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McCain Surgery Puzzles Melanoma Experts, But Some Clues Found In Reporters' Notes

By Paul Goldberg

A massive scar that begins on John McCain's left temple, bisects his cheek and runs down his neck is a graphic reminder of a melanoma surgery he had eight years ago.

Experts in treating the deadly cancer say this scar is difficult to explain. In August 2000, when the Arizona Senator received his surgery at the Mayo Clinic in Scottsdale, he possibly could have been spared the disfigurement had he gone to a major academic center with a strong melanoma program.

Could the scar be interpreted as indication that the 72-year-old Republican Presidential candidate had more advanced disease than the campaign acknowledged? Could it be that he received "VIP care" that

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In the Cancer Centers:

MSKCC Receives Interest In Geoffrey Beene; Baylin, Jones Win Workman Memorial Award

MEMORIAL SLOAN-KETTERING Cancer Center received a membership interest in Geoffrey Beene LLC, the business and fashion company of the designer **Geoffrey Beene**. Revenues from the gift will be used to support the Geoffrey Beene Cancer Research Center, established two years ago at Memorial Sloan-Kettering with funds from Beene's estate. The new contribution brings the total value of gifts from the various Beene entities to Memorial Sloan-Kettering to over $100 million. "We are especially grateful to **Tom Hutton** and his colleagues at Geoffrey Beene LLC, for recognizing the significance of the work being done here and for making this extraordinary new investment to help move it forward," said **Harold Varmus**, president of MSKCC. Programs that will be supported include translational research, core research labs, and the establishment of senior and junior faculty chairs, graduate fellowships, and the Geoffrey Beene Symposium. Activities of the Geoffrey Beene Cancer Research Center are overseen by an executive committee that includes Varmus as chairman, **Thomas Kelly**, director of the Sloan-Kettering Institute, and **Robert Wittes**, physician-in-chief, Memorial Hospital. . . . **STEPHEN BAYLIN** and **PETER JONES** will receive the David Workman Memorial Award from the Samuel Waxman Cancer Research Foundation for their research identifying molecular processes that silence genes which suppress tumors, thereby aiding the growth of cancers. Baylin is deputy director of the Sidney Kimmel Comprehensive

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Press "Pool" Reports Appear To Support Stage IIA Diagnosis

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bypasses normal procedures, but sometimes ends up producing worse outcomes for John McCain than for Joe the Plumber?

A pro-Obama group recently took out a full-page ad in The New York Times demanding a full release of information on McCain's health. Last May, the campaign allowed a pool of 20 reporters to review 1,173 pages of medical documents. Reporters could take notes, but were precluded from making copies of documents that included the pre-operative plan and the surgery report.

McCain's doctors spoke with the press at a campaign-organized telephone conference May 23, the Friday before Memorial Day. After that, Mayo doctors weren't allowed to respond to further questions.

Trying to glean clinical information from media reports, melanoma experts seemed to be more confused than Joe Sixpack.

—"It's hard for people in the medical field who do melanoma for a living, without more information, to understand exactly what was done and why," said Vernon Sondak, a melanoma surgeon and chief of the Division of Cutaneous Oncology at H. Lee Moffitt Cancer Center in Tampa.

—Michael Atkins, a melanoma expert at Harvard, takes this a step further. "It is difficult to reconcile [McCain's] reported diagnosis with the treatment," said Atkins, director of the Cutaneous Oncology and Biologic Therapy Programs and director of the Cancer Clinical Trials Office at Beth Israel Deaconess Medical Center and leader of the Kidney Cancer Program at the Dana-Farber Cancer Institute.

—Donald Morton, the surgeon who pioneered a less invasive surgery that is commonly used to stage melanoma, said his procedure, called sentinel node biopsy, was the standard of care at top melanoma centers by August 2000, when McCain received his disfiguring treatment.

"If he had seen me, I would have probably done a sentinel lymph node dissection and saved him the morbidity of the parotidectomy and neck dissection," said Morton, chief of the Melanoma Program at John Wayne Cancer Institute.

Generally, McCain's aggressive surgery would be more common for a higher-stage melanoma with positive lymph nodes, experts said. Also, press reports cited a document that raised the possibility that McCain had a "satellite" tumor, which would have placed him at a higher risk of recurrence. "I don't know whether he had Stage IIA or IIIB," said Lynn Schuchter, interim chief of the Division of Hematology/Oncology at the University of Pennsylvania Abramson Cancer Center and a melanoma expert.

