solving the riddle of Type 1 diabetes have received funding through an initiative that first tapped the creativity of Harvard’s schools and affiliated institutions just over a year ago.

It was in February 2010 that the Harvard Clinical and Translational Science Center, known as Harvard Catalyst, launched a bold crowd-sourcing experiment called the Ideation Challenge. Some 40,000 faculty, staff and students, along with the general public, were invited to answer the question: What do we not know to cure Type 1 diabetes?

A panel of experts reviewed 190 suggestions and zeroed in on 12 outstanding responses—some of them from nonexperts, including a student at Harvard College and a human resources manager at HMS. Each of the dozen contest winners received $2,500 and agreed to release their idea and intellectual property to Harvard.

Luft Award to Dean Flier

HMS Dean Jeffrey S. Flier (above, with Karolinska Institutet President Harriet Wallberg-Henriksson) received the international Rolf Luft Award in March for seminal research on insulin and leptin physiology and the mechanisms underlying their defective action in metabolic diseases.

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In this portrait of Pablo Picasso, the differing positions of the points of light in the artist’s eyes suggest their misalignment.

both eyes, are more common among artists than non-artists. Moreover, according to the team’s assessment of photographs of established artists, artists’ eyes often show misalignment, especially when compared to a control population of non-artists. Eye misalignment, a condition known as strabismus, contributes to poor stereopsis.

The unexpected advantage gained by overriding the brain’s tendency to layer depth into the tandem views captured by the eyes has long been recognized by teachers of art. Budding representational artists are often counseled to close one lid and peer through a single eye at the subject of their attention. Shuttering one eye, says Livingstone, defeats stereopsis and heightens visual cues for depth, such as shading and perspective.

In their two-part study, Livingstone, Bevil Conway, HMS lecturer on neurobiology and assistant professor of neuroscience at Wellesley College; and former Wellesley student Rosa Lafer-Sousa tested stereoscopic accuracy among 403 art students from two U.S. art schools noted for their emphasis on representational rendering. They then compared those results with the same measurements for 190 non-artist peers at two universities. Next, the investigators assessed stereopsis among established artists by adapting an eye alignment test and using it to measure alignment in photographed eyes. The researchers used photographs of notable artists drawn from respected archives, the National Gallery of Art and the Smithsonian American Art Museum. As a control, the team measured eye alignment in photographs of an age- and gender-matched group of U.S. congressional representatives.

The team not only found poorer stereoscopic accuracy among the art students as compared to the non-artists, but also found a prevalence of eye misalignment among the established artists, indicating an increased incidence of strabismus.

Does all this mean poor eye alignment is necessary for artistic success? No, cautions Livingstone, “You can get the same effect simply by closing one eye. But, at a minimum, if poor stereopsis doesn’t contribute to artistic talent, it certainly doesn’t detract from it.”

—Ann Marie Menting

For more information, students should contact Margaret Livingstone, professor of neurobiology at margaret_livingstone@hms.harvard.edu.

The eye of the Beholder

Neurobiology sheds new perspective on the artist’s gaze

One of the challenges of learning to paint the world is figuring out how to collapse the three dimensions of life onto a two-dimensional canvas. Part of that difficulty is technical; the evolving artist must grasp the subtleties of paint, stroke and dimensions of life onto a two-dimensional canvas.

In photographs of an age- and gender-matched group of U.S. congressional representatives.

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TRaA MiLs I3o d y AMICs. A n CuTu TROL O F CHOLLARa I NHA TI: An p iEeMiC M oD 4L
Andrews JR, Basu S. Division of Infectious Diseases, Massachusetts General Hospital and HMS; HSPH Center for Communicable Disease Dynamics. Official projections of the cholera epidemic in Haiti have not incorporated existing disease trends or patterns of transmission, and proposed interventions have been debated without comparative estimates of their effectiveness. We used a mathematical model of the epidemic to provide projections of future morbidity and mortality, and to produce comparative estimates of the effects of proposed interventions. We conclude that a decline in cholera prevalence in early 2011 is part of the natural course of the epidemic, and should not be interpreted as indicative of successful intervention. Substantially more cases of cholera are expected than official estimates used for resource allocation. Combined, clean water provision, vaccination and expanded access to antibiotics might avert thousands of deaths. Lancet 2011 March 16.

