

Melanoma Horizons

This is a semiannual newsletter from M.D. Anderson Cancer Center to referring physicians about the latest advances in melanoma cancer research.

Issue 11

February 2011

Announcing Competitive Renewal of MD Anderson SPORE in Melanoma – Elizabeth Grimm, Ph.D.

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Skin Cancer is the most common form of cancer in the United States. Of the three major types of skin cancers; two are generally curable and are called basal cell and squamous cell carcinoma. Melanoma is the third and most serious form of skin cancer, which if recognized and removed early from the skin has a high cure rate (over 80%), but if allowed to invade, it spreads quickly throughout the body and results in metastasis. Melanoma metastasis are notoriously resistant to standard therapies. Fortunately, our research on personalized cancer therapies, tailor-based on individual patient's tumor characteristics and treatment responses, are fast becoming the new standard in cancer treatment. M.D. Anderson Cancer Center is a pioneer in this field, where we conduct cutting edge research to bring these exciting discoveries into the clinic.

As part of our efforts to improve and support this type of research, we are pleased to announce our recent renewal of funding for another five years, for the NIH grant entitled "UT MD Anderson Cancer Center SPORE in Melanoma", which will further strengthen our efforts to promote highly collaborative translational research to develop new therapies and improve outcomes for our patients with melanoma. Specialized Programs of Research Excellence (SPORE) are highly competitive National Cancer Institute's funded research programs, specifically designed to support interdisciplinary research activities to bring novel and diverse approaches to early detection, diagnosis, treatment and prevention of cancer. There are approximately 50 SPOREs active in any given time in the country. Our first melanoma SPORE was awarded in 2003 and funded in 2004, and now this recent renewal will keep projects moving forward through 2015, with \$2,300,000 total and \$1,455,696 direct costs awarded per year from the NCI for each future year.

The UT MDACC SPORE in Melanoma is led by Elizabeth A. Grimm, PhD, deputy division head for Research Affairs in the Division of Cancer Medicine and professor in Melanoma Medical Oncology, along with co-directors Jeffrey E. Lee, MD chair of Surgical Oncology; Jeffrey Gershen-

wald, MD, professor in Surgical Oncology, and Patrick Hwu, MD, chair of Melanoma Medical Oncology. The Melanoma SPORE has five new projects, which are supported by three core facilities. Developmental projects will fund highly innovative research ideas, which will form the foundation for future research. The five projects are:

1. Patrick Hwu, MD, Chairman of Melanoma Medical Oncology and Richard Royal, MD, professor in Surgical Oncology will devise novel strategies to use the patient's immune system to fight against melanoma. In this project, they are testing a novel anti-microbial peptide as an adjuvant, produced in our body, to generate a systemic immune response to destroy tumors.

2. Amy Heimberger, MD, associate professor in Neurosurgery and Waldemar Priebe, PhD, professor in Experimental Therapeutics will work with drugs that specifically target signaling pathways predominantly used by cancer cells to proliferate and survive. Their studies may provide new insights to treat melanoma patients with highly fatal brain metastasis.

3. Elizabeth A. Grimm, PhD, Suhendan Ekmekcioglu, PhD, associate professor in Melanoma Medical Oncology, Kevin Kim, MD, associate professor in Melanoma Medical Oncology, and Victor Prieto, MD, PhD, professor in Pathology will collaborate to identify molecular patterns/signatures that predict patient survival. By analyzing these patterns/signatures and comparing them across several patients, they will identify targets, which are usually altered or abnormally expressed in tumors such as nitric oxide synthase. They exploit this information to develop novel treatment regimens for improved outcomes in patients with metastatic melanoma and other skin cancers.

4. Menashe Bar-Eli, PhD, professor in Cancer Biology, Wen-Jen Hwu, MD, PhD, professor in Melanoma Medical Oncology, Gabriel Lopez-Berestein, MD, professor in Experimental Therapeutics, and Chuan Ng, associate professor in Diagnostic Radiology will be using nanoparticles to deliver small molecule therapeutics to treat

Fifth Annual DoCM Faculty Recognition and Award Program

Congratulations to **Kevin Kim, M.D.**, Associate Professor, on his nomination for the Melvin L. Samuels Awards for Excellence in Patient Care for the Division of Cancer Medicine's annual Faculty Recognition and Award Program in December 2010.



