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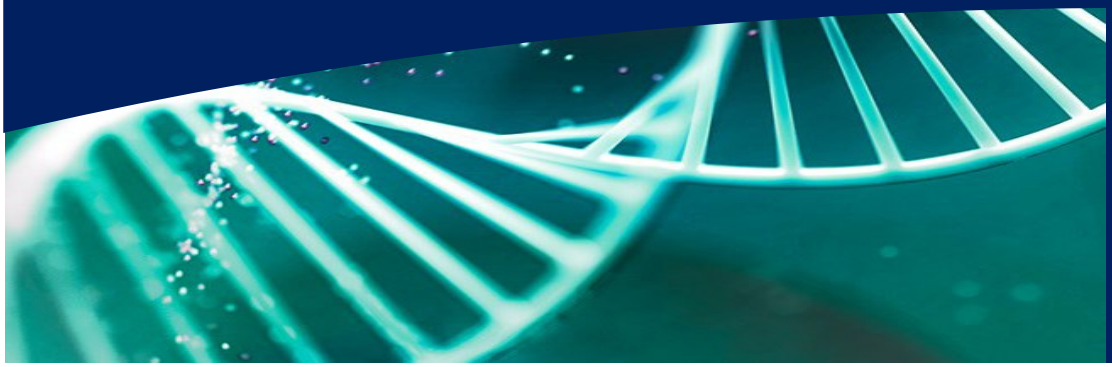
Newsletter of the Donald A. Adam Melanoma & Skin Cancer Center of Excellence

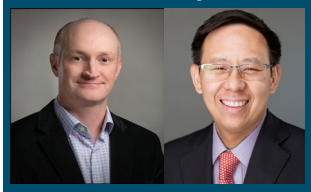
MOFFITT CANCER CENTER

Donald A. Adam Melanoma and Skin Cancer Center of Excellence

"To promote transformative research and new clinical trials that improve outcomes for skin cancer patients."



Leadership Corner



Keiran Smalley, PhD
Kenneth Tsai, MD, PhD

Welcome to the summer edition of the CoE newsletter! There is a lot to celebrate. In this issue we highlight new two publications from CoE faculty that unravel the mechanisms of metastasis in uveal melanoma and then tumor progression in cutaneous melanoma. In terms of funding, the CoE group has been recently awarded three significant new grants that will help develop new cellular therapies for patients with melanoma, uncover new mechanisms of melanoma progression and develop the new generation of personalized therapies for rare melanomas. In May, we held our annual retreat, in which CoE faculty had the opportunity to showcase their latest research and forge new collaborations. We are also happy to announce an exciting new partnership between the CoE and a local patient group who are fundraising for uveal melanoma research. Wishing you all a fun and productive summer and don't forget that sunscreen!

CoE/Cutaneous Oncology Annual Scientific Retreat

On May 5th, 2026, faculty and trainees from the Department of Cutaneous Oncology and the Melanoma and Skin Cancer Center of Excellence came together at the Tampa aquarium for a daylong retreat. Sessions focused on cutting edge theme such as the development of new cell therapies for melanoma, the use of AI in research, rare melanomas and skin cancers, and new targeted therapies for melanoma. The program also included a talk from Sara DiNapoli, Director of Scientific Programs at the Melanoma Research Alliance, who gave details of new funding opportunities. The afternoon session introduced several new CoE faculty including Dr. Golnaz Morad and Dr. Christopher Medina. The program provided a great overview of the exciting research ongoing in the CoE and offered many new opportunities for collaboration among the group.

Publication: Study Identifies Protein that Helps Eye Cancer Spread to the Liver

Key Highlights

- GDF15, a protein that can be secreted by uveal melanoma cells, helps the cancer spread from the eye to the liver. Uveal melanoma is the most common form of eye cancer in adults.
- The protein disrupts the activities of liver support cells, which, when healthy, help repair damage.
- Communication between the cancer cells and liver cells generates changes to the liver's microenvironment, including promoting the growth of new blood vessels that supply tumors with the nutrients and oxygen they need to thrive.
- In animal studies, shutting down GDF15 resulted in fewer and smaller liver tumors.
- The study pinpoints potential new ways to stop or slow the spread of cancer from the eye to the liver.

