

University of Chicago Cancer Research Center

In the News: Our Members in the Media

The University of Chicago Cancer Research Center (UCCRC) publishes this newsletter periodically to provide its members, University of Chicago Cancer Research Foundation members, and other associates with informative articles or press releases regarding cancer and research by our members. If you wish to include a media story in the next issue, please e-mail us at pbutera@medicine.bsd.uchicago.edu.

APRIL 10, 2009

Two Takes: Should Stem Cell Research be Permitted?

U.S. News and World Report

President Barack Obama repealed a federal funding ban on human embryo stem cell research. Advocates say that it could cure afflictions that include spinal cord injuries and Alzheimer's disease, but critics say it involves destroying human life. Should such research proceed?



Janet Rowley, Professor of Medicine at the University of Chicago and member of the President's Council on Bioethics

Yes: The decision to end many restrictions on embryonic stem cell research has removed a key barrier

to research and discovery. Scientists are driven by the desire to succeed as fervently as our most success-driven businessmen, entrepreneurs, or lawyers. But for years they have contended with research limits that prevent innovation but do not serve a clear moral purpose. A responsible expansion of embryonic stem cell research can advance a vital goal—the search for new medical treatments—while respecting the dignity of human life.

At present, there are about 400,000 human embryos in the freezers of in vitro fertilization clinics. Many are destined to be thawed and discarded and thus die. It is a true moral dilemma, but science offers a way to bring something good from a flawed situation. The parents of these embryos could allow them to die, or they could donate the embryos for research that someday might benefit patients with incurable diseases. This is a high purpose, one that promotes both human health and understanding.

Scientists have worked tirelessly to develop useful alternatives to these rare sources of embryonic stem cells. Through trial and error, they have developed a cocktail of genes that can transform adult human skin cells (from you and me) into cells closely resembling embryonic stem cells. But make no mistake—these are not embryonic stem cells. They are induced pluripotent stem cells. The study of these cells is in its infancy.

The hope is that induced pluripotent cells could be developed from individuals who have genetic disorders like juvenile diabetes, Parkinson's, and muscular dystrophy. Having stem cells with these defects could dramatically help scientists in their efforts to understand the basic, underlying problems in cells with these mutations. That's because stem cells offer a unique window into cell development—and they can shed light on how development goes awry in serious diseases. However, investigators also desperately need embryonic stem cells developed from patients with these genetic disorders to confirm that studies



Tony Perkins, President of the Family Research Council, promoting "the sanctity of human life in national Policy"

No: Proponents of embryonic stem cell research must view the future with great hope. After all, on Monday,

President Barack Obama reversed President George W. Bush's decision to shut the door on such research in August 2001 when he restricted federal research funds to a limited number of embryonic stem cell lines. One might also think that with all the talk about the promise of human embryonic stem cell research since 1998 (mouse embryonic research started in 1981), patients would be seeing some benefit using these stem cells by now. After all, stem cells have now been used to treat human patients for a variety of diseases. Keon Penn was treated for sickle cell anemia. Stephen Sprague was treated for leukemia. Barry Goudy has gone without multiple sclerosis symptoms for over five years, and 13 patients with type 1 diabetes have gone off of their insulin shots. Jacki Rabon walked again with the aid of braces after being treated with stem cells for a spinal cord injury. However, the stem cells used to treat these and thousands of other patients in the recent past use cord blood or adult stem cells—not human embryonic stem cells.

Why haven't embryonic stem cells been used to treat any patients? Is it a lack of funding? Hardly. Under President Bush, from 2002 to 2008 roughly \$300 million of federal funds went to human embryonic stem cell research. States like California—which passed a \$3 billion 10-year bond program—and the private sector also fund this kind of research. But still, this line of inquiry has produced no treatments for any diseases.

In truth, there are major, inherent biological obstacles to any potential use of embryonic stem cells for human therapies. These are serious, long-standing scientific problems, well known and nowhere close to being solved. The very characteristic so prized by some scientists, their flexible (or pluripotent) nature, makes these cells difficult to control for actual clinical use; the result is that they tend to form tumors, even reverting to uncontrolled growth after they have been specialized.

And because these are from genetically different

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with induced pluripotent cells faithfully reproduce the genetic disorders. Scientists in the United States have developed such cell lines from embryos with genetic defects that were identified by genetic analyses. They have developed cell lines using money from private philanthropy because they have been prohibited by the previous administration from using federal money to carry out this important research.