Congratulations to **Agop Bedikian, M.D.**, Professor, on his nomination for the John Mendelsohn Lifetime Scientific Award for the Division of Cancer Medicine's annual Faculty Recognition and Award Program in December 2010.



Congratulations to **Michael Davies, M.D., Ph.D.**, Assistant Professor, on his nomination for the Emil Frei III, Award for Excellence in Translational Research for the Division of Cancer Medicine's annual Faculty Recognition and Award Program in December 2010.



American Legion Auxiliary Fellowship



Jessica Chacon, GSBS student is the proud recipient of the American Legion Auxiliary Fellowship in cancer research. The award is a \$5000 fellowship awarded to pre-doctoral students that can be renewed for up an additional 2 years. The Graduate School of Biomedical Sciences hosted a luncheon on November 5, 2010 for the recipients of the Award, along with their mentors, to meet the leadership of the American Legion Auxiliary. The American Legion Auxiliary is an organization of women who have served in the armed forces, as well as wives, mothers, sisters, daughters and granddaughters of members of the American Legion.

SPORE in Melanoma – continued

metastatic melanoma patients. This new approach can be combined with conventional chemotherapy to achieve better outcomes.

5. Jeffrey E. Lee, MD, Qingyi Wei, MD, PhD, professor in Epidemiology, Christopher Amos, PhD, professor in Epidemiology and John Reveille, MD, professor Internal Medicine and director of Division of Rheumatology and Clinical Neurogenetics at The University of Texas Medical School of Houston, will work towards the determination of the most important genetic polymorphisms influencing melanoma progression. This will enable the doctors to personalize the treatment by accurately identifying high-risk patients for adjuvant therapies and improve the clinical outcomes.

The SPORE also includes an Informatics, Tissue Resource and Pathology Core led by Drs. Jeffrey Gershenwald, Victor Prieto and Michael Davies, MD, PhD, assistant professor in Melanoma Medical Oncology and the Biostatistics and Bioinformatics Core currently led by Donald Berry, PhD, professor in Biostatistics. This core is not only an NCI requirement for SPOREs, but also has been the key to much of our success. Recently, the research and results from a most recent manuscript (Ellerhorst, Greene, Ekmekcioglu, et al., Clinical Correlates of NRAS and BRAF Mutations in Primary Human Melanoma, *Clinical Cancer Research*, Jan 15th; 17:229-35) was made possible by the careful documentation and processing of 297 of these valuable cutaneous primary tumor samples provided by this Core.

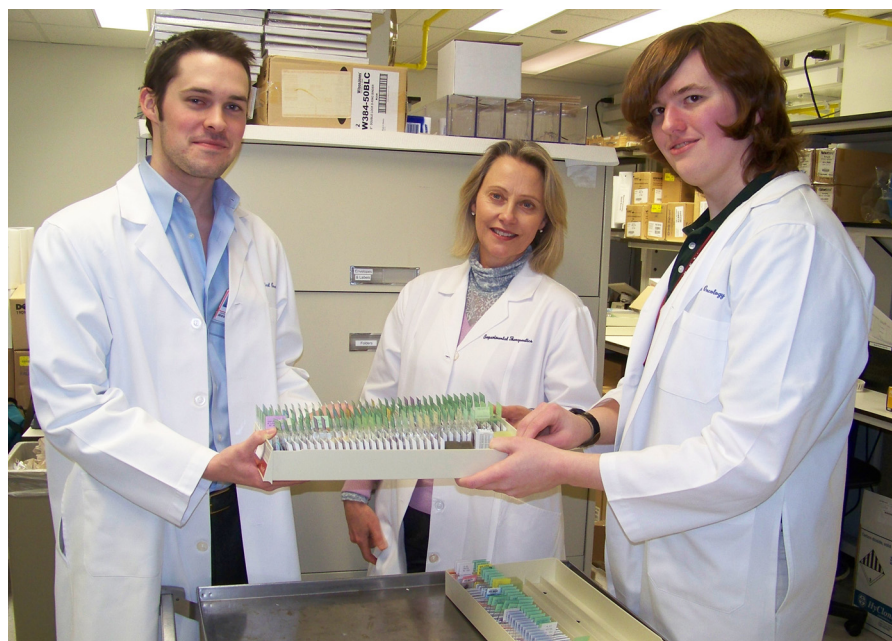
With the thorough analyses of data generated from two of the five projects and statistical analyses by our Biostatistics and Bioinformatics Core staff Roland Bassett, Ping Liu and Dawen