s HORTC ts T O MA kln C A R 6 0 M nDy T o s
Xu H, BA, Chien KR. Cardiovascular Research Center, Massachusetts General Hospital; Harvard Stem Cell Institute, Department of Stem Cell and Regenerative Biology, Harvard University. The adult human heart lacks sufficient regenerative capacity to recover after a myocardial infarction. Cell-based therapy has emerged as a potential treatment for the failing heart; however, a key issue for the success of future cell-based therapies is the ability to obtain patient-specific high-quality cardiomyocytes in a fast and efficient manner. Recent progress has been made towards this goal using reprogramming-based approaches. Nature Cell Biology. 2011 March;13(3):191-9.

X C H I R O M D O s M D aD y A COM P s a T I d e s v i a n H A s C e d TR A s a C R I P T I O N e L D e s a F T I d e s r D r a a s p h a
Larsen E, Bishop ER, Kierstanova IV, Cara LJ, Li JP, Park PJ, Kuroda MR. Division of Genetics, Department of Medicine, Brigham and Women’s Hospital. The evolution of sex chromosomes has resulted in the X chromosome of (female) complex increases transcription on the single (male-specific lethal) chromosome requiring dosage compensation. MS 2011 March 23. (8)(26):115-4.

R eL A T I O n s b H iP B eTw W en a q uA L I T Y O F CA R e s d n aL I g G en e C o T I g L I t I d e s r s u N s R a l n G H O Ms. Student DM, Spaital NA, Mello MM, O’Malley AJ, Stevenson DG. Melbourne School of Population Health, University of Melbourne; HMS Department of Health Care Policy. It is unclear whether high-quality health care institutions are less likely to be sued for negligence than their low-performing counterparts. We linked information on tort claims brought against 1,465 nursing homes between 1998 and 2006 to 10 indicators of nursing home quality drawn from two U.S. national data sets. We conclude that the best-performing nursing homes are sued only marginally less than the worst-performing ones. Such weak discrimination may subvert the capacity of litigation to provide incentives to deliver safer care. New England Journal of Medicine. 2011 Mar 31;364(13):1243-50.

Focus on understanding Cancers

HMS affiliates are advancing our understanding of cancer to improve human health

MuTAble Lung T uMoRs s Hed Lig HT O n Res i T aN Ce
A detailed analysis of lung tumors that became resistant to targeted drugs revealed two previously unreported resistance mechanisms. In the March 21 Science Translational Medicine, investigators from Massachusetts General Hospital Cancer Center and HMS also describe how the cellular nature of some tumors actually changes in response to treatment and find that resistance-conferring mutations can disappear after treatment is discontinued. The findings support the importance of monitoring the molecular status of tumors throughout treatment.

“Very remarkably, how much we oncologists assume about a tumor based on a single biopsy,“ said lead author Lecia Sequist, HMS assistant professor of medicine at Mass General. Non-small-cell lung cancer (NSCLC) is the leading cause of cancer death, and in about 12 percent of patients the tumor is driven by a mutation in the epidermal growth factor receptor (EGFR). Targeted drugs called tyrosine kinase inhibitors (TKIs) block EGFR activity and can halt the growth of such tumors, but resistance usually develops.

To better understand why, the research team analyzed the genotype and the phenotype of tumor samples from 37 NSCLC patients, taken both before TKI treatment and when resistance first appeared. The results validated previously reported mechanisms of resistance and identified two more genetic changes: mutations in another oncogene called FGFR4 and overproduction of the EGFR molecule itself.

ToLoMeRaSe In HIBOTOR PinX1 seen T o su Ppress TuMoRs
It’s been nearly 10 years since Beth Israel Deaconess Medical Center scientists Kan Ping Lu and Xiao Zhen Zhou discovered PinX1, the first potent endogenous protein shown to inhibit telomerase in mammals. Now the scientific team has discovered a critical new function for this telomerase inhibitor. The investigators reported March 23 in the Journal of Clinical Investigation that low levels of PinX1 contribute to cancer development, providing the first genetic evidence linking telomerase activation to chromosome instability and cancer initiation, and suggesting a new avenue of treatment for cancers.