Today, scientists are free of this impediment. But like all research, work on stem cells needs firm ethical guidelines. That's why scientists have joined with ethicists, lawyers, and patient advocates to develop the very strict rules that are currently in place to govern this area of study. I was part of a multidisciplinary group under the auspices of the National Academy of Sciences that met numerous times to develop guidelines that help ensure such work proceeds only within well-defined limits. The rules were adopted by California in 2005 to guide its stem cell initiative, and they have since been modified in response to California law and vigorous public debate.

One of the guiding principles in these policies is the intrinsic value of human life. The guidelines call for careful ethical oversight of all research using human oocytes (eggs), embryos, or cell lines derived from these tissues. The cells and embryos must be obtained with informed consent, with no money paid for oocytes or embryos. All proposed research must be reviewed by a separate board that has scientists who are knowledgeable about embryonic stem cell research, as well as ethicists and the lay public.

During this whole process of developing guidelines, scientists have been active and willing participants. Rather than demanding to do their work unfettered, scientists realize that strict guidelines will enable our society, which is supporting their work, to know that the research respects our shared values.

Thus the scientific community now has many of the tools and resources needed to pursue stem cell research much more effectively than would have been possible only a few years ago. As we work to refine guidelines, it is critical that the rules be consistent between states, with national guidelines most likely issued by the National Institutes of Health. It is noteworthy that under President Bill Clinton, an eminent committee chaired by Shirley Tilghman (now president of Princeton University) wrote guidelines for NIH-funded stem cell research. The guidelines were due to take effect in 2001, but their implementation was canceled by President George W. Bush.


Everyone benefits when science works with the political system, rather than being kept at the margins. At a time when the promise and challenges of new technology are greater than ever, we need a national conversation driven by sound science and our common values. Scientists don't expect to dictate all the rules for stem cell research or for any field with complex moral issues. But we should have a clear voice in the democratic exchange, to help ensure that our research guidelines give us the best chance of finding new treatments and enriching life.

We've lost eight years; let's get started! Only by harnessing our intellectual and financial resources nationally will we be able to realize the potential of stem cells as the therapeutic tool we all hope they will be. 

embryos, they can be rejected by a patient's immune system. To skirt this problem, some even advocate the highly controversial prospect of human cloning. President Obama stated he opposes reproductive cloning, meaning the birth of human clones, but he clearly supports cloning human embryos for experiments.

Canada, France, Germany, and the United Nations are right to prohibit human cloning for destructive research as well as reproductive purposes. I agree with their argument that it will be virtually impossible to prevent baby cloning once we take the first step down that path. The problem of human research cloning is also practical. Human cloning requires women to risk their health by donating huge numbers of eggs. Because of the problem of obtaining women's eggs, some researchers are trying to mix human cells with animal eggs in efforts to get human-animal hybrid embryos. President Obama's executive order could end up funding research on stem cells taken from clones or even human-animal hybrids. What's the difference? Proponents of embryonic stem cell research complained that Bush's policy was too restrictive, that he should have allowed funding for research on cells derived from destroying so-called leftover embryos (ones that parents don't plan to implant) instead of just those stem cell lines that existed in 2001. President Obama goes well beyond funding embryonic stem cell research with "leftover" embryos; he would fund this kind of research with cloned embryos or human-animal hybrid embryos.

The problem for some is that even this is not far enough! The ink on Obama's order was barely dry before politicians started calling for repeal of the Dickey-Wicker amendment, first signed into law by President Bill Clinton. This provision prevents federal funding for any research that harms or destroys human embryos, whether created through in vitro fertilization, cloning, or other means. Apparently, some folks feel it's not enough to provide dollars for stem cells from embryos or clones; they now want taxpayer money to create and destroy the embryos in the first place! What to do about this controversy? What if you could create embryonic stem cells without using embryos? Well, researchers can. Since November 2007, Japanese and U.S. scientists have used reprogramming to turn normal cells into embryonic-like stem cells that are identical to embryonic stem cells, without using human embryos, eggs, or cloning.

Researchers call these cells induced pluripotent stem cells. They function like the human embryonic variety, can be created for disease-specific lines, and would genetically match the patients. How significant is this alternative? When the creator of Dolly the cloned sheep, Ian Wilmut, turns away from human cloning to pursue this kind of research, you know you're on to something big. Federal resources are vast, but they are limited. Federal funding should prioritize stem cell research on what is benefiting patients now. One piece of legislation everyone can agree to is that sponsored by Reps. J. Randy Forbes, a Virginia Republican, and Daniel Lipinski, an Illinois Democrat. It would direct funding to build on the successes over the past years to the benefit of patients. Putting patients first is a strategy we can all embrace. 