Sui, the following abstracts have been submitted and/or presented for 2011 national or international meetings:

- Eastern North American Region (ENAR) of the International Biometrics Society Spring Meeting, New Orleans, LA, March 2010. A Genome-wide Association Approach on Detecting CNVs for SNP Genotyping Data. Yaji Xu, Bo Peng, Emily Y. Lu and Christopher Amos.
- 19th Annual International Genetic Epidemiology Society (IGES) Meeting, Boston, MA, October 10-12. Genome-wide Algorithm for Detecting CNV Associations with Diseases. Yaji Xu, Bo Peng, Emily Y. Lu and Christopher Amos.
- 60th American Society of Human Genetics (ASHG) Annual Meeting, Washington, DC, November 2-6, 2010. Genome-wide Association Study to Detect CNV Associations with Cutaneous Melanoma. Yaji XU, Elizabeth Pugh, Bo Peng, Audrey Schnell, Emily Y. Lu, Kurt
- 71st Society of Investigative Dermatology (SID) Annual Meeting, Phoenix, Arizona, May 4-7, 2011 and the 102nd American Association for Cancer Research (AACR) Annual Meeting, Orlando, Florida, April 2-6, 2011. Inducible nitric oxide synthase suppresses the expression of CXCL10 and hence leads to the poor outcome of Stage III malignant melanoma. Keiji Tanese, Suhendan Ekmekcioglu, and Elizabeth Grimm.
- 22nd World Congress of Dermatology, in Seoul Korea, May 17 - 20, 2011. "Novel nitric oxide-associated post-translational modification of p53 (S-nitrosylation) inhibits DNA binding in Melanoma" John Kwon and Elizabeth Grimm.

Tissue transactions in MelCore

Pictured (left to right) **Jared Malke**, Research Assistant in Surgical Oncology, **Dr. Vicky Greene**, Research Scientist in Melanoma Medical Oncology, and **Garrett Matejka**, Research Assistant in Surgical Oncology.



Current Clinical Advances in Melanoma Medical Oncology

Below is a list of open and approved Melanoma Oncology clinical trials as of 1/3/2011. To refer a patient please see page 6.

Single Center Clinical Trials

Adjuvant

[Pegylated Interferon + Peptide \(2006-0816\)](#) Phase I

Principal Investigator: Wen-Jen Hwu, MD, PhD

Research Nurse: Tracey Moffatt, RN

Patients must be free of disease after surgical resection for AJCC stage II or III (N1a) melanoma (T2b, T3a, T3b, T4a, T4b and N1a or N2a). Patients must be HLA-A0201 positive and have had surgical resection within 90 days.

Chemo-Naïve Patients (no previous chemotherapy)

[IPILIMUMBAB plus Temozolomide in Patients with Metastatic Melanoma \(2009-0408\)](#) Phase II

Principal Investigator: Agop Bedikian, MD

Research Nurse: Suzanne Cain, RN

For patients with unresectable Stage III/IV melanoma. No previous cytotoxic drugs, targeted therapies or anti CTLA4. Patients with brain lesions will be evaluated by the principal investigator or his designee as to eligibility.

[Biochemotherapy with Abraxane \(2009-0124\)](#)

Principal Investigator: Nicholas Papadopoulos, MD

Research Nurse: Suzanne Cain, RN

Patients with unresectable Stage III or advanced Stage IV metastatic melanoma with measurable disease.