“Although telomerase is activated in 85 to 90 percent of human cancers, little has been known about the significance of telomerase activation in chromosome instability and cancer initiation,” explains Lu, the paper’s senior author and HMS professor of medicine at BIDMC. “We have discovered, for the first time, a novel role for abnormal telomerase activation in cancer initiation. This suggests that telomerase inhibition using PinX1 or other small molecules may be used to treat certain cancers with activated telomerase.”

Notably, the discovery that most PinX1-mutant mouse tumors share tissues of origin with human cancer types linked to alterations in chromosome 8p23 suggests a possible role for deregulation of the PinX1/telomerase complex in treating several common carcinomas, including breast, lung, liver and gastrointestinal cancers.

Multiple independent lung tumors metastasized from breast cancer in PinX1 mice. It’s a rare development in single-gene knockout mouse tumor models, says j orden- ick Bronson, an HMS lecturer on pathology who collaborated with researchers at Beth Israel Deaconess Medical Center.

MultiPL e MyLOMA gen OMe y ields u nE x pE c t e d i n s gHiTs
Scientists have unveiled the most comprehensive picture to date of the full genetic blueprint of multiple myeloma, a form of blood cancer. A study of the genomes from 38 cancer samples has yielded new and unexpected insights into the events that lead to this form of cancer and could influence the direction of multiple myeloma research. This work, led by scientists at the Broad Institute of MIT and Harvard and Dana-Farber Cancer Institute, appeared March 24 in Nature.

Multiple myeloma is the second most common blood cancer in the United States, with about 20,000 new cases diagnosed in this country each year. The emerging genome-wide picture of multiple myeloma reveals genes never before associated with cancer as well as multiple mutations that disrupt just a handful of common pathways, or chains of chemical reactions that trigger a change in a cell. Individually, each mutation is fairly uncommon and might have remained undiscovered had researchers not looked at such a large collection of samples.

“Already, we can see that mutations are tumorigenic within a limited number of pathways,” said co-senior author Todd Golub, director of the Broad’s Cancer Program and Charles A. Dana Investigator in Human Cancer Genetics at Dana-Farber Cancer Institute. “This is a demonstration of the value of looking at more than just a single tumor at great depth.”

—From the news offices of Mass General, Beth Israel Deaconess and Dana-Farber
Compost It

HMS prepares to celebrate Earth Day, removes food from waste stream

It was 20 degrees outside, but the compost piles were steaming at Brick Ends Farm, in Hamilton, Mass. Harvard students toured the farm on March 26 to learn about post-consumer composting and discover what happens to apple cores and soup containers after they leave Harvard’s cafeterias.

The tour was part of the gearing-up for Earth Day on April 22. All month long, Harvard’s faculty, students and staff will be raising awareness of sustainability. At HMS, the focus is on “post-consumer” composting in the Courtyard and Atrium cafes. On April 18, HMS Campus Operations, Restaurant Associates and Harvard’s Office for Sustainability will provide information and a video in the cafes, where volunteer “composting ambassadors” will demonstrate how to compost correctly, creating a waste stream of food scraps, napkins and compostable take-out containers.

Match day 2011

Medical schools across the country hosted annual Match Day ceremonies on March 17, during which 16,559 medical school seniors learned where they are going to spend the next three to seven years for their residency training. At HMS, approximately 170 seniors matched to residency programs across the country, with the greatest number matching in internal medicine.

Family medicine program matches increased the most at HMS. This trend held true nationwide, with family medicine programs experiencing the strongest growth in the number of positions filled, according to the National Residency Matching Program (NRMP). Pediatrics, internal medicine, emergency medicine, anesthesiology and neurology also increased in popularity. The most competitive fields, according to the NRMP, were dermatology, orthopaedic surgery, otolaryngology, plastic surgery, radiation oncology, thoracic surgery and vascular surgery.

The 2011 match offered more than 23,000 first-year residency positions, and more than 95 percent of those were filled. Nationwide, 81 percent of those students matched to one of their top three choices. The NRMP is a non-profit organization sponsored by several national medical societies in order to provide an orderly and fair way to match applicants to U.S. residency positions.