"Pool Report" Notes Prove Informative

Though several reporters who covered McCain's health were physicians, their accounts of the information were written on tight deadlines and calibrated for a lay audience. This didn't help melanoma experts, who craved unfiltered clinical information.

After the news cycle moved on, some reporters returned to the story, most recently Lawrence Altman of The New York Times. His most recent story, which includes an account of his wrangling with the McCain campaign over access to the Senator's health information, appeared on Oct. 20.

Yet, unbeknownst to most melanoma experts, additional clinical information was, in fact, publicly available, posted on the Web in the form of "pool reports" prepared by journalists at the campaign's May 23 information dump.

One report, which deals most directly with the surgery, is posted at http://i.usatoday.net/news/mmemmottpdf/mccain-health-pool-2-5-23-2008.pdf. Another report, which covers the aftermath of the surgery as well as McCain's general health, is posted at http://marcambinder.theatlantic.com/archives/2008/05/mccains_health_records.php. Though more valuable to

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physicians than any news story, these notes have been available only to those who followed the right blogs or knew the right search words.

Melanoma expert Atkins found these notes more informative than any past news story on the subject. In his view, the documents, which he didn't see until they were shown to him by The Cancer Letter, suggest that McCain's tumor would most likely be classified as Stage IIA, which is consistent with information disclosed by the campaign.

Also, the surgery that produced McCain's massive scar could be explainable because of the size of the excision around what was likely a wide area of melanoma on the temple, Atkins said.

While some of the documents have been cited in the press, they were abridged and placed in a different context. A pool report by The Washington Post health reporter David Brown, basically his raw notes, includes a document from two pathologists at the Armed Forces Institute of Pathology, who examined a biopsy of a melanoma taken off McCain's temple.

"The vertical orientation of this lesion with only focal epidermal involvement above it is highly suggestive of a metastasis of malignant melanoma and may represent a satellite metastasis of S00-9572-A," which was a "skin, left temple, lateral" biopsy, the document reads.

If indeed McCain had a satellite lesion and no positive lymph nodes, his disease would be staged IIIB.

Stage IIA includes lesions $\geq$ 1 mm and $\leq$ 2 mm thick with ulceration of the overlying epithelium and those >2 mm and $\leq$ 4 mm thick without epithelial ulceration.

Stage IIIB includes patients with one to three microscopically involved lymph nodes (N1a or N2a) in a patient whose primary tumor is ulcerated, or one to three macroscopically involved lymph nodes (N1b or N2b) in a patient with a non-ulcerated primary tumor, or patients with in transit and/or satellites without metastatic lymph nodes (N2c).

However, documents partially copied in the pool report state that the new tumors arose in the proximity of an excisional biopsy that was performed in 1996.

Putting these two pieces of information together, Atkins said that it's most likely that the two lesions that arose in 2000 were leftover melanocytic tissue from the 1996 biopsy.

"They both could be considered, therefore, one primary melanoma in that whole area rather than two melanomas, and rather than satellite lesions," said Atkins, who describes himself as a Democrat. "But the real answer to whether that's actually the case or not would likely require a review of the wide local excision pathology to see whether there was evidence between those two lesions of the scar from the prior biopsy. You should stage these in an incompletely excised melanocytic tumor that has a local recurrence. Even though this might, in fact, be a local recurrence, data suggest that when it results from incomplete initial surgery, the staging can be based on the tumor information from the second surgery. So, if this scenario is correct, his staging would probably be most accurately characterized as Stage IIA."

The post-operative pathology report, a document needed to confirm this hypothesis, was not among documents covered in Brown's notes.

Aggressive vs. Conservative Surgery

McCain's massive scar brings back memories of one of the great controversies in the treatment of melanoma, the move from aggressive surgery, the elective lymph node dissection, to a conservative procedure, the sentinel node biopsy.

Unlike most Stage IIA patients who received melanoma surgery in 2000, McCain ended up with an elective lymph node dissection, which entailed removal of at least 33 lymph nodes.

By contrast, the sentinel node biopsy usually requires removal of one to four lymph nodes.

