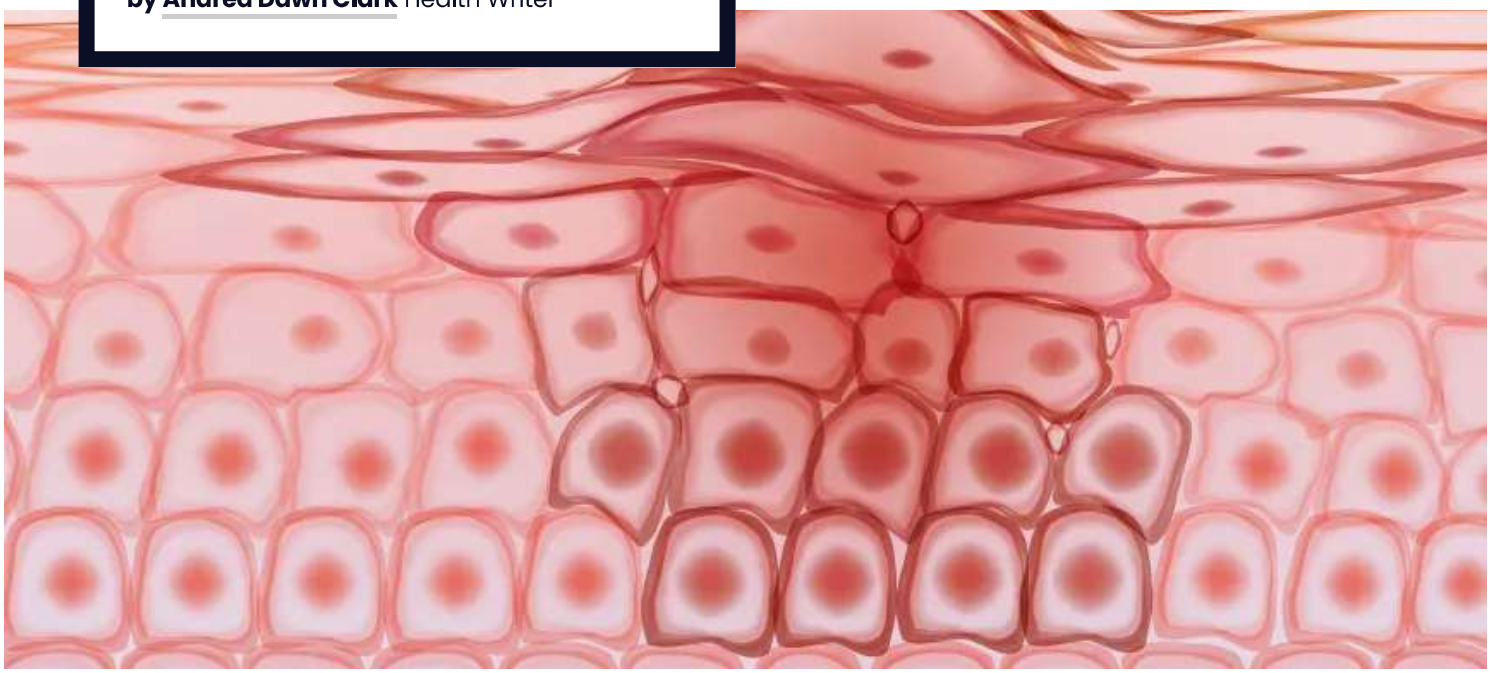
MELANOMA

What Is Melanoma Inhibitory Activity?

The MIA protein impacts how melanoma spreads. Here's what you need to know.

by **Andrea Dawn Clark** Health Writer



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ONE OF THE scariest aspects of most any cancer diagnosis is having to face the possibility of the disease spreading throughout your body. In the case of melanoma, a potentially life-threatening form of skin cancer that starts in your pigment-making cells (or melanocytes), it's an especially pressing concern as melanoma tends to spread faster than other types of skin cancer, per the American Cancer Society.

That's why researchers are focused on staying a step ahead of the disease. One way they're looking to do that is by potentially blocking and regulating a key element which contributes to melanoma's spread—namely, the melanoma inhibitory activity (MIA) protein.

"Melanoma inhibitory activity, or MIA, is a protein involved in the metastasis, or spread, and immunosuppression in melanoma," explains Hysem Eldik, M.D., a board-certified dermatologist at Marmur Medical in New York City. In other words, the MIA protein, which is secreted by melanoma tumor cells, not only fuels the progression of the cancer, but also suppresses the immune system's ability to fight it. A double jeopardy for your cancer prognosis, indeed.

Remind Me: What Are the Causes and Symptoms of Melanoma?

Basically, melanoma forms when melanocytes grow out of control. This can occur wherever these pigment-making cells exist in the body—and that's not only on the stretches of skin that get the most sunshine: In rare cases, melanoma can also occur in the melanocytes under your nails, inside your eye, or within the mucus lining of your nose, throat, or GI tract.