Current Controversies in Oncology: The Timing of Chemotherapy in Early- Stage, Muscle Invasive Bladder Cancer

ASCO News and Forum
Walter M. Stadler, MD, FACP
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It is acknowledged that outcome following surgical extirpation of locally advanced bladder cancer is poor. It is furthermore acknowledged that the only level 1 evidence supporting the addition of cisplatin-based systemic therapy to improve overall time to recurrence and survival comes from neoadjuvant trials. Nevertheless, it will be argued here that the use of adjuvant (something that enhances the effectiveness of a medical treatment) cisplatin-based therapy is not only rational but should be preferred. This argument is based on analysis of the biologic rationale on which systemic therapy is based, the prognostic and predictive value of surgical pathologic data, and data from randomized adjuvant studies performed to date.

Neoadjuvant systemic therapy (treatment administered to cancer patients prior to surgery or radiotherapy to help reduce the size of the cancer) can theoretically improve recurrence-free and overall survival through improved local control and/or eradication of clinically unsuspected micro-metastases. Despite the improvement in pT0 rate observed following neoadjuvant treatment, it is highly unlikely that the overall benefit is due to improved local control. First, the majority of recurrences in bladder cancer are due to systemic disease and local recurrence alone following surgery occurs in only 6 to 13 percent of patients. Secondly, the addition of radiotherapy to surgery, which can only impact local control, has been subject to five randomized clinical trials and a meta-analysis demonstrated that radiotherapy did not impact survival. Systemic therapy thus likely eliminates subclinical systemic disease, and there is no theoretical advantage to administering it prior to surgery.

In the neoadjuvant setting systemic therapy must be administered indiscriminately to all patients with locally advanced disease, resulting in a

very modest overall improvement in long-term survival of approximately 5 percent.

This represents the outcome of a heterogeneous population in which treatment benefit is great in some and non-existent or perhaps even harmful in other patients. One would thus prefer to select and treat patients with the greatest benefit/risk ratio. Despite multiple efforts, accurate clinical and laboratory biomarkers for predicting benefit from cisplatin-based DNA and DNA-repair targeted therapy have not yet been identified. However, if the relative benefit is equivalent across this heterogeneous patient population, then patients with the worst prognosis will have the largest absolute benefit. Data from the completed adjuvant trials in bladder cancer support the concept that relative benefit is equivalent across prognostic groups. In the analogous smoking-related disease, lung cancer, the relative benefit of cisplatin-based adjuvant chemotherapy was in fact higher in higher stage, poorer prognosis patients. For locally advanced bladder cancer, standard staging remains the most important prognostic factor and pre-surgical staging remains highly inaccurate, even in modern surgical series. It is only through full pathologic analysis of the resected specimen that poor prognosis patients, who can enjoy the greatest absolute benefit from systemic therapy, can be accurately identified.

Despite these theoretical considerations, one does need to consider the available data. There is certainly strong data that adjuvant chemotherapy improves time to recurrence, but whether this leads to improved survival continues to be debated. The debate centers around one basic argument: namely, the studies done to date are simply not large enough to detect the survival advantage even if one exists. To this end, two meta-analyses of the available randomized studies have been performed, and both support the contention that adjuvant chemotherapy improves survival.

In sum, the unimportance of



Walter M. Stadler, MD, FACP

local therapy timing in regards to the likely mechanism of subclinical disease control by systemic therapy, the ability to better select the patient population with the largest absolute benefit from a highly toxic therapy, and supporting data from analysis of available trials all support the contention that the most rational approach to systemic therapy in locally advanced bladder cancer is to administer it in the adjuvant setting.



EDITOR'S NOTES:

This issue of "In the News" highlights the important contributions our members are making in all phases of cancer research and outreach.

In the article on pages 1 and 2, Janet Rowley, MD, provides some context on the recent changes in stem cell regulations.

On page 3, Walter Stadler, MD, FACP, discusses his views on the timing of chemotherapy in early-stage bladder cancer.

On page 4, Rick Kittles, PhD, is quoted in an article that examines the social, cultural, and political influences of our DNA.

On page 5, Scott Eggener, MD, is featured in an article on low-risk prostate cancer treatments. Also, Janet Rowley, MD, is quoted in a story on embryonic stem cell research.

