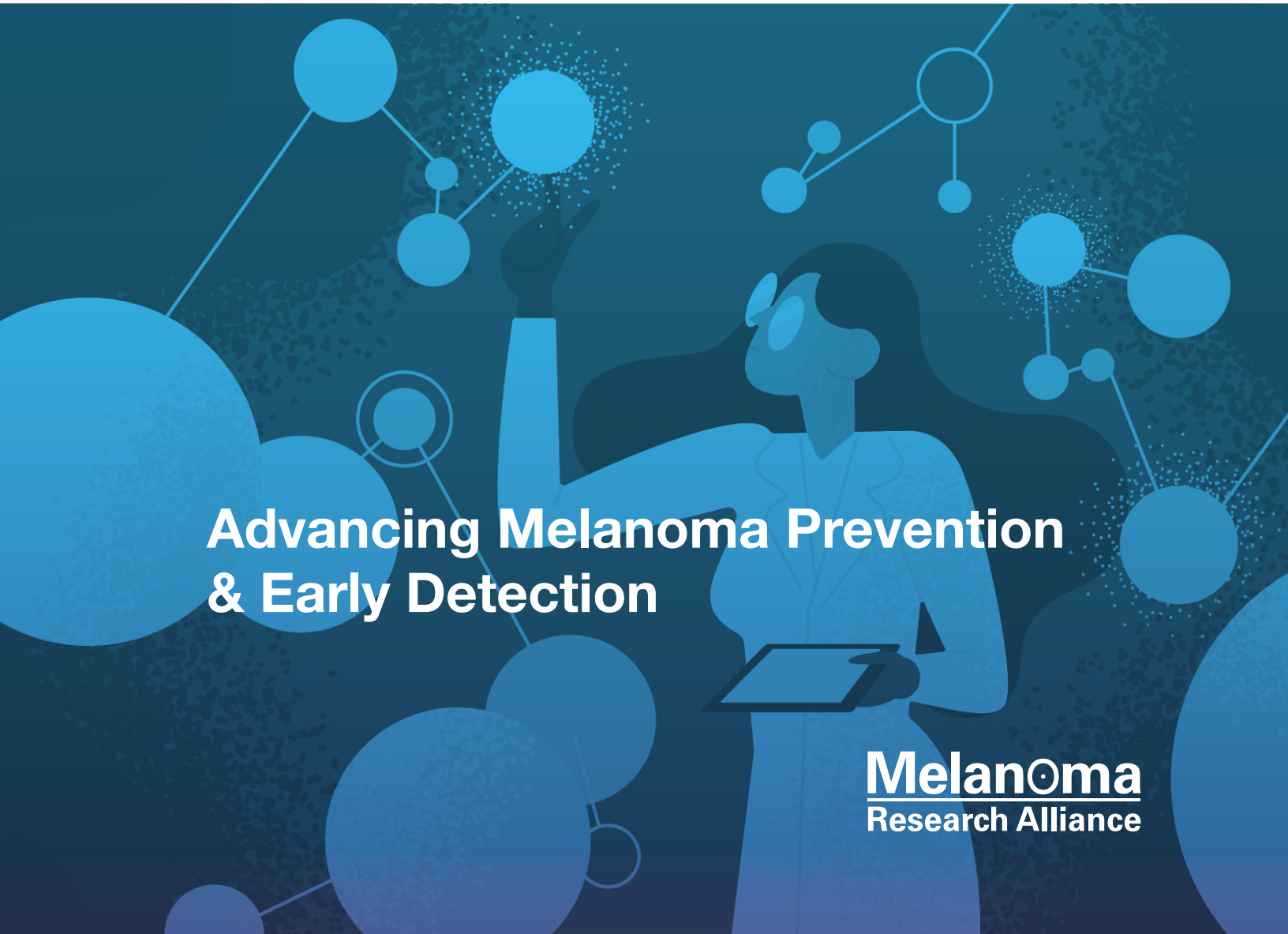
the next generation

MRA's Dermatology Research Fellowship Awards



Advancing Melanoma Prevention & Early Detection

Melanoma Research Alliance

2019 Dermatology Fellow Award Recipients

Shirin Bajaj, New York University School of Medicine

Development of an enhanced telemedicine-based melanoma diagnostic platform

Maria Graciela Cascio, Joan & Sanford I. Weill Medical College of Cornell University

