



MMHCC Newsletter March 2009

MouseLine

Moving Ahead with the Stimulus Funds

With President Barack Obama's signing of the American Recovery and Reinvestment Act (ARRA) on February 17, 2009, came newfound hope in many circles that our economy can start down the road to recovery. As the President himself has said, it will not be easy. This recovery package is just the first step and, undoubtedly, just one of many interventions.



The economic stimulus package presents a tremendous opportunity for the biomedical research establishment. Under the new law, NIH will receive approximately \$10.4 billion for use in fiscal years 2009 and 2010, \$8.2 billion of which is specifically tagged for research.

Of that \$8.2 billion, approximately \$1.26 billion will go to NCI. The total funding for cancer research could increase if NCI grantees successfully compete for "challenge grants," comparative effectiveness research monies, and other infrastructure funds administered by the NIH Office of the Director and the National Center for Research Resources. I believe this sizable figure is a profound affirmation from President Obama and the American people of the importance of tackling the cancer burden and a sign of their confidence that we are well suited to meet that challenge. As you are well aware, I continually remind our leaders in the executive and legislative bodies of our government that an investment in cancer research, whether in basic scientific discovery or behavioral studies of populations, is an investment in a model for gaining an understanding of all diseases.

As I wrote recently, an investment in research does more than just create new scientific knowledge and advances in clinical medicine. That investment also translates into support for research projects at institutions large and small across the country, and those projects in turn create jobs and a plethora of new business opportunities by generating patents, products, and biotechnology start-up companies. In fact, on average, a single NIH research grant supports seven jobs. And according to one analysis, for every \$1.00 spent on research in a given community, \$2.25 in local economic activity is generated.

The White House is requiring an unprecedented, but certainly appropriate, level of transparency and accountability with regard to how ARRA funds are used. These funds will be kept separate from our general operating budget secured via the standard appropriations process.

To help achieve this transparency, new NCI reporting mechanisms are being developed for the grantees and institutions that receive funds from the stimulus package. These 2-year awards will be supported via three primary mechanisms:

- Already reviewed, highly meritorious R01 applications that make scientific sense to fund for only 2 years, as well as new R01 applications that have a reasonable expectation of making progress in 2 years
- Administrative and competitive supplements to current grants
- Challenge grants, which are intended to provide jumpstart funds for projects that address defined health and science challenges, and where it is believed reasonable





progress is feasible in a 2-year time frame

NCI's leadership is working under an accelerated timetable to create a spending plan that meets the stimulus package goals, while striking an all-important balance between increases in the number of grants for individual investigators, where there are long-term financial obligations, and a greater commitment to solicited, team-science projects—such as IT-related efforts like caBIG, BIG Health, and efforts related to the development of electronic medical records.

We will widely report—via the NCI Web site, the *NCI Cancer Bulletin*, teleconferences, professional meetings, and other avenues—on the research opportunities created by these funds, the specific projects they support, the scientific knowledge and advances they generate, and the number of jobs they provide. NCI is committed to ensuring that the cancer community and general public can easily trace the return on this unprecedented investment.

The bottom line is this: NIH and NCI leadership are prepared to do our part toward the economic recovery of this great country by quickly distributing stimulus funds via a science- and merit-driven process and, in so doing, supporting not just new science but crafting new approaches that alter the course of cancer while preserving and creating jobs.

It's rewarding to witness members of Congress—particularly Senator Arlen Specter, who championed the need for these funds—and the President's confidence in the potency of biomedical research in the recovery process. Many in the cancer community toil behind the scenes, in basic research laboratories, community clinics, and the offices of advocacy organizations. But we are all committed to reducing the cancer burden, and this influx of funds recognizes the remarkable work we have done and the important achievements the American people believe we can accomplish.

Indeed, during the signing ceremony last Tuesday, while talking about the support for scientific research in the stimulus package, President Obama said that he hoped "this investment will ignite our imagination once more, spurring new discoveries and breakthroughs." I am confident that we as a community have the people and strategies in place to live up to that hope, to achieve important progress that will better the lives of millions in the process.

Dr. John E. Niederhuber
Director, National Cancer Institute

Source: NCI Cancer Bulletin

<http://www.cancer.gov/ncicancerbulletin/022409/page4>

Blocking Protein Leads To Fewer, Smaller Skin Cancer Tumors

ScienceDaily (Feb. 19, 2009) — New research suggests that blocking the activity of a protein in the blood could offer powerful protection against some skin cancers.

In the study, normal mice and mice that had a genetically engineered protein deficiency were exposed to almost a year of ultraviolet light that mimics chronic sun exposure. The mice that lacked the protein developed fewer, smaller, less aggressive and less vascular skin cancer tumors than did the normal mice.





Because a low-dose drug that blocks the protein's activity in the blood is currently under investigation by a Pennsylvania pharmaceutical company, the researchers hope that someday, a simple pill might help prevent or treat nonmelanoma skin cancer in people at highest risk for the disease.