DNA Tests Show there's More to A Person's Race and Ancestry Than Meets the Eye

The Herald News
March 29, 2009

We're all pegged by a color - black, white, red, brown, yellow. As the saying goes, never judge a book by its cover. Yet that's what we've done best in our few hundred years as a nation. "We know not only culturally but biologically that it's a melting pot -- everybody knows that," said Rick Kittles, PhD, a University of Chicago geneticist. "However, socially, politically there's a strict dichotomy."

Our new president is the son of a Kenyan immigrant and a white woman from Kansas and once called Indonesia home. Tiger Woods rose to the top of a traditionally white man's game, identifying himself on the links as "Cablinasian" -- Caucasian, black, Native American and Asian. Still, Woods and Barack Obama are known as black men who broke white racial barriers. As the country becomes more overtly diverse, those men represent a shift toward multiracial identity. Could our history of black and white be graying?

Since the presidential campaign, readers occasionally have asked why the press identifies Obama as black or why we let others identify him that way when his heritage is more complicated than that. Obama's prominence may have prompted many to wonder, but the truth is all of us have a heritage more complicated than one color label.

We invited four Southland men, whose various racial identities often are pigeonholed by stereotypes, to swab their cheeks and send their DNA to be tested through an ancestry database to see if color really summed up who they are. Our test subjects are Jose Garibay, son of Latino immigrants, from Chicago; Josh Wellington, of Polish roots, who lives in Home-wood; Leroy Palmer, an African-American from Chicago; and Willie Winters, an Irish-man from Chicago's Beverly community. What we found was as broad as it was similar.

Though we can't say for sure, it is likely these men have blood from countries they never dreamed possible. Their earliest ancestors bring the four men to parts of Asia, Africa - countries to which none laid claim before starting on their genealogy quest.

Palmer's roots could link to the most significant effect on our world today.

The movement of his people of west and sub-Saharan Africa across the continent "played a striking role in the population and cultural evolution of our world in the last few thousand years," his findings showed. But that is far removed from Palmer's life today. Though his maternal grandparents, who grew up in Montgomery, Ala., likely had many stories and recollections of their time growing up in the



Rick Kittles, PhD

racially divided Deep South, Palmer knows little about it.

Even after discovering more, Palmer, who works at MetroSouth Medical Center in Blue Island, believed it meant little to his place in the world, perhaps because of how distanced his genealogy is from his life here in Chicago.

Fast forward to the present day and their genealogy showed all four men could be related to people from Australia to Finland. "It just shows how distanced we are in so many ways from where we came," said Winters, Executive Director for the jail diversion, crime prevention division of the Cook County sheriff's police. "At the same time the vast majority come from the same place, and the divisions we put between us are contrived and really don't mean anything."

Winters has met the last living

male Winters relative in Ireland, Liam, who shares the name of Winters' son. Garibay, who also works at Metro-South, has Latino roots that link him to Puerto Rico, where his maternal grandparents were born, but he also found distant relatives in Hawaii, the coast of Brazil and the eastern Malaysian state of Pahang.


Wellington discovered for the most part he is that "classic western European white person," as he dubbed himself. "I sort of equate whatever I am with the boring," he said. Race seems to matter least to Wellington; he's more interested in learning of his multiracial friends' ancestors than his own.

It's no surprise Wellington feels that way, as much of the movement toward a multiracial society is being led by minorities, of course, but largely by Asians and Latinos, who fall between the white and black divide and have migrated by the thousands since the mid 1960s, said Jennifer Lee, an Associate Professor of Sociology at the University of California-Irvine.

"They're so much evidence that shows that race determines your life chances," Lee said. "Non-whites wear their ethnicity; they wear their race every day. It matters to them every day in the way that they're perceived."

It is expected that the 2010 U.S. Census will show Latino and Asian communities growing disproportionately to the black community, she said. Already the Latino community has become the country's largest minority group.

Interracial marriages and a rise in immigration have played a part in this growing integration of cultures. Nine years ago, respondents to the 2000 Census for the first time had the ability to identify with multiple races. Nearly 7 million people did, out of about 282 million.

Yet Obama's ascension to the nation's highest public office in many ways has reflected that shift. "Part of what made Barack palatable to the majority of the US was he wasn't purely black," said geneticist Kittles, creator of www.africanancestry.com. "People are starting to embrace beyond the black-white nature; that paradigm is being broken." 

'Watchful Waiting' Safe With Low-risk Prostate Cancers

**US News and World Report
March 16, 2009**

Refusing immediate treatment can be safe for men with low-risk prostate cancer if they're closely monitored, new research finds. The multi-center study of American and Canadian patients was conducted between 1991 and 2007.