Patients with previous chemotherapy

[T-Cells +/- Dendritic Cells \(2004-0069\)](#) Phase II

Principal Investigator: Patrick Hwu, MD

Research Nurse: Sandy Mahoney, RN

In this study, T-cells capable of recognizing and killing melanoma will be isolated from tumor biopsies and expanded in the laboratory. The T-cells will then be reinfused into the patients with or without dendritic cells, which are immune cells capable of potentially activating T-cells. This study is for patients with a good performance status, with measurable metastatic melanoma, and a site that can easily be biopsied.

[Trial of High Dose Interleukin-2 \(HDIL-2\) with Recombinant MAGE-A3 Protein Combined with Adjuvant System AS15 in Patients with Unresectable or Metastatic Melanoma \(2010-0113\)](#) Phase II NCT

Principal Investigator: Jade Homsy, MD

Research Nurse: MaryAnne LaFontaine, RN

Patients with at least one biopsible lesion and/or access to paraffin-embedded tissue block sample.

[Teseaxel \(2009-0624\)](#) Phase II

Principal Investigator: Agop Bedikian, MD

Research Nurse: Karen Woodard, RN

Patients with advanced melanoma and normal serum

LDH. Unresectable disease or metastatic Stage IV disease. No CNS or ocular disease allowed.

[Activation of pDCs at tumor and vaccine sites with TLR agonist \(2008-0416\)](#) Phase II

Principal Investigator: Patrick Hwu, MD and Richard Royal, MD

Research Nurse: Abby Yu, RN

For patients with metastatic melanoma with measurable disease, Stage IIIC (in transit lesions) or Stage IV (M1A). Patients must be HLA-A201 and DP4 positive to participate and have at least 4 biopsiable lesions. No previous exposure to gp100 or MAGE-3 peptide.

[TPI in Combination with Temozolomide \(2009-0357\)](#) Phase I/II

Principal Investigator: Agop Bedikian, MD

Research Nurse: Maryanne LaFontaine, RN

This study combines the cytotoxic agent Temozolomide with a novel microtubule inhibitor TPI287. Patients with unresectable Stage III or Stage IV, including bulky stage III and M1-3. Patients who have brain metastases must be off drugs for at least a week.

[Decitabine and PEG Intron \(2007-0450\)](#) Phase I/II

Principal Investigator: Wen-Jen Hwu, M.D.

Research Nurse: Anna Vardeleon, R.N.

The purpose of the study is to determine the safety and tolerability of the combination of drugs at 6 pre-determined dose levels in patients with advanced melanoma and to determine clinical benefit and progression-free survival. Patients may have one prior chemotherapy.

[LOC-Paclitaxel \(2009-0432\)](#)

Principal Investigator: Agop Bedikian, MD

Research Nurse: Karen Woodard, RN

Patients who have failed all conventional therapies and no other therapies are available. No CNS metastases allowed.

Patients with Metastatic Choroidal Melanoma

[Study of Genasense-Carboplatin-Paclitaxel-combination in Uveal Melanoma \(2010-0188\)](#) Phase II

Principal Investigator: Agop Bedikian, MD

Research Nurse: Tracey Moffatt, RN

Patients must have histologic or cytologic confirmation of malignant uveal melanoma and documented metastatic disease with measurable disease. Patients may have had previous treatment except hepatic chemoembolization is not allowed. Patients with brain metastases or history of brain metastases are not allowed.

[Hepatic Arterial Infusion of Abraxane \(2006-0603\)](#) Phase I

Principal Investigator: Dr. Agop Bedikian

Research Nurse: Karen Woodard, R.N.

Patients must have at least one clearly measurable metastatic lesion in the liver that is more than 2cm in the largest dimension. Patients must not have received prior systemic chemotherapy with regimens including taxanes. Prior adjuvant treatment with immunotherapy or vaccine therapy is allowed provided there is documentation of disease progression in the liver.

Multi-Center Clinical Trials

Neoadjuvant

[Temozolomide alone or with Pegylated interferon-alpha 2b \(2005-0143\)](#) Phase II

Principal Investigator: Wen-Jen Hwu, MD, PhD

Research Nurse: Tracey Moffatt, R.N.

Temozolomide is a drug that is designed to work by stopping

cancer cells from making new DNA. Pegylated Interferon Alpha-2b is a protein made by the human immune system that helps to fight viral infections regulate cell function. Patient should not have any prior systemic chemotherapy.