—Angela Alberti

Toward Better Child Care

Summit yields strategies for change

From saving lives to expanding knowledge to shaping global policy, the challenges of a career at HMS and its affiliates are immense and rewarding. From saving lives to expanding knowledge to shaping global policy, the challenges of a career at HMS and its affiliates are immense and rewarding.

But for faculty, staff and students balancing work and family, another challenge can be overwhelming: arranging child care in a community where demand far outstrips supply.

That challenge drew 180 participants on Jan. 25 to “Child Care Summit: Future Directions,” organized by the Joint Committee on the Status of Women at HMS and the Harvard School of Dental Medicine. At the Summit, or to learn more about the Joint Committee on the Status of Women, including how to join, visit www.hms.harvard.edu/jcsw.

Summit organizers shared conclusions that emerged from breakout sessions at the summit, from expanding options for flexible work hours to building information networks across institutions.

The NRMP is a non-profit organization sponsored by several national medical societies in order to provide an orderly and fair way to match applicants to U.S. residency positions.

—R. Alan Leo

To read the full report from the Child Care Summit, or to learn more about the Joint Committee on the Status of Women, including how to join, visit www.hms.harvard.edu/jcsw

On Jan. 25, a child care summit drew about 180 participants from across the Harvard community to the Joseph B. Martin Conference Center.

At Brick Ends Farm, Harvard students get a tour of the compost fields from Peter Britton, who founded the farm in 1975 to improve local farm land and divert food waste from landfills.

"To be successful, everyone must make a conscious behavior change," said Longwood Sustainability Manager Claire Berezowitz. At HMS, cafeterias compost waste from food production, but a challenge, Berezowitz said, is to recognize and dispose of non-compostables, such as coffee cups from outside vendors. For inspiration, she points to the Harvard School of Public Health, which kept 103.3 tons of material out of landfills last year, saving $2,289 in trash-hauling fees.

Composting has benefits beyond the environmental and financial. At Brick Ends Farm, the product is bagged by Bass River, an organization for disabled adults. Bag labels were designed by patients from Children’s Hospital Boston through Kids B Kids, a non-profit children’s art group. Proceeds go to Children’s to fight childhood cancers, said Kids B Kids co-founder Jan Weinshanker. The 20-pound bags were set to go on sale in April at local grocery and garden stores.

—Angela Alberti

For a full list of Harvard-wide Earth Day events, visit green.harvard.edu.
How can it be that physicians and nurses worked actively in collaboration with government leaders to sterilize and kill “undesirables” during the Nazi era? How did those health care professionals come to subordinate their obligation to individual patients to a perceived obligation to the state-as-patient? What were the intertwined ideological and scientific origins of “racial hygiene”? And what lessons might we draw for contemporary medicine and society?

These questions that will confront visitors to “Deadly Medicine: Creating the Master Race,” an exhibition by the United States Holocaust Memorial Museum that opens April 14 at the Countway Library, Harvard Medical School has partnered with the museum to bring the exhibition and its provocative questions to health care professionals in training, including students of medicine, nursing, law and public health, as well as their faculties, staff members and the public. To inspire and lead debate, the museum and HMS will sponsor related public forums and events on campus and across Boston.

Few adults are ignorant of the virulent anti-Semitism of the Third Reich and the Nazis’ attempted annihilation of Europe’s Jews. Most are familiar with the horrors of medical experimentation attached to the concentration camps, and the name Josef Mengele remains a notorious synonym for monster-physician. What far fewer people know is that, in the Nazi era, the medical profession and its opinion elites played a central role in conceiving and promoting the concept of “racial hygiene,” which became the ideological foundation for Hitler’s efforts to purify the German nation. Indeed, a symbiotic relationship existed between medical professional elites and the Nazi regime: Nazi policies supported public health measures that many physicians already had come to embrace years before, while the profession’s imprimatur and active involvement became the literal means of effecting Hitler’s plans.

For example, in addition to eliminating “non-Aryans”—Jews, Gypsies and others who differed from Nazi stereotypes of the ideal German—it was seen as important for the health of the nation to eradicate “feeblemindedness,” physical deformity, alcoholism, blindness and deafness. More than 400,000 German men and women were sterilized, many through orders issued by “heredity health courts” comprising geneticists, physicians and anthropologists, who offered a patina of respectability to the unconscionable process.