"I do think it's important for the public to know that it's not just skin cancer, and that there was a question about the seriousness of the melanoma, and I think that's relevant information," said Schuchter, who signed a recent petition seeking release of McCain's medical information.

"The standard of care for Stage IIA would not be to do an elective lymph node dissection," she said. "And I think that the doctors may have been influenced by the AFIP report, which raised the question of whether this was an in-transit, and so elected to be extra-aggressive.

"I think they may have taken into account that this was not just IIA. I think they may have been influenced by that pathology report. I think that's why he had a more aggressive surgery. They were hedging their bets.

"Often our surgery is done assuming worst-case scenario. Mayo Clinic reviewed it, and AFIP reviewed it, and it wasn't clear-cut how you interpret the second lesion, and so I think they said let's be safe and do the most aggressive surgery. If you were concerned that it was an in-transit, you very well may have done this

surgery. If you were confident that it was a IIA, then you wouldn't do the surgery."

At leading melanoma centers in 2000, a patient with a 2.2 mm-thick melanoma, the disease McCain and his physicians say he had, would have been treated with a wide local excisions and a sentinel-node biopsy, which in head-and-neck cases entail removal of up to four lymph nodes.

The procedure entails injecting a blue dye and an isotope into the tumor, then sweeping a Geiger counter over the adjacent area to find the closest lymph node. An incision is made over the hot spot, and the node that has taken up the dye is removed for analysis under the microscope. If the lymph node is found to contain microscopic disease, more extensive surgery is performed to remove multiple nodes, usually at a later time.

If he was indeed at Stage IIA, McCain had a 20 to 25 percent chance of having node-positive disease in his parotid gland or his neck. "You would know that one in four or one in five of these patients would have metastases in their nodes, but you couldn't tell which ones they were," Morton said.

Before Morton developed his procedure, to find patients who had microscopic metastases in the lymph nodes, the standard of care was to perform an elective node dissection.

"When I looked at this problem back in the 1980s, I said, 'That's crazy. If you don't have known metastases, you can't possibly benefit from the procedure,'" Morton said. "So, out of every 100 patients you do this on, 75 to 80 are not going to benefit, and yet they will have the morbidity of the operation."

Morton first presented his procedure at the Society of Surgical Oncology in 1990, published the definitive paper in the Archives of Surgery in 1992, then worked the political structures in surgery to get the procedure into clinical practice.

At the same time, a randomized trial by Charles Balch, then of M.D. Anderson Cancer Center, found that overall five-year survival was not significantly different for patients who received the elective node dissection compared to those who were randomized to observation. According to a 1996 paper in the Annals of Surgery, "patients older than 60 years of age who had [elective lymph node dissection] actually had a lower survival trend than those who had nodal observation."

McCain's surgery was performed by Michael Hinni, an otolaryngologist at the Mayo Clinic campus in Scottsdale, Arizona.

Hinni's preoperative plan, as described in the pool report, reads: "Certainly there needs to be wide local excision of the primary melanoma, and certainly the lymph nodes need to be assessed. Certainly, given the cervical parotid incision that would be required for rotation flap closure of this defect (I think the best cosmetic result ultimately will come from that as opposed to skin grafting), it seems feasible to use this incision to remove all of the lymph nodes in his neck that are at risk, as he is going to incur the morbidity of the incision. The morbidity of the neck dissection is limited. . . . If a malignancy should be found at any lymph node, then I would want to remove the deep lobe of the parotid gland as well with primary resection."

Hinni's notes were dated Aug. 18, 2000, the day before the surgery.

At the May 23 press conference, Hinni explained that since the lesion was two centimeters across, he needed to make a "6-by-6 centimeter island of skin, a fairly sizable wound" to excise it.

After examining the pool report, Atkins said the complexity of the case justified this unusual plan.

"They had to do such a big surgery because the two melanoma lesions on his temple were probably separated a bit from each other, and they had to get around both of them with one excision," Atkins said. "Rather than doing a large 6 cm skin graft, they chose for cosmetic reasons to close the excision wound with a huge flap of skin rotated up from the back of his neck.

"Why did he have all those nodes removed? There is actually an answer to it from Dr. Hinni's comments in that note, where he says, as long as I'm going to have to expose all the nodes to create this flap, I might as well remove them all, because it's not such a big procedure to remove them once I expose them.