More than 1 million cases of nonmelanoma skin cancer are diagnosed in the United States each year, according to the National Cancer Institute. The two most common types are basal cell carcinoma, which forms in small cells in the base of the outer layer of skin, and squamous cell carcinoma, which forms in cells that compose the surface of the skin.

The protein is called macrophage migration inhibitory factor, or MIF. It is a pro-inflammatory cytokine present in human blood that generates inflammation in response to infection, offering protection against some pathogens. But in this research, MIF emerged as a contributor to the chronic inflammation that precedes the development of skin cancer after long-term sun exposure. Previous studies have implicated MIF in other cancers, as well.

"Our data show that MIF appears to be affecting multiple pathways that are important for tumor generation and progression. It also is clear here that there is a link between inflammation and cancer," said Abhay Satoskar, associate professor of microbiology at Ohio State University and a coauthor of the study.

"No one else has shown this in a skin cancer model."

The scientists exposed normal mice and mice deficient in MIF to ultraviolet B light, the type of radiation from the sun that damages the skin. The mice were exposed to the light three days per week for 46 weeks, with doses increased regularly after week 13 to account for skin adaption to UVB exposure. The exposure in the study was designed to accelerate tumor growth and far exceeded the UVB exposure that humans experience over the same time period.

By week 37, more than two-thirds of the mice exposed to UVB light had developed at least one tumor, and all mice had developed tumors by week 45. The MIF-deficient mice averaged 2.89 tumors per mouse at the end of the exposure, compared to an average of 5.27 tumors per normal mouse. Overall, the MIF-deficient mice on average had about half as many tumors and significantly smaller tumors than did the normal mice. The tumors on the MIF-deficient mice were also less likely to be malignant than were tumors on normal mice.

Satoskar and colleagues compared a number of tumor characteristics on the two groups of UVB-exposed mice to confirm the MIF deficiency's role in lowering the incidence of skin cancer.

The MIF-deficient mice had almost twice as many tumor-suppressor cells of the p53 gene than did normal mice, suggesting that the presence of the MIF protein interferes with this tumor suppressor's ability to do its work. The MIF-deficient mice also had lower concentrations of the protein vascular endothelial growth factor (VEGF) than did normal mice. VEGF has previously been found to promote the development of blood vessels in certain types of cancer tumors, so the lower amount of the protein in MIF-deficient mice means the tumors they did develop had less vascular support to grow, Satoskar said.

Finally, MIF-deficient mice exposed to UVB rays had lower levels of three markers for inflammation, indicating an important link between MIF and the inflammatory response in skin that follows UVB exposure.

The scientists also observed that the MIF deficiency did not cause any significant side effects in the mice. Under normal circumstances, the amount of MIF in the blood remains constant.

"Some MIF is not bad, but we think that if it goes above a certain threshold, it starts doing crazy things,"





Satoskar said. "We're not aware of the natural existence of a MIF deficiency in humans, but in a mouse, we don't see any toxic effects."

MIF is also an important target for skin cancer research because previous studies have identified five polymorphisms in the MIF gene in humans. Polymorphisms are mutations in genes that, in the case of MIF, might make some individuals produce higher or lower levels of the protein, which could influence their susceptibility to skin cancers.

Satoskar and colleagues plan to examine biopsies of patients who have been diagnosed with squamous cell or basal cell carcinoma to see if these patients have a polymorphism on the MIF gene that would suggest a genetic predisposition toward the cancer.

"If we find a correlation, a MIF-gene polymorphism could become a biomarker to predict skin cancer. That would mean people who have a polymorphism that makes them high MIF producers would be more likely to develop skin cancer if they are exposed to the sun," Satoskar said. "We don't know yet whether there is a correlation, however."

The researchers also plan to begin tests of the drug under development in their MIF-deficient mouse model. The drug is based on a small molecule that blocks the activity of MIF in the blood and has been effective in other animal models of inflammatory diseases at a very low dose.

"Our goal is to move forward to see whether this molecule is a new target for prevention and/or treatment of this disease," Satoskar said.

The study is scheduled for publication in the March 2009 issue of the Journal of the Federation of American Societies for Experimental Biology. This work was supported by an Ohio State University Comprehensive Cancer Center seed grant.

Source:

<http://www.sciencedaily.com/releases/2009/02/090217104648.htm>

Publication:

Macrophage migration inhibitory factor (MIF) plays a critical role in pathogenesis of ultraviolet-B (UVB) - induced nonmelanoma skin cancer (NMSC).

Martin J, Duncan FJ, Keiser T, Shin S, Kusewitt DF, Oberyszyn T, Satoskar AR, Vanbuskirk AM.