Dependence of metastasizing melanoma cells on different NAD kinase isoforms

Sixue Liu, University of California, Los Angeles

Metastatic origin and adjuvant therapeutic efficacy of stage III melanoma

Enrica Quattrocchi, Mayo Clinic

Melanoma staging by artificial intelligence

Ofer Reiter Agar, Memorial Sloan Kettering Cancer Center

Differentiating change over time in melanoma as compared to benign nevi

Aditi Sahu, Memorial Sloan Kettering Cancer Center

Exploring differential PARP1 expression for non-invasive melanoma diagnosis

Qi Sun, New York University School of Medicine

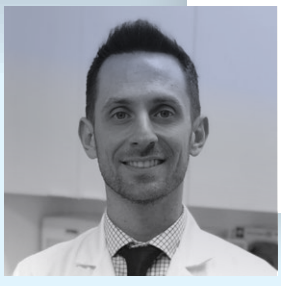
Transcriptional profiling and marker identification of early stage melanoma

Matthew Vesely, Yale University

Determining the immune inhibitory landscape in melanoma

Carl Winge, Stanford University School of Medicine

Rac-1-interacting proteins as diagnostic biomarkers for melanoma



Names correspond to photographs counterclockwise from left

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Melanoma Research Alliance

Founded in 2007 with the generous support of Debra and Leon Black, the Melanoma Research Alliance (MRA) is the largest nonprofit funder of melanoma research. MRA's mission is to end suffering and death due to melanoma by collaborating with all stakeholders to accelerate powerful research, advances cures for all patients and prevent more melanomas. MRA has dedicated $122 million to date in support of the fight against melanoma.

MRA thanks the Anna-Maria and Stephen Kellen Foundation for their generous support of all 2019 Dermatology Fellowship Awards.

www.curemelanoma.org

A New Generation
of Melanoma Dermatology Experts

The Melanoma Research Alliance (MRA)—the largest non-profit funder of melanoma research—has been a catalyzing force, forever changing the melanoma landscape as well as challenging and propelling the melanoma field immeasurably forward.

Over the last decade, MRA has directly invested more than $122 million in research and helped usher in a new era of melanoma treatment with 12 new FDA-approved treatment options.

Although the availability of immunotherapies and molecularly targeted therapies for patients have significantly improved survival rates, there remains a substantial need to better prevent, detect, and diagnose melanoma. Dermatologists can play a critical role in prevention and early detection and can help to fill remaining research gaps.

To address this, MRA launched the Dermatology Fellowship Award pilot program in 2019. The pilot funded nine fellows from the seven institutions represented by MRA's Dermatology Council. In 2020, the program was expanded to include all institutions in the United States with an established pigmented lesion clinic/program.

The research grants focus on one of two areas:

1) prevention or
2) detection, diagnosis, staging, and early intervention treatments.

Through this work, MRA is helping to bring forth a new cohort of dermatology researchers to pick up their torches and blaze new trails. This funding—a scarce rarity for young researchers at this stage of their careers—creates a pipeline of promising scientists specialized in melanoma and supports not only the next generation of researchers but also to improve detection and prevention outcomes in melanoma.

"The new MRA Dermatology Fellows Program will provide critical support for young scientists and dermatologists to explore new avenues of investigation, providing financial backing not generally available at this point in their careers."

Denise Kellen,
MRA Board Member & Melanoma Survivor

Shirin Bajaj

A Personal Journey, A Virtual Platform

When Dr. Shirin Bajaj was still in high school her beloved grandmother developed what appeared to be a red rash across her breast. At the time the family was unaware that this could be a sign of inflammatory breast cancer—the body only showing a glimpse of the chaos just beneath the surface.

By the time they received a diagnosis, the prognosis was poor. It wasn't long before Bajaj's grandmother—a woman who helped raise her—was gone.

It was a turning point for Bajaj. She always had an interest in medicine, but now it was personal.

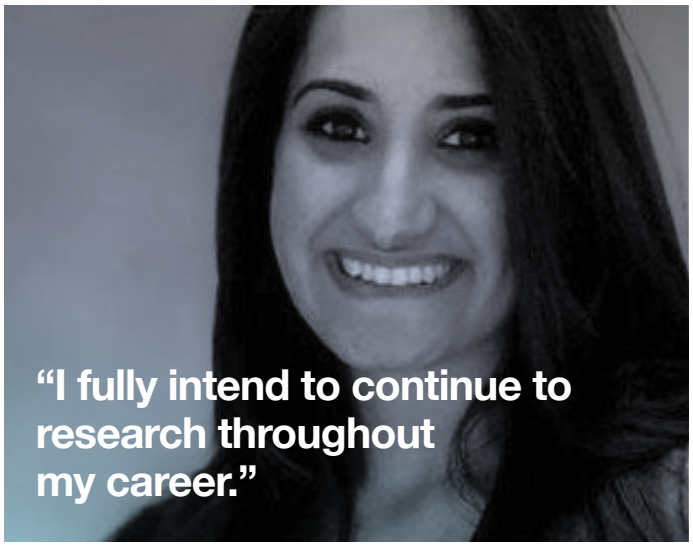
Bajaj went on to attend Northwestern University's Feinberg School of Medicine and is now a third-year resident at NYU's School of Medicine.