"We would probably still not remove them, because it has been shown not to be clinically useful," Atkins said. "On the other hand, I could see how somebody faced with this decision in this patient might view this as a reasonable approach to minimize the need for potential future surgeries."

The scarring is so massive because the surgeon "took a big patch of skin from behind his ear, and exposing the whole neck, flipped it forward to cover the left side of his cheek after they removed all the cheek skin," Atkins said. "This left exposed his neck and all the neck nodes. So before they go and close that up, they said, 'We might as well remove the nodes.' That isn't what we would do, but it's not an unacceptable thing."

Still, the elective node dissection procedure is extremely unusual for a patient like McCain. Moffitt's

Sondak estimates that he performs the more invasive procedure in no more than two percent of cases he sees.

"If the reconstruction was a complicated one, we might be faced with the situation where you had to cut through all the lymph nodes and scar up that area," Sondak said. "In that case, you have a real problem on your hands going forward. How would you know if they recurred in those lymph nodes? How would you deal with it if they did? There are times where we would say, 'Nope, if we are moving this tissue around and we are going to cut through those lymph nodes, we are not going to cut through them, get rid of them, then do our reconstruction.' So we would be a little bit more aggressive for a little bit better likelihood of control in the short term."

Sometimes sentinel nodes simply cannot be found. "In my career, with many thousands of surgeries, I had that happen half-dozen times," Sondak said. In such cases, the surgeon acknowledges that the nodes couldn't be identified, and the patient is usually followed closely through watchful waiting.

This wouldn't be an option in the case of a VIP patient.

"You can imagine that if they couldn't find his sentinel node, rather than saying to the world that they couldn't do it, they said, we went in and we took out every damned lymph node, so no one could ever say we didn't take out the right lymph node," Sondak said.

According to notes copied from the three-page surgery report, Hinni used blue dye to identify a sentinel node, after which the node was taken to the pathology laboratory for frozen section, and the surgery continued.

"All frozen section margins on the skin edges circumferentially an on the nodes demonstrated no evidence of cancer," the report sates. A pathology report from intraoperative review of the tissue states that the sentinel node was negative for malignancy.

Atkins said it's unusual to combine the sentinel node biopsy and the excision into one procedure.

"It wasn't exactly the way one would normally do it, but it was an acceptable way of doing a sentinel node with blue dye and looking at it in a frozen section, and they have that information now to know that at least there was no tumor in the sentinel node, which actually makes his staging more akin to the contemporary approach," Atkins said. "This switches him to more recent staging data that is based on knowing the status of the sentinel lymph node, and likely provides more accurate information on risk of recurrence than previous systems, in which sentinel node status was unknown."

DuPont Guerry, former director of the University of Pennsylvania Cancer Center's Melanoma Program, who similarly read the pool report forwarded by The Cancer Letter, said the document appears to support the Stage IIA diagnosis.

"My 'best guess,' based on incomplete and imperfect data, is that the patient had a 'precursor' lesion treated in 1996," Guerry said in an e-mail. "This may have been incompletely removed. It underwent tumor progression over time and presented in 2000 as a complex primary melanoma that on the two biopsies had invasive components that were in the one case thin (the .23 mm specimen) and in the other thick (the 2.2 mm lesion).

"I doubt the latter was a satellite. I think he was then clinical Stage IIA (T3a)."

However, the surgery appeared to be more aggressive than warranted, said Guerry.

"He had a wide excision and a sentinel lymph node biopsy to drive what I infer to have been non-standard decision making," Guerry said. "The intent apparently was not to avoid a node dissection. Rather it was to do a 'big procedure' if the frozen section was positive, and to do a lesser node dissection, if it was negative.

"Happily, it was negative and this was confirmed on the permanent sections of the sentinel lymph node biopsy (you cannot make a definite negative call on a frozen section of a SLN). As well, the multiple nodes that made up the node dissection were negative. Hence, the patient was pathological Stage IIA [T3a, N0, S0, M0]. Thus, his surgeon did more surgery than is standard and this resulted in more morbidity (e.g., swelling). It produced neither greater or lesser efficacy.

"It was not a bad thing to do, but it was not optimal—or not optimal for the usual patient with Stage IIA disease," said Guerry, who declined to discuss his political affiliation.

