Lighting up Melanoma (One Cell at a Time)

"I'm really passionate about cancer biology and working on early detection in cancer," says Aditi Sahu, a post-doctoral fellow at MSKCC.

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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 Aditi Sahu, a post-doctoral fellow at Memorial Sloan Kettering Cancer Center working under the mentorship of Milind Rajadhyaksha, PhD, 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 number 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.”

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