"When or if to treat men with low-risk prostate cancer has always been a challenging question that faces patients and urologists," study author Dr. Scott Eggener, an Assistant Professor of Surgery at the University of Chicago Medical Center, said in a news release from the University. "Some men may be rushing into treatment that won't necessarily benefit them, prevent problems or prolong life. Close observation in certain patients may provide and maintain quality of life without increasing the chances of the cancer spreading."

Between 20 percent and 50


percent of American men diagnosed with prostate cancer will eventually die from a cause other than their prostate cancer, he noted. This shows that a large number of patients don't benefit from treatment for their prostate cancer.

The 262 men in this study who decided on "watchful waiting" instead of immediate treatment met the following criteria: under age 75; prostate specific antigen (PSA) below 10 ng/ml; clinical stage T1-T2a; Gleason score 6 or below; and three or fewer positive cores at diagnostic biopsy. The patients underwent a restaging biopsy and had no treatment for six months following the repeat biopsy. They then had physical exams and PSA tests every six months with biopsies recommended every one to two years.

Of the men in the study, 43 eventually decided to have treatment or had evidence of cancer progression that prompted a doctor's recommenda-

tion to begin treatment. Following radiation or surgery, all but one of those 43 patients were cured of their prostate cancer. The remaining 219 patients remained on watchful waiting without evidence of cancer progression.

"Active surveillance with delayed treatment, if necessary, for select patients appears to be safe and associated with a low risk of metastatic spread," the researchers concluded. The study was published in the March 16 issue of *Urology*.

"Active surveillance is not a total disregard for patients with prostate cancer. Instead, it identifies men unlikely to be affected by their cancer and encourages frequent monitoring, and then starting therapy at a later appropriate time if needed. Cure rates appear to be identical when these men choose immediate treatment or delayed treatment when prompted by new information about their condition," Eggener said. 

Chicago Area Scientists Applaud Repeal of Funding Limits on Embryonic Stem Cell Research

**Chicago Tribune
March 8, 2009**

As Chicago-area scientists got the word that President Barack Obama will repeal federal restrictions on embryonic stem-cell funding Monday, the response was less a celebration than a sigh of relief.

"It's a wonderful thing to see science now being in the hands of scientists, to see it becoming less politicized," said Dr. John Kessler, Chairman of Neurology at Northwestern University's Feinberg School of Medicine.

Embryonic stem cells excite scientists for their ability to form virtually any tissue in the human body, meaning they potentially could be used to heal spinal-cord injuries or grow a healthy kidney. But they remain controversial because they are derived from fertilized embryos.

In August 2001 President George W. Bush limited federal funding of the research to the few cell lines already in existence. His decision meant no new stem cell lines could be created in labs receiving federal research dollars.

That decision slowed American stem-cell research, scientists said. In some cases, labs had to set up separate facilities, one funded by the National Institutes of Health and one funded by private money, said Dr. Janet Rowley, a University of Chicago Professor of Medicine who served on The President's Council on Bioethics in Bush's administration. "That is very wasteful," she said.

The restrictions also gave a competitive edge to countries such as Japan and Korea, where funding for the research continued. American scientists made do with limited funding from states such as California and Massachusetts and the stem-cell lines approved for federally funded research, but advances were limited.

"The cell lines that we have access to have remained the same and are getting a little older when there are shinier new cars on the lot," said Dr. Timothy Kamp, a cardiologist and Co-Director of the University of Wisconsin Stem Cell & Regenerative Medicine Center. The repeal "gives us more tools to work with to help move medicine forward."

The landscape of stem-cell research has changed dramatically since Bush announced his restrictions. James Thomson, another Co-Director of the Wisconsin center, recently discovered a way to reprogram adult skin cells to behave like stem cells, suggesting an alternative to cells derived from embryos. But Kamp, who studies the use of stem cells to treat heart disease, said the scientific value of embryonic stem cells has not diminished.

Even as local scientists expressed excitement about Obama's action, they reminded the public not to expect fast results. "I applaud it, but I also worry that much of the public may think this means that this will translate instantly into a brand-new treatment," Kessler said. "That's not the way science works."

Regulatory and technical details will have to be worked out before research can proceed, Rowley said, and funding will need to be obtained—no easy task in this economic climate. After "everybody gets finished drinking the champagne," a lot needs to happen, Rowley said. "You need resources." 