TAMPA, Fla. — A study led by researchers at Moffitt Cancer Center explain why uveal melanoma, the most common form of eye cancer, often spreads to the liver. The uvea is the middle layer of the eye, including the iris.
The findings, published in Cancer Research, identify an important role for tumor-derived growth differentiation factor 15 (GDF15), a stress-response signaling protein, in enabling metastasis to the liver.
Researchers found that eye cancer cells release unusually high levels of GDF15 when they reach the liver. When stellate support cells, which help repair liver damage, were exposed to the GDF15, they produced elevated levels of collagen and fibronectin, molecules that are important for normal repair. Excessive buildup, however, can create conditions that allow tumors to establish themselves within the liver.
The interaction between GDF15 and stellate cells also promoted the growth of new blood vessels that deliver oxygen and nutrients to the liver tumors, supporting their expansion. When the researchers blocked GDF15 in uveal melanoma cells, there were fewer, smaller liver tumors

Q&A with Keiran Smalley, Ph.D., senior author and director of the Donald A. Adam Comprehensive Melanoma Research Center of Excellence at Moffitt.

What does this discovery mean for patients with uveal melanoma, both before the cancer possibly spreads to the liver and after it has spread?
Patients with class 2 uveal melanoma have a high risk of developing liver metastases. There are currently no FDA-approved strategies to prevent this from occurring. It is possible that early therapeutic targeting of GDF15 through anti-GDF15 antibodies could either delay or even prevent the outgrowth of liver metastases. In patients with established liver metastases, GDF15 could be required for the maintenance of liver metastases, but this would need to be tested through further studies.

Why does this type of eye cancer spread to the liver far more often than to other organs?
It is not clear why uveal melanoma has this unique preference for liver metastasis. Some studies have suggested that uveal melanoma cells can spread to multiple organs but only really grow in the liver.

Keiran Smalley, PhD
Skin Cancer CoE,
Senior Member, Tumor Microenvironment &

"It is possible that early therapeutic targeting of GDF15 through anti-GDF15 antibodies could either delay or even prevent the outgrowth of liver metastases." - Keiran Smalley, Ph.D.

Why did you focus on GDF15?
GDF15 is a signaling molecule that can be secreted by tumor cells and influence other tissues, making it a strong candidate for promoting communication between cancer cells and the liver. We focused on it because earlier research showed that uveal melanoma cells associated with liver metastases produce high levels of GDF15.

Could this discovery be used to develop new drugs or treatments to reduce or even prevent the spread of this form of eye cancer to the liver?
Antibodies that block the function of GDF15 have been shown to be highly effective at treating cancer cachexia, a condition that includes reduced desire to eat and weight and muscle loss. It is likely that these antibodies could be repurposed and evaluated as a therapy for uveal melanoma.

Can you envision this finding applying to other cancers?
Yes, GDF15 levels are known to be very high in colorectal carcinoma, renal cell carcinoma , lung cancer, and urothelial carcinoma. It is likely that GDF15 plays a similar role in these other cancers. If so, targeting GDF15 may offer new ways to target distant metastases.
This study was supported by the National Cancer Institute (R01CA256193; P30 CA076292; P30 CA247796; P30 CA142543), National Eye Institute (P30 EY030413), Cancer Prevention and Research Institute of Texas (RR220010), Research to Prevent Blindness, Inc., and appropriations from

Publication: Identification of MAFG as a driver of melanoma development and progression

Florian Karreth, PhD
Vice Chair,
Department of Molecular Oncology
Associate Member,

Melanoma, an aggressive form of skin cancer, can change its behavior over time in ways that make it harder to treat. This shape-shifting ability is controlled by a key protein called MITF, which acts like a master switch for how melanoma cells behave. CoE Researchers, led by Dr. Florian Karreth, have now discovered that another protein, MAFG, plays an important role in controlling MITF.

MAFG is found at unusually high levels in melanoma, and patients with more of it tend to have worse outcomes. The study shows that MAFG physically connects with MITF and changes where MITF operates in the cell's DNA, effectively hijacking its instructions. When MAFG was experimentally removed from melanoma cells — both in the lab and in animal models — cancer cells were less able to grow and spread. MAFG also appears to play a role in the early stages of melanoma development, helping benign moles turn into full-blown cancer.