So, what influences melanocytes to go haywire? "The development of melanoma is thought to be through a combination of genetic and environmental factors," explains Erum Ilyas, M.D., a board-certified dermatologist with the Schweiger Dermatology Group in King of Prussia, PA. Genetics plays a role in who develops melanoma in that this cancer can run in families, and those with fair skin and/or more moles are at higher risk for it. As for the environmental part of the equation, exposure to ultraviolet (UV) rays from sunlight or tanning beds is known to increase your risk.

Frequently, the first signs of melanoma are a change in an existing mole or the formation of an unusual-looking or strangely-pigmented mole. "It most often presents as a changing or darkening mole or freckle however it can present without pigment as well," says Dr. Ilyas.

Dermatologists recommend assessing any suspicious growths with the same ABCDE checklist that they themselves employ to identify melanomas. "We use this acronym to remind people to look for an [A] asymmetrical shape, [B] borders that are irregular, [C] colors that are uneven or dark, a [D] diameter that's larger than six millimeters, and [E] evolving signs and symptoms," says Dr. Eldik. "It's also important to mention that about 25% of melanomas arise within pre-existing moles. This means that just because you have had a spot since childhood or adolescence does not mean it cannot become melanoma." The remaining 75% of melanomas will be growths that appear anew.

Your dermatologist can remove any suspicious moles or growths and send them to a lab for a biopsy. If melanoma is detected, the next step is to determine which stage of development the cancer is in to guide the best course of treatment. In its most advanced stage, that is, stage 4, the melanoma is said to have metastasized, meaning that it has spread to other organs and is not considered curable.

While that may sound harrowing, early detection and treatment of melanoma can maximize one's chance of making a full recovery. That's why experts recommend monthly self-checks of your skin and having a standing appointment with your dermatologist for an annual skin-cancer screening.

Understanding the MIA Protein and Its Link to Melanoma

Ready for a quick biochemistry lesson? It's important to note that the MIA protein which appears to accelerate melanoma is "absent in normal human melanocytes," per a study in the journal *Carcinogenesis*. In other words, research shows that the MIA protein is produced once a malignant melanoma tumor has formed but markedly absent in both benign tumors and normal skin biopsies.

While Dr. Ilyas notes that there are not a lot of research on what actually induces the release of MIA, we do know how it works: "In melanoma, MIA is believed to regulate a protein called p54, which works in the nucleus of skin cells, potentially upregulating cell turnover," she explains. Think of it as a deadly domino effect—MIA nudges p54 into action and it's p54 that spurs the cancerous cells to proliferate and thereby speed the growth of melanoma.

In addition, this same process lowers your immune system's response to melanoma by inhibiting cellular anti-tumor reactions. "This helps increase the spread by decreasing the body's defense systems," says Dr. Ilyas

How MIA Can Be Used to Help Detect and Suppress Melanoma

When researchers first found the MIA protein, it opened a much-needed door to cancer patients and the therapies that could be offered to them. "Practitioners finally had a key indicator on how melanoma could spread," says Dr. Ilyas. "And, that's not just for melanoma. MIA may play a role in other malignancies such as squamous cell carcinoma, cervical cancer, lung cancer, and esophageal cancer—which is incredible and valuable knowledge that can save lives."

The presence of MIA is detected through a blood test. Doctors do a quantitative analysis of a patient's blood sample to see the level of MIA protein circulating—the higher the level, the greater the odds that the melanoma has metastasized, explains Dr. Eldik. "[The level of MIA] can be used to determine prognosis and be a factor of consideration when determining the aggressiveness of a tumor," he says. Indeed, in a study conducted in Germany with 100 melanoma patients, MIA showed a clear sensitivity to detect disease progression, allowing doctors to monitor patients with melanoma that has metastasized.

Because melanoma can be aggressive and highly invasive, it can be hard to treat with conventional methods like straight-forward surgical removal of the cancer. That's why understanding the production and function of MIA has been a game changer. "Recognizing that blocking MIA production helps stop malignant cell migration and invasion helped facilitate different treatment courses," says Dr. Ilyas. "Patients can have their blood analyzed for MIA production—which helps determine the aggressiveness of a tumor—and be put on life-saving immunotherapy drugs that could help stop tumor growth and formation." Dr. Eldik notes that multiple clinical trials have shown that this approach of blocking MIA not only leads to a decrease in the number of melanoma metastases, but also a decrease in the immunosuppression which MIA causes.

Keep in mind, MIA is not used to diagnose melanoma, which still likely requires a biopsy. "Hopefully in the future, MIA can be used as part of the clinical work-up for patients that have melanoma," says Dr. Eldik. "It can be very informative regarding a patient's case and their best clinical course."

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Andrea Dawn Clark

Andrea Dawn Clark is the Editorial Director at John Jay College, City University of New York (CUNY). With over 20 years of professional publishing experience, she's worked at numerous consumer magazines as an Executive Editor... more