The Question of Risk

Recently, in a full-page ad that ran in The New York Times, a group of doctors urged McCain to release his medical records.

The petition, paid for by a Democratic political action committee, was signed by 2,908 physicians, including 64 oncologists and 43 dermatologists. The list is posted at www.therealmccain.com/doctors.

"I'd love to see his records, but we should be careful, because if we had a patient who has melanoma, none of us would want that patient discriminated against, fired from his job, told they couldn't apply for

a promotion," said Sondak, who didn't sign the petition, and who declined to discuss his political affiliation. "We have to be careful that we don't create a stigma that ought not be there."

At the time of diagnosis, a Stage IIA melanoma patient would have a 77.7 percent chance of being alive five years later and a 67.3 percent chance of 10-year survival.

A Stage IIIB patient with a satellite tumor and no node involvement would have a 67.6 percent chance of five-year survival and a 59.2 percent chance of 10-year survival.

These projections are based on a Nov. 1, 2005, paper by Gimotty, PA *et al*., a validation of the American Joint Committee on Cancer melanoma staging system, Journal of Clinical Oncology. The paper is posted at http://jco.ascopubs.org/cgi/content/full/23/31/8065

Schuchter said the number of patients staged IIIB is so small that a prediction of their survival would be unreliable.

For example the Stage IIIB cohort in the Gimotty et al. paper included 405 patients, about 1 percent of the total number analyzed. By year 10, this population diminishes by 40.8 percent, and you end up with 240 of these patients.

As time passes, follow-up becomes less reliable.

"Way out there, the curves get sort of floppy, so how good is statistical information at the end of those curves?" said Guerry, a co-author of the paper. "It's less than at the beginning of those curves. You have fewer and fewer people to work with, in part because they've been lost to follow-up, and in part because they've died of their cardiac disease, jumped off the buildings, have been run over by cars. But mainly because people aren't good at keeping records beyond five or 10 years.

"We don't have a robust model that would tell us what a population of people like McCain will have happened to them," Guerry said. "Whatever the initial prognosis, for those free of disease after eight years, the prognosis is good; how good, we don't know with any precision."

Melanoma experts agree that as patients with more aggressive tumors die, those who remain have an increasingly improving outlook. And, as survival curves flatten out, the difference in absolute risk of Stage IIA vs. Stage IIIB likely diminishes.

"While the risks vary greatly by stage at time of diagnosis, at eight years out disease-free, the risks of subsequent relapse tend to converge," said Atkins. "In his case, the risk of relapse over the next four to five years would likely be less than 10% in either case."

Experts agree that even though McCain has had four melanomas, their risk isn't cumulative, which means that his overall risk is determined by the lesion removed eight years ago.

Morton said McCain faces competing morbidities that are more significant than the melanoma.

"In my opinion, his longevity with the melanoma and without the melanoma will be the same," said Morton, who declined to discuss his political affiliation. "We are all going to die of something. What's it going to be? And early on, in the first five years [after melanoma diagnosis], the chances of him having a recurrence and dying of melanoma is greater than his chances of having a heart attack or something else."

Records indicate that McCain has had difficulties with his scar.

It had swelled after the surgery, causing him to return for a "scar revision." He has used cosmetic products and facial masks. According to a doctor's notes, "he has used the compression device for the facial scar, but he has not used it routinely. It makes sleeping difficult."

Speaking with reporters at the campaign-organized press conference May 23, the surgeon Hinni said:

"He is not interested in considering other therapies or operations to correct this, being relatively pleased with how things have gone, and states quite openly that he is quite pleased with this institution, and describes it as a wonderful place."

NIH News:

One Resubmission Enough, NIH Tells Grant Applicants

Starting next year, researchers will be allowed to resubmit their grant applications to NIH only once, instead of twice.

NIH will phase out second amendments for new applications submitted beginning Jan. 25.

"This new policy will help ensure earlier funding of high-quality applications and improve efficiencies in the peer review system," according to an NIH statement. The change is part of a series of actions stemming from a year-long assessment of the peer review system.

An analysis by the institutes found that an increasing number of meritorious applicants that were ultimately funded had to resubmit their applications multiple times, which increased the amount of work for applicants and reviewers.