Overall, this research reveals a previously unknown partnership between MAFG and MITF that drives melanoma's ability to change states and become more aggressive, opening a potential new target for future treatments. This work was recently published in *Nature Communications*. Link https://www.nature.com/articles/s41467-026-73291-x

New funding relationship with Your Next Step is the Cure

Your Next Step is the Cure are a charitable foundation that supports research into uveal melanoma based in Plant City. The group hold an Annual 5K race in Aldermans Ford Park, Plant City as their main fundraising event. We are excited to announce that Your Next Step is the Cure is partnering with the CoE to fund uveal melanoma research at Moffitt. To celebrate this partnership, we had a visit from Bernadette and Linda, the organization founders, who met CoE faculty and had lab tours. For details on the run and how to sign up see: https://runsignup.com/Race/FL/PlantCity/YourNextStepistheCure

New Grants

New NCI R01 awarded to Dr. Florian Karreth
Title: Defining the role of MAFG in melanocyte transformation and melanoma development
Amount: $3,036,245

Melanoma remains one of the most aggressive and treatment-resistant cancers, particularly once it reaches the metastatic stage. While oncogenic mutations have long been the focus of melanoma research, it is increasingly clear that non-genetic mechanisms, including epigenetic reprogramming, transcriptional dysregulation, and post-transcriptional gene control, play equally powerful roles in driving tumor initiation and progression. Because these mechanisms are dynamic and potentially reversible, they represent compelling targets for therapeutic intervention. The new R01 from Dr. Karreth and his team focuses on MAFG, a basic leucine zipper transcription factor that they identified as a critical regulator of melanomagenesis (see accompanying article on their recent paper in *Nature Communications*). In their new R01, Dr. Karreth and his co-workers will pursue three interconnected aims. First, using the ESC-based GEMM platform, they will comprehensively evaluate MAFG's contributions across the full arc of melanoma development, from melanocyte transformation through metastasis. Second, the investigators will dissect the transcriptional complexes through which MAFG operates, including its cooperation with MITF and the canonical binding partner BACH2, to define the molecular pathways underlying its oncogenic activity. Third, they will leverage acute MAFG depletion strategies and CRISPR-based screening to identify upstream regulators of MAFG that may represent actionable therapeutic targets. Together, Dr. Karreth's studies aim to establish MAFG as a central node in the non-genetic rewiring of melanoma and to lay the groundwork for novel treatment strategies targeting transcriptional dependencies in this disease.

Florian Karreth, PhD
Vice Chair,
Department of Molecular Oncology
Associate Member,

Lilit Karapetyan, PhD
Assistant Member,
Departments of Cutaneous Oncology & Translational Pathology

Member, Immuno-Oncology & Immune-cell Therapy Programs

Florida Innovation award to Dr. Lilit Karapetyan
Title: CD40L-41BBL Augmented Tumor-Infiltrating Lymphocytes (TIL) for Advanced Melanoma: Phase I Evaluation of Safety, Feasibility, and Preliminary Clinical Activity
Amount awarded: $1,915,651.00.

Although recent advances in immunotherapy and targeted treatments have improved survival for many melanoma patients, about half of those with unresectable stage IV melanoma do not respond, and others eventually relapse. New therapies are urgently needed for patients whose cancer continues to progress despite standard treatments. This new study led by Dr. Karapetyan plans to evaluate a next-generation form of tumor-infiltrating lymphocyte (TIL) therapy, a personalized treatment made from a patient's own immune cells. These cells are collected from the patient's tumor, expanded in the laboratory, and then reinfused to attack the cancer. The research team has developed an improved TIL growth method that adds two natural immune signals, CD40L and 4-1BBL, which enhance T-cell growth, strength, and persistence. Laboratory studies show that this dual-signal approach produces more effective cancer-fighting immune cells compared with current methods. The team are now conducting a Phase I clinical trial to test the safety and feasibility of this enhanced TIL therapy in patients with advanced melanoma who have exhausted other treatment options. Researchers will also analyze blood and tumor samples to understand how the therapy works and to identify markers that predict which patients are most likely to benefit. If successful, this study will lay the groundwork for larger clinical trials and position Florida as a leader in developing innovative immune therapies for melanoma.

New DoD Focused Program Award – Rare Melanomas: Dr. Keiran Smalley (Moffitt) and Dr. Andrew Aplin (Thomas Jefferson)

Title: Identification and Evaluation of Immune and Targeted Therapies for Acral Melanoma

Amount awarded: $2.8M

The new 4-year DoD Focused Program Award will evaluate new approaches to treat acral melanoma. The program is led by Dr. Keiran Smalley at Moffitt in partnership with Dr. Andrew Aplin at Thomas Jefferson University, Philadelphia. As an immunotherapy strategy, Dr. Smalley's team will use a specialized type of immune cell called CAR-T cells, which will be engineered to recognize unique proteins expressed on the surface of acral melanoma cells and selectively kill these cells. They will evaluate whether CAR-T cells directed against B7-H3 can eliminate acral melanoma in animal models. B7-H3 (CD276) is a cell surface protein that modulates interferon release. It has limited expression in normal human tissues but high expression levels in multiple cancers, making it an ideal immunotherapy target. For targeted therapy, Dr. Aplin and his group will test a new class of drugs that directly target active forms of RAS called RAS^{multi}(ON) inhibitors. RAS is broadly activated in acral melanoma through RAS gene mutations as well as amplification or deletion of genes in the RAS pathway. They will test whether RAS^{multi}(ON) inhibitors can effectively shrink acral melanomas in mice. Through synergies between the projects, the collaborative team will determine whether acral melanomas develop resistance to these immune-based and targeted treatments and will define how this may occur.