PMID: 18952710





Meetings

March 18 – 20, 2009

Advanced Surgical Techniques in Mice: Jugular Vein & Carotid Artery Catheterizations

La Jolla, California

Meeting Information: http://courses.jax.org/2009/adv_surg_2.html

Mar 20, 2009

**Advanced Surgical Techniques in Mice: Thymectomy, Nephrectomy & Kidney Capsule Implant-
Second Session**

La Jolla, California

http://courses.jax.org/2009/adv_surg_4.html

March 23 – 25, 2009

CHI's-3rd Annual MicroRNA In Human Disease & Development

Boston, Massachusetts

Meeting Information: <http://www.healthtech.com/mrn/overview.aspx>

April 7 – 8, 2009

CHI's-Inaugural Kinase Inhibitor Chemistry: Charting the Chemical Space

San Diego, California

Meeting Information: <http://www.DrugDiscoveryChemistry.com>

April 6 – 10, 2009

CHI's-5th Annual PEGS – Protein Engineering Summit

Boston, Massachusetts

Meeting Information: <http://www.pegsummit.com/>

Apr 13 - Apr 17 2009

Colony Management: Principles and Practices

Bar Harbor Maine

Meeting Information: http://courses.jax.org/2009/colony_barharbor09.html





AACR Meeting

April 18 – 22, 2009

AACR-100th Annual Meeting

Colorado Convention Center

Denver, Colorado

Meeting Information:

<http://www.aacr.org/home/scientists/meetings--workshops/aacr-100th-annual-meeting.aspx>

NCI/NIH-Sponsored Session at the AACR Meeting

Monday, April 20, 10:30 am - 12:00 pm

cancer Biomedical Informatics Grid[®] (caBIG[®]) Resources to Support Life Sciences and Translational Research

The Cancer Biomedical Informatics Grid[®] (caBIG[®]) is a virtual network that connects data, research tools, scientists and institutions to leverage the combined strengths and expertise in an open environment using common standards. Data and analytical services are available through caGrid, which makes it possible for the databases at multiple institutions to be interconnected to support data sharing and integration. We will start with an introduction to the caBIG[®] program, followed by presentations on tools developed to support integrative biomedical and translational research. We will also discuss experiences in the caBIG[®] technology adoption. Applications featured in this session and additional caBIG[®] resources will be discussed in more detail at the caBIG[®] learning center later the same day.

Notices and Funding Opportunities

Continuation of the NCI Program for Rapid, Independent Diagnostic Evaluation (PRIDE) of Cancer Biomarkers

NOT-CA-08-023

National Cancer Institute

<http://grants.nih.gov/grants/guide/notice-files/NOT-CA-08-023.html>

IACUC 101 Workshop and PRIM&R 2009 IACUC Conference: March 28-31, 2009 in San Diego, CA

NOT-OD-09-048

National Institutes of Health

<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-09-048.html>

Request for Information (RFI): Priorities for Biomarkers For Cancer Detection, Diagnosis, and Prognosis

NOT-CA-09-014

National Cancer Institute

<http://grants.nih.gov/grants/guide/notice-files/NOT-CA-09-014.html>





Change in Application Due Date for RFA-RR-09-002 Mutant Mouse Regional Resource Centers (U42) applications

NOT-RR-09-006

National Center for Research Resources

<http://grants.nih.gov/grants/guide/notice-files/NOT-RR-09-006.html>

New Technologies for Liver Disease STTR (R41/R42 and R43/44)

PA-09-094 and PA-09-095

Multiple Institutes

<http://grants.nih.gov/grants/guide/pa-files/PA-09-094.html>

<http://grants.nih.gov/grants/guide/pa-files/PA-09-095.html>

caBIG™ Tools

caBIG® Announces the Release of caTissue Suite 1.1

We are pleased to announce the release of caTissue Suite 1.1 - the fifth release of the caTissue line of software developed under the caBIG® program.

Many congratulations to the development team at Washington University in St Louis led by Mark Watson and Rakesh Nagarajan and the assistance of end user and testing teams at Thomas Jefferson University Indiana University University of Pennsylvania University of Pittsburgh Yale University Project management support was provided by LiMing Shen of SAIC and Linda Schmandt of the University of Pittsburgh.

caTissue Suite 1.1 is an open-source, web and programmatically accessible tool for managing biospecimens collected in support of basic and clinical research. caTissue Suite helps users manage inventory, annotation and sample tracking, and the derivation and aliquoting of samples for follow-up analysis. caTissue Suite also supports clinical and pathology report annotation and provides query capabilities for researchers to identify and find samples for their own research projects. caTissue Suite also features Dynamic Extensions, allowing biobanks to develop and share annotations customized for their institution.

New capabilities of caTissue Suite 1.1 include:

- The ability to support multiple repositories across an institution using a single installation of caTissue while supporting appropriate data security and patient privacy
- Advanced query capabilities including: Time between events, patient age and other key annotations
- Compatibility with caGrid, allowing users to share and access data locally or across the caBIG® network
- Enhanced clinical annotation capabilities including the ability to create customized forms
- Performance improvements including improved user interface and workflow.

caTissue Suite is built on a common set of Open Source technologies for ease of installation and maintenance and is interoperable with other caBIG® tools and technologies. A Java-based Application Programming Interface (API) and a caGrid compatible Grid Service are provided for programmatic access to data.

More information about caTissue, including user and technical documentation is available from

<https://cabig.nci.nih.gov/tools/catissuesuite>.





MMHCC
*the Mouse Models
of Human Cancers Consortium*



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