Chemo-Naïve Patients (no previous chemotherapy)

[DTIC vs Abraxane \(2007-0750\)](#) Phase III

Principal Investigator: Jade Homsy, MD

Research Nurse: Suzanne Cain, RN

The primary objective of this study is to compare the following regimens with respect to antitumor activity in patients who are previously untreated with cytotoxic chemotherapy for metastatic malignant melanoma.

Patients with previous chemotherapy

[Phase II Study of E7080 \(2010-0356\)](#)

Principal Investigator: Kevin Kim, MD

Research Nurse: Abby Yu, R.N.

Patients not previously treated with targeted therapy, measurable disease.

[Phase I/II GSK BRAFi - MEKi \(2009-0949\)](#)

Principal Investigator: Kevin Kim, MD

Research Nurse: Abby Yu, R.N.

Expansion Part C BRAF mutation (+) tumors, archived tissues,

no previous MEK or BRAF inhibitors.

[\(BRF113710\) A Single-arm, Open-Label Study of GSK2118436 in Previously Treated BRAF Mutant Metastatic Melanoma \(2010-0350\)](#) Phase II

Principal Investigator: Kevin Kim, MD

Research Nurse: Deborah Sanders, RN

Patients must have confirmed cutaneous metastatic melanoma (Stage IV) with BRAF mutation-positive. No active gastrointestinal disease. No history or evidence of brain metastases. No previous treatment with a BRAF or MEK inhibitor.

[GSK1120212, a MEK Inhibitor, in BRAF Mutation-positive Melanoma Subjects \(2009-0839\)](#) Phase II

Principal Investigator: Kevin Kim, MD

Research Nurse: Deborah Sanders, RN

No active gastrointestinal disease. No previous use of MEK inhibitor such as GSK1120212, AZD6244, PD0325901. Stable, treated (surgery, stereotactic radiosurgery) brain metastases for at least 8 weeks by MRI. Archived tissue or biopsy required for analyses to be enrolled.

[CHIR-265 \(2005-0949\)](#) Phase I/II

Principal Investigator: Dr. Kevin Kim

Research Nurse: Suzanne Cain, R.N.

RAF265 is a novel small molecule with potent inhibitory activity against mutant B-Raf kinase, VEGFR-2 and also to a lesser degree, PDGF-alpha, and c-kit.

Melanoma Philanthropic Funding

We would like to thank the following Donors who have generously donated over \$ 384,450 between July-December 2010.

Blue Water Express
Bradley O'Martin Melanoma Foundation
Claffey Pools
D. Durvasula
Dallas Associated Dermatologists, P.A.
Dr. Carl Plager
Floors Inc.
Fulbright & Jaworski L.L.P.
Jim and Miriam Mulva
KDC
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Swingle, Collins & Associates
Texas Star Commercial Maintenance Inc.
The Arena Energy Foundation

Proceeds Benefiting Melanoma Research at MD Anderson

AIM FOR A CURE MELANOMA WALK AND FUN RUN



SAVE THE DATE!

Saturday, September 24, 2011

MD Anderson Campus • Houston, Texas

Registration: 6:30 am • Walk/Run: 8:00 am

To Schedule an Appointment –

Call 713-563-9716 or 1-877-MDA-6789

Self Referral Form

<https://www2.mdanderson.org/sapp/contact/selfreferral/index.cfm>

Physician Referral Form

<https://my.mdanderson.org/>

If you are a patient or physician and wish to track appointments, view reports, and send secure messaging please register for on-line access at:

<https://my.mdanderson.org/>

You Can Make a Difference – How to Help

Gifts from individuals provide a significant portion of the funding needed to get new research off the ground. The Melanoma Oncology and Research Team is dedicated in helping our patients get the best treatment possible. Your contribution will help with our new research studies in the laboratory and the clinic, including studies of cancer vaccines, T-cell therapy, and new agents.

To make a donation by phone please call 713-792-3450 or 1-800-525-5841 and specify **Melanoma Vaccines** for your gift.

To make a donation online, you may visit our secure website page at

<http://www.mdanderson.org/melanomaresearch>

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