"I've been interested in research in different capacities but given this personal circumstance I always veered towards cancer research," says Bajaj.

She particularly enjoyed her dermatology rotation and was quickly fascinated by melanoma: "I found it so interesting that it was one of few cancers that can visually be seen and thus hopefully diagnosed at the earliest stages," she explains. It promised empowerment rather than powerlessness, "Other cancers often present with symptoms when disease is later stage. With melanoma, if you are able to intervene early, you can catch them at their earliest stages when they can more often be treated curatively."

Indeed, when found at early stages, melanoma is a largely curable disease. In underserved communities, however, there is limited access to skin care specialists, which often leads to later-stage tumors at diagnosis and worse overall survival. But with the advent and accuracy of telemedicine technology, Bajaj realized that it doesn't have to be this way.

Encouraged by her mentor, Bajaj applied for and received a 2019 MRA Dermatology Fellow Research Award. "This is such an amazing way to launch your career, right when you are at the beginning of your training…. Learning all the nuts and bolts of a grant process, it's incredibly useful



and I fully intend to continue to research throughout my career," says Bajaj.

Her study is entitled "Development of an Enhanced Telemedicine-Based Melanoma Diagnostic Platform," and is still underway with patient recruitment. The telemedicine platform transmits images of a patient's skin to dermatologists for diagnosis and management recommendations as a way to remotely deliver specialized care. Bajaj will then compare the accuracy of the telemedicine evaluation to an in-person evaluation by a trained dermatologist—the current standard of care—for concerning, possibly cancerous skin lesions.

With this study, Bajaj hopes to determine the utility of a telemedicine system as a screening tool for patients living in medically underserved areas, build upon this preliminary data for larger follow-up studies and, ultimately, improve the detection of melanoma and patient survival.

After this study, Bajaj is interested in further exploring the telemedicine model in a rural population and perhaps in a walk-in setting or pharmacy so that it is assessible to people regardless of where they live.

"It's exciting to fund dermatologists in this way and I want to give a big thank you to Debra and Leon Black for putting MRA together. I love how 100% of the money is going towards research and that is so meaningful. I think it's so important they are funding dermatology residents and helping them network with the right people…and for those of us interested in research, it means getting the funding to actually be able to do it. I am so grateful."

Enrica Quattrocchi

Bridging the Knowledge Gap Through AI

Two years ago, Dr. Enrica Quattrocchi was still writing research papers and living in Sicily, Italy but soon that all changed. “I have a passion for research and wanted to do something that had a real impact on peoples’ lives,” says Quattrocchi.

“Then melanoma found me,” she explains.

After graduation, Quattrocchi came to work at the Mayo Clinic where she found a mentor in Dr. Alexander Meves, and pulled her nose out of the books and moved into the lab.

Today, she is a clinical dermatology research fellow and translational scientist in the Dermatology Department.

When an email about the MRA Dermatology Fellowship Award Request for Proposals came through, Quattrocchi jumped at the opportunity. She is quick to recount a Winston Churchill quote about not fearing failure nor losing enthusiasm. It is with this mindset that she jumped all-in on her research project entitled “Melanoma Staging by Artificial Intelligence (AI).”

“Our current staging system,” explains Quattrochi, “has a number of weaknesses. The sizes and concepts don’t always work well.” Quattrocchi is referring to the American Joint Committee on Cancer (AJCC) 8th edition guidelines—the current classification system for describing the extent of disease and prognosis—which is heavily dependent on the tumor invasion depth or thickness (otherwise known as Breslow depth). “New methods are needed to better identify patients who are likely to relapse but remain unidentified using conventional staging parameters. This is where AI can help.”

In particular, Quattrocchi’s study examines cutaneous melanoma by applying AI to distinguish between biologically indolent (or slow growing) and aggressive melanomas. This work would help not only identify melanomas, but also patients at higher risk of relapse who might have been overlooked using conventional staging parameters.

“Too many patients die for something that is mistaken as a simple mole while others have unnecessary invasive surgeries,” explains Quattrocchi. When staging is inaccurate, patients may also miss out on treatment opportunities, such as the ability to undergo adjuvant therapy following surgery or to consider enrolling into a clinical trial.