Keiran Smalley, PhD
Skin Cancer CoE,
Senior Member, Tumor Microenvironment & Metastasis

ASCO

Investigators from the Department of Cutaneous Oncology/the CoE were well represented at the ASCO Annual meeting in Chicago, IL. Below are some of the presentations from the group.

Final results of a first-in-human study of MC1R-targeting radiopharmaceutical 225actinium MTI-201 (255Ac-MTI-201) in metastatic uveal melanoma (mUM)	Nikhil Khushalani
Health-related quality of life following tumor-infiltrating lymphocytes (TIL) therapy with commercial lifleucel in metastatic melanoma: Real-world longitudinal patient reported outcomes	Kimberly Ward
A phase II trial of olaparib in combination with pembrolizumab in metastatic uveal melanoma	Nikhil Khushalani
Outcomes of neoadjuvant immunotherapy (NeoIO) in Merkel cell carcinoma	Lacey Mead
Phase 2 sequential treatment of percutaneous hepatic perfusion with melphalan/hepatic delivery system followed by tebentafusp in the treatment of metastatic uveal melanoma	Jonathan Zager
Novel adaptive versus continuous dosing of encorafenib and binimetinib in combination with nivolumab in advanced BRAF V600E mutant melanoma.	Zeynep Eroglu
Immunologic determinants in procured melanoma tissue as drivers of durable response in tumor-infiltrating lymphocyte therapy	Lilit Karapetyan
A phase II study of neoadjuvant ipilimumab-nivolumab-retatlimab (INR) combination immunotherapy in high-risk resectable melanoma	Ahmad Tarhini

Upcoming grant deadlines: Department of Defense

The Melanoma Research Program (MRP) of the Department of Defense has been re-issued for 2026. $40M has been allocated for the program. Below are the details of the types of awards available, along with the pre-application and application deadlines.

Title of Program				
Focused Program Award - Rare Melanomas	FY26 MRP Focused Program Award - Rare Melanomas Program Announcement	05-21-2026	07-13-2026 - (Pre-application - Pre-Proposal) 10-14-2026 - (Application)	**Login to Apply**
Idea Award	FY26 MRP Idea Award Program Announcement	05-21-2026	07-13-2026 - (Pre-application - Pre-Proposal) 10-14-2026 - (Application)	**Login to Apply**
Melanoma Academy Scholar Award	FY26 MRP Melanoma Academy Scholar Award Program Announcement	05-21-2026	09-22-2026 - (Pre-application - Letter Of Intent) 10-14-2026 - (Application)	**Login to Apply**
Survivorship Research Award	FY26 MRP Survivorship Research Award Program Announcement	05-21-2026	09-22-2026 - (Pre-application - Letter Of Intent) 10-14-2026 - (Application)	**Login to Apply**
Team Science Award	FY26 MRP Team Science Award Program Announcement	05-21-2026	07-13-2026 - (Pre-application - Pre-Proposal) 10-14-2026 - (Application)	**Login to Apply**

For more details and application instructions go to https://cdmrp.health.mil/funding/mrp

Monthly MSCCoE Research Meetings

Meetings recur on the second Thursday of each month at 3:00pm in SRB Atrium 4 and via Zoom. Invited guest speakers at date/time as noted.

Upcoming MSCCoE Monthly Research Meetings – Featured Presenters and Invited Speakers

July 9 : Nikhil Khushalani, PhD
Assistant Center Director, Clinical Research Review and Partnerships
Vice Chair & Senior Member, Department of Cutaneous Oncology

August 13 : Marcelo Bonini, PhD
Department Chair, Department of Metabolism and Physiology

September 10 : Golnaz Morad, DDS, PhD
Assistant Member, Department of Tumor Microenvironment & Metastasis

October 8 :

November 12 : Amer Beg, PhD
Senior Member, Department of Immunology

December 10 : Ignacio Garrido-Laguna, MD, PhD, MBA
Department Chair, Department of Early Therapeutics

October 8th is available if you'd like to speak, please contact Keiran Smalley.

With Our Most Heartfelt Thanks…

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