Likewise, convinced that maintaining “non-productive” members of society within institutions at government expense was a waste of resources, Hitler instituted a secret, so-called euthanasia program that some physicians and nurses helped implement. More than 200,000 Germans, including 5,000 children, were killed between 1935 and 1945. These murders of German citizens began before and continued during the Holocaust.

Of course, not all health care professionals supported Hitler’s plans. Of what relevance to medicine today are the lessons of eugenics? Join this month’s discussion at the HMS Idea Lab, a virtual laboratory for sharing opinions on research, academic medicine, medical education and more.

Exhibit explores lessons in eugenics from the Nazi era

Guest essay by Mildred Solomon and Scott Podolsky

Solomon is an associate clinical professor of medical ethics in the departments of Global Health and Social Medicine (GHSM) at HMS and of Anesthesia at Children’s Hospital Boston, and director of the Fellowship in Medical Ethics within the HMS Division of Medical Ethics. Podolsky is an assistant professor of social medicine in GHSM and director of the Center for the History of Medicine at Countway Library. The opinions expressed are those of the authors and not necessarily those of Harvard Medical School, its affiliated institutions or Harvard University.

Models of racial types (near left) served as teaching aids in racial hygiene classes at the Berlin School for the Blind, where students (far left) were taught Gregor Mendel’s principles of inheritance and their applications to heredity. In Nazi Germany, German-born blind children were urged to submit to sterilization.

Of what relevance to medicine today are the lessons of eugenics? Join this month’s discussion at the hMS Idea Lab, a virtual laboratory for sharing opinions on research, academic medicine, medical education and more.
Melanoma

Continued from page 1

Melanoma has a poor prognosis when diagnosed late. In the United States, there were about 68,000 new cases and 8,700 deaths in 2010. Mutations in BRAF, a core characteristic of the Zon lab’s model, are seen in about 50 to 60 percent of human melanomas. But BRAF mutations are also seen in benign moles and are by themselves insufficient to cause cancer; other mutations must also be present. The team set out to pinpoint other candidates in a region of chromosome 1 called 1q21 in which a stretch of 54 genes are amplified in about 30 percent of melanoma patients. Of those 54, SETDB1 stood out: It was the only gene that worked with BRAF to fuel tumor development.

By THOMAS MARSH

“Along with being a creative approach, it was truly a brute force scientific effort to home in on SETDB1,” said Leonard Zon, director of the Harvard Catalyst Linkages Program.

According to HITI Co-directors Arlene Sharpe, the George Fabyan Professor of Comparative Pathology, and Larry Turka, HMS lecturer on medicine at Beth Israel Deaconess Medical Center, the goal of these seven research projects is threefold: to better understand the origins of these diseases, to formulate immune-based assays to support human clinical trials and improve diagnostics, and, ultimately, to develop novel therapies.

Most of the winning entries involve the creation of new, multidisciplinary teams that introduce new investigators to the study of Type 1 diabetes.

“Assembly of these groups is in itself an important metric of success,” said Eva Guinan, director of the Harvard Catalyst Linkages Program.

For more information, students may contact Leonard Zon at zon@enders.tch.harvard.edu. For more information, students may contact Leonard Zon at zon@enders.tch.harvard.edu.
The team identified the critical enzyme by looking in petri dishes for proteins whose absence caused normal breast cells to become cancerous. “We were looking for genes that pushed the cells over the edge,” explained Stephen Elledge, the Gregor Mendel Professor of Genetics and a professor of medicine at Harvard Medical School.

One of tyrosine phosphatases’ primary jobs is to turn off another group of enzymes critical for growth called receptor tyrosine kinases. The researchers reasoned that, if they could identify the enzymes that were switched on in the absence of PTPN12, they could pinpoint critical drug targets that might be used to develop therapies for patients with triple-negative breast cancer.

To identify these proteins, the team turned to HMS Professor of Cell Biology Steven Gygi. By taking a look at all proteins activated in cells lacking PTPN12, the researchers found two enzymes crucial for breast cancer’s progression, or metastasis, EGFR and HER2.