Quattrocchi is partnering with Meves on the study as well as Dr. Dennis Murphree, Co-Director of the Mayo Clinic’s Office of Artificial Intelligence in Dermatology. Murphree has expertise in applying quantitative methods to solve real-world problems.

“Right now, our predictive model is close to 83% [accurate] and we are continuing to make refinements,” says Quattrocchi. If the model is able to distinguish between slow-growing cancers and those that will aggressively metastasize, it could revolutionize the prevention, diagnosis, and treatment of melanoma.

“Research is progress. It advances patient care. To do it, however, requires stamina, originality, and persistence. I’ve been blessed to be on a wonderful team of people who are passionate. My word for this project is ‘excitement.’ I am so excited and so thankful for my mentor and for MRA for believing in me,” says Quattrocchi.

“For me, this funding means hope for new therapies and enthusiasm for the next challenge ahead.”

Aditi Sahu

Lighting up Melanoma (One Cell at a Time)

"Some non-cancerous skin lesions can look like cancer, and because melanoma can be deadly, often doctors biopsy many more lesions to prevent missing melanomas," explains Dr. Aditi Sahu, a post-doctoral fellow at Memorial Sloan Kettering Cancer Center working under the mentorship of Dr. Milind Rajadhyaksha, who pioneered the development and use of confocal microscopy for skin cancer detection.

Typically, melanoma is identified through 1. visual inspection or 2. surface magnification (also known as dermoscopy). Other identification methods, however, also exist, such as Reflectance Confocal Microscopy (RCM), which enables a very high magnification of the tissue and has led to improved detection of melanoma and reduced biopsy of non-cancer lesions.

Both dermoscopy and RCM, however, look at visual changes of melanoma and, therefore, cannot always detect it at its earliest stage, especially the melanomas that arise in non-cancerous moles.

In Sahu's study, entitled "Exploring Differential PARP1 Expression for Non-Invasive Melanoma Diagnosis" she poses the question: Can technology beyond dermoscopy and RCM improve early detection of melanoma? In particular, Sahu asks whether the florescent molecule known as PARPi-FL may be effective in doing so.

PARP1 is a DNA repair enzyme that is important for repairing breaks in the DNA that occur as a normal part of cell division. PARPi-FL targets and binds to cellular protein PARP1, which is produced in greater quantities in cancerous cells than in non-cancerous cells.

PARP1 expression has been used as a quantitative biomarker for oral, oropharyngeal, esophageal, and brain cancers and has been visualized using PARPi-FL. Sahu's research hypothesizes that PARPi-FL may also be applied to help visualize melanoma in order to detect and identify it earlier than is possible with existing methods.

PARPi-FL is a cell-penetrating, fluorescent, imaging agent. It binds PARP directly in cells, and can be applied topically. Because PARP1 protein is produced in greater quantities in cancer as compared to normal tissues, positive PARPi-FL signal creates a kind of visual "roadmap" of where higher PARP1 is present and where cancerous cells are likely to be present.

In short, under a special type of fluorescent imaging microscope called a "fluorescence confocal microscopy (FCM)," the cancerous cells upon PARPi-FL staining will glow akin to a "send help here" message, letting researchers and providers alike know where to focus their clinical attention.

"So far we have looked at 20 samples," says Sahu, "and the results look promising. We are hoping to do 100 more so we have enough of a statistical sample." Sahu is grateful for the opportunity delivered with a Dermatology Fellows award—one she admits is so rare for someone so early in their field and for a researcher without preliminary data. "This helps us create experience and become sufficient as principal investigators. I'm so grateful to MRA—for their mission, this funding, and this collaboration," says Sahu.

The goal for Sahu's study is to prove that PARPi-FL is a viable diagnostic method and that in doing so, they are able to:

- improve testing so that melanoma can be identified earlier,
- improve the accuracy of diagnoses,
- reduce the amount of surgeries on non-cancerous skin lesions that patients must undergo; and
- ultimately reduce morbidity related to melanoma.

"I'm really passionate about cancer biology and working on early detection in cancer," says Sahu. "With early detection, cancer is often curable and there is a high survival rate. We have to do everything we can to detect cancer at its absolute earliest and give people the best chance at life."

MRA is grateful to the leadership and support of its Dermatology Council. The council serves as a critical advisory body and helps guide MRA's research agenda as it relates to dermatology, prevention, and early detection of disease.

The MRA Dermatology Council was created and convened under the MRA Board of Directors and is co-chaired by **Denise Kellen** and **Daisy Helman.**

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Melanoma Research Alliance

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