The previous policy allowed research applicants two attempts (amended applications known as A1

and A2 resubmissions) to improve upon their original application (known as A0 submission) based on feedback from peer reviewers.

In times of budgetary constraint, however, the number of awards made to original applications decreased. An increasing number of projects were funded only after one or more resubmissions. This trend has been increasing over recent years. In 2006, successful applicants needed to apply on average twice as many times than in 2002 to get funded.

NIH posted supporting data for this analysis at http://enhancing-peer-review.nih.gov/resubmission.html#data.

"Over the past several years, the number of applications submitted each year to NIH has doubled and the number of investigators applying for grants has increased by over 75 percent, increasing stress on the system, especially when confronted with stagnating budgets," NIH Director Elias Zerhouni said. "This has led to scientists spending more time rewriting their applications and undue delays in the funding of outstanding projects."

The application must go through more rounds of submission today than it did just five years ago. In 2002, an investigator had a 17 percent chance of a first submission being funded as compared to a 7 percent chance in 2006.

"To implement the recommendations of the peer review panel, we found after careful analysis that eliminating the second amended application is the best way to help ensure that we fund the best science earlier and reduce administrative burden on meritorious scientists and their projects," Zerhouni said.

The new policy applies to all NIH grant programs and is posted at http://grants.nih.gov/grants/guide/notice-files/NOT-OD-09-003.html.

Tobacco Use Banned On NIH Campus

NIH Became tobacco-free on Oct. 1. Forty-four years, eight months, and 20 days after the Surgeon General's 1964 report on smoking, the use of all tobacco products, including cigarettes, cigars, pipes, and smokeless tobacco, is prohibited on the NIH Bethesda campus.

The new policy is part of the "Tobacco-free HHS" initiative. Information on smoking cessation programs is available at http://tobaccofree.nih.gov.

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MARIE BERNARD, the Donald W. Reynolds Chair in Geriatric Medicine and professor and chairman of the Donald W. Reynolds Department of Geriatric Medicine at the University of Oklahoma College of Medicine, was named deputy director of National Institute on Aging, said **Richard Hodes**, director of NIA. . . . **JOHN JONES** was named NIH chief information officer, said NIH Director **Elias Zerhouni**. Jones will advise the director in areas of computational bioscience, computer engineering, and information technology. He will also continue as acting director of the Center for Information Technology until a permanent CIT director is appointed. . . . **MYRTLE DAVIS** was appointed chief of the Developmental Therapeutics Program's Toxicology and Pharmacology Branch in NCI's Division of Cancer Treatment and Diagnosis. Before joining NCI, she worked at Eli Lilly Research Laboratories as a research advisor in toxicology in their Investigative Toxicology Group, where she focused on the development of kinase inhibitors as therapeutic agents. Prior to that, Davis was an associate professor in the Department of Pathology at the University of Maryland School of Medicine, where her research explored the mechanisms of toxin-induced apoptosis.

In the Cancer Centers:

UCSF Begins Clinical Trial Matching Service Online

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Cancer Center at Johns Hopkins University. Jones is director of the University of Southern California/Norris Comprehensive Cancer Center. The award, given every two years, includes $50,000 to support a two-year research project. . . . **UNIVERSITY OF CALIFORNIA**, San Francisco, Center of Excellence for Breast Cancer Care has begun BreastCancerTrials.org, a free, non-profit, clinical trial matching service. The online database includes information about clinical trials at more than 1,100 medical facilities. The site is an outgrowth of a regional pilot begun by the UCSF Carol Franc Buck Breast Care Center, and is funded by a grant from The Safeway Foundation. . . . **OHIO STATE UNIVERSITY** Comprehensive Cancer Center-James Cancer Hospital and Solove Research Institute named Theres Dinardo Brown as chief communications officer, reporting to **Michael Caligiuri**, cancer center director. She is president of Brown Communications Inc. . . . **ROSWELL PARK CANCER INSTITUTE** will bring together national cancer experts to discuss "The Future of Cancer Research: Science and Patient Impact" during a Centennial Symposium sponsored by the American Association for Cancer Research, Oct. 27-28. **Frank Torti**, recently appointed FDA principal

deputy commissioner and chief scientist, is the keynote speaker. "Roswell Park is privileged to host the AACR Centennial Symposium honoring the contributions of individuals and organizations which have contributed to a century of progress in cancer research," said **Donald Trump**, president and CEO of RPCI. "This event offers a significant opportunity for a distinguished roster of national leaders in cancer to gather and share their insights into future opportunities for advances in cancer prevention, research, education and treatment."