In addition, the team used biochemical methods to identify a third receptor enzyme, called PDGFR-β, that was also regulated by PTPN12.

Together, these results suggest that the improper activation of these three tyrosine kinases could be the major cause of triple-negative breast cancer. “We’ve grabbed a molecular foothold in triple-negative breast cancer,” said Westbrooke, who discovered PTPN12 as a postdoctoral fellow in Elledge’s laboratory. “We are now starting to understand the disease better. Even more important, we have a rationale for a combined drug therapy for the disease.”

Their idea: to treat the disease, turn off the trio of enzymes with drugs.

**FeA-APPROved Options**

To test their strategy, the team took advantage of two drugs already being used to battle other types of cancer: laptanib (Tykerb), which turns off EGFR and HER2, and sunitinib (Sutent), which turns off PDGFR-β.

The team treated mice with triple-negative breast cancers with either sunitinib or laptanib, or both. In mice treated with sunitinib alone, tumors shrank by nearly 80 percent. But in mice treated with both drugs, tumors shrank by more than 90 percent—and life expectancy more than doubled.

These results suggest that sunitinib and laptanib (or similar drugs) together may be a promising therapy for people with triple-negative breast cancer. And because both drugs are already FDA-approved and sitting on pharmacy shelves, they can be tested immediately in these patients.

“This research underscores the relation of basic bench science to human health,” said Elledge. “If you know what’s driving the cancer, you can think about targeting that for therapy.”

The team hopes to launch a phase II trial for triple-negative breast cancer by the start of 2012.

---Michelle Pfamm

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**When Medicine Has Nothing More to Offer**

The transition to end-of-life care tests patient and doctor

I pulled back the curtain to reveal my patient, dying quietly on a gurney. Death had stalked him. Almost a year earlier, as his wife was dying of metastatic cancer, he himself began to develop symptoms that could not be ignored: night sweats, malaise, fevers. As his wife’s primary caregiver, he stayed with her to the end. And despite attempts to properly evaluate his new symptoms, he missed most of his own medical visits, the short time with his wife too precious.

Days after his wife’s death, he came to the clinic and was admitted quickly for dehydration and expedited evaluation. In such situations, I have learned to hope for infection as the cause; the alternative almost always is cancer. The diagnosis was grim: Stage IV Hodgkin’s lymphoma. Over the next year, he went from one chemotherapy regimen to the next, each failing to slow the progression of disease. Most days he was hopeful, and sometimes his optimism troubled me. How could he feel so well when the PET scans clearly indicated he was losing this battle?

By the time he had reached the final chemotherapeutic option—at this stage his treatment could be considered “extreme salvage”—the reality of his imminent death had begun to set in. Clearly, if this treatment failed him, and odds were it would, we had nothing more to offer.

Nothing more to offer. To this nascent clinician, the concept seemed foreign. Even in the age of antibiotic resistance, we can almost always do something, irrespective of the diminishing returns.

The patient’s health declined rapidly, and symptom management, or palliation, became the goal of his care. A few days before his final admission, he had sounded upbeat as he described a steak meal, a stark contrast to how we found him, awaiting admission for end-of-life care.

On the gurney, he was groggy, a side effect of medications to ease his pain and nausea. His face was gaunt. He looked feeble, a shadow of the stocky, healthy man he had been so recently. At first, he did not appear to recognize us, and I feared that I would not get a chance to say goodbye, or that he would be too confused or withdrawn to comprehend. My mentor, who had known the patient and his wife for the better part of a decade, held his hand and spoke to him, asking gently: Was he in pain? Did his family understand the extent of his illness? Did he need to speak with anyone? Was he at peace?

---Erica Seiguer Shenoy, MD-PhD ’07, is a fellow in infectious disease at Massachusetts General Hospital and Brigham and Women’s Hospital.

The opinions expressed in this column are not necessarily those of Harvard Medical School, its affiliated institutions or Harvard University.
Deadly Medicine
Continued from page 5

racial hygiene policies, the ideology of genetic determinism, or programs of sterilization and euthanasia. “Deadly Medicine” creates an opportunity to reflect not only on the social, political and economic determinants of these events, but also on the moral choices that individual professionals face today on a range of issues.

Visiting the exhibition and its website (www.usihm.org/deadlymedicineboston) and participating in related forums will prompt more questions than answers. We hope that people will not view the Nazi story as an aberration of the deep past, far removed from contemporary circumstances, an impossibility anywhere else. Nazi physicians believed they were acting in the people’s interest, on behalf of public health; they were blind to their own excesses. Most people are, including, and perhaps especially, esteemed professionals.

Therefore, the exhibition should remind us to remain alert to our inherent biases and the possibility of committing or participating in wrongful acts that we haven’t recognized as wrong. On the other hand, it can be easy to overgeneralize and make simplistic comparisons to modern health policies. For example, the very use of the term “euthanasia” could introduce confusion, leading some people to mistakenly equate the current ethical framework in the United States for making decisions about the use of sustaining technologies near the end of life with the Nazi program of systematized murder. Careful analysis of similarities and differences between contemporary events and Nazi policies can head off overly broad generalizations and the demagoguery that might result.

A notable
Ruhul Abid, HMS assistant professor of medicine at Beth Israel Deaconess Medical Center, will be recognized April 26 with the 2011 Werner Rusch New Investigator Award in Vascular Biology. His paper, “Endothelium-dependent Coronary Vasodilation Requires NADPH Oxidase-derived ROS,” was selected as the most outstanding paper published during 2010 in the vascular biology section of the journal Arteriosclerosis, Thrombosis and Vascular Biology.

Donna Berry, HMS associate professor of medicine and director of the Center for Research in Nursing and Patient Care Services at Dana-Farber Cancer Institute, will accept the Oncology Nursing Society’s Distinguished Researcher Award at the 2011 DNS Congress in Boston on April 28. Berry is widely recognized for her research involving patient-centered oncology care and leadership within oncology research.

Constance Cepko, HMS professor of genetics and professor of ophthalmology, has received the 2011 Alfred W. Bressler Prize in Vision Science. The prize, announced March 8 by the Jewish Guild for the Blind, recognizes her discoveries of the causes of retinal degeneration in retinitis pigmentosa (RP) and possible future therapeutic benefits to humans. The Cepko lab discovered in a mouse model of RP that cone cell death is primarily caused by a nutritional deficit resulting after rod death. Cone life can be prolonged by injecting the mice with insulin. Future applications may allow people with RP to maintain daylight and color vision longer.

Jeffrey S. Flier, dean of the Faculty of Medicine, received the international Roßl Prize Award from the Karolinska Institute in Sweden on March 18 for seminal contributions to the understanding of the physiology of insulin and leptin and the mechanisms underlying their defective action in metabolic diseases. Flier gave the prize lecture, “Hormone Resistance in Diabetes and Obesity: Insulin, leptin and FGFR2.”

Flier’s contributions to the understanding of obesity and insulin resistance have had a significant impact on lipid research, particularly in the arena of leptin action and resistance. He is credited with the groundbreaking observation that leptin is likely to be the key signal that informs the brain of the transition between the adequately nourished and the starved state. Flier has also made substantive contributions to research on the metabolic syndrome as well as on insulin action and resistance.

Previous I Uff honorees at HMS include C. Ronald Kahn, Mary K. Lecouca Professor of Medicine at Brigham and Women’s Hospital and Joslin Diabetes Center; Bruce Spiegelman, the Stanley J. Kornmeyer Professor of Cell Biology and Medicine at Dana-Farber Cancer Institute; and Lewis Cantley, the William Bosworth Castle Professor of Medicine at Beth Israel Deaconess Medical Center.

American Institute for Medical and Biological Engineering’s College of Fellows on the basis of his major contributions to cell and tissue engineering, angiogenesis and cancer research, systems biology, and nanobiotechnology. Ingber, the Judah Folkman Professor of Vascular Biology in the Department of Pathology at Children’s Hospital Boston, is recognized for his pioneering efforts in the emerging field of biologically inspired engineering.

AAMC Call for nominations
The American Association of Medical Colleges invites nominations for its 2011 research and education awards, including the Flexner Award for Distinguished Service to Medical Education. Nominations are due May 2. For more information, visit www.aamc.org/initiatives/awards.