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SUSAN G. KOMEN FOR THE CURE awarded 2008 grants to institutions that include the following:

M. D. ANDERSON Cancer Center received a total of $19 million for breast cancer research. Ranging from $120,000 to $7.5 million, the grants will be allocated across 11 different translational breast cancer research studies. Basic and clinical research will be conducted on issues such as diagnostic and prognostic biomarkers, endocrine therapies, immunotherapies and nutritional prevention. Researchers will examine discrepancies in treatment response, the spread of cancer to other organs, effects of obesity on cancer, the ability to identify who is at risk for developing cancer, the efficacy of a breast cancer vaccine and how to detect breast cancer at the earliest possible stage. "The grants will enable M. D. Anderson to build on its historic strengths in translational research and multidisciplinary care and continue to rapidly advance patient treatment," said M.D. Anderson President **John Mendelsohn**.

UNIVERSITY OF TEXAS Medical Branch at Galveston received $600,000 grant for research on breast cancer metastasis. **Binhua Zhou**, assistant professor at Sealy Center for Cancer Cell Biology and Department of Pharmacology and Toxicology, will lead a multidisciplinary team on the roles played by Snail, a transcriptional regulatory protein that controls cell movement, and Beta-Catenin, a signaling protein, in the initiation and progression of metastasis.

UNIVERSITY OF COLORADO Cancer Center researchers were awarded a $599,999 grant, over three years, to study a diabetes drug in breast cancer. "We're exploring the relationship between pre-diabetes syndrome or type II diabetes, obesity and breast cancer risk," said **Steve Anderson**, professor of pathology at the University of Colorado Denver, and primary investigator. Other UC Denver scientists include **Paul MacLean**, associate professor of endocrinology, diabetes and metabolism; **Pepper Schedin**, associate professor of medical oncology; **Ann Thor**, professor of pathology; and **Natalie Serkova**, associate professor of anesthesiology and director of the UCCC animal imaging and metabolomics shared core services. UCCC is a consortium of three state universities that includes Colorado State University, University of Colorado at Boulder and University of Colorado Denver and six institutions.

CITY OF HOPE received a three-year, $600,000 grant for research to reduce side effects and prevent drug resistance during treatment of hormone-dependent breast cancer. **Shiuan Chen**, principal investigator, and co-leader of the Breast Cancer Research Program, is studying the regulatory mechanism of aromatase expression in breast cancer cells. The grant will examine the combined use of LBH589 and aromatase inhibitors such as letrozole.

Funding Opportunities:

American Cancer Society International Fellowships

The American Cancer Society offers 12-month, $45,000 fellowships intended for beginning investigators and clinicians who are in the early stages of their careers. Application Deadline: Dec. 1.

Funding preference will be given to candidates who conduct cancer research projects into the preclinical, clinical, epidemiology, psychosocial, behavioral, health services, health policy and outcomes and cancer control areas. The initiative would promote research knowledge, experience, expertise, and innovation between countries. Inquiries: fellows@uicc.org. and http://www.cancer.org.

NIH Cancer Research Opportunities:

RFA-CA-09-503: Cancer Care Outcomes Research and Surveillance Consortium. U01. Application Receipt Date: Dec. 16. Full text: http://www.grants.nih.gov/grants/guide/rfa-files/RFA-CA-09-503.html. Inquiries: Neeraj Arora, 301-594-6653; aroran@mail.nih.gov.

PA-09-010: Basic and Preclinical Research on Complementary and Alternative Medicine. R01. Full text: http://www.grants.nih.gov/grants/guide/pa-files/PA-09-010.html. Inquiries: Cindy Davis, 301-594-9692; davisci@mail.nih.gov.

NOT-CA-09-001: Reaching Out to Potential Users on Non-Grant Shared Resources of the NCI Division of Cancer Treatment and Diagnosis. Full text: http://www.grants.nih.gov/grants/guide/notice-files/NOT-CA-09-001.html. Inquiries: Jason Cristofaro, 301-594-5318; cristofaroj@mail.nih.gov.

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