Promising new drug stops spread of melanoma by 90 percent

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Credit: Michigan State University

Michigan State University researchers have discovered that a chemical compound, and potential new drug, reduces the spread of melanoma cells by up to 90 percent.

The man-made, small-molecule drug compound goes after a gene's

ability to produce RNA molecules and certain proteins in melanoma tumors. This gene activity, or transcription process, causes the disease to spread but the compound can shut it down. Up until now, few other compounds of this kind have been able to accomplish this.

"It's been a challenge developing small-molecule drugs that can block this gene activity that works as a signaling mechanism known to be important in melanoma progression," said Richard Neubig, a pharmacology professor and co-author of the study. "Our chemical compound is actually the same one that we've been working on to potentially treat the disease scleroderma, which now we've found works effectively on this type of cancer."

Scleroderma is a rare and often fatal autoimmune disease that causes the hardening of skin tissue, as well as organs such as the lungs, heart and kidneys. The same mechanisms that produce fibrosis, or skin thickening, in scleroderma also contribute to the spread of cancer.

Small-molecule drugs make up over 90 percent of the drugs on the market today and Neubig's co-author Kate Appleton, a postdoctoral student, said the findings are an early discovery that could be highly effective in battling the deadly skin cancer. It's estimated about 10,000 people die each year from the disease.

Their findings are published in the January issue of *Molecular Cancer Therapeutics*.

"Melanoma is the most dangerous form of skin cancer with around 76,000 new cases a year in the United States," Appleton said. "One reason the disease is so fatal is that it can spread throughout the body very quickly and attack distant organs such as the brain and lungs."

Through their research, Neubig and Appleton, along with their

collaborators, found that the compounds were able to stop proteins, known as Myocardin-related transcription factors, or MRTFs, from initiating the gene transcription process in melanoma cells. These triggering proteins are initially turned on by another protein called RhoC, or Ras homology C, which is found in a signaling pathway that can cause the disease to aggressively spread in the body.

The compound reduced the migration of melanoma cells by 85 to 90 percent. The team also discovered that the potential drug greatly reduced tumors specifically in the lungs of mice that had been injected with human melanoma cells.

"We used intact melanoma cells to screen for our chemical inhibitors," Neubig said. "This allowed us to find compounds that could block anywhere along this RhoC pathway."

Being able to block along this entire path allowed the researchers to find the MRTF signaling protein as a new target.

Appleton said figuring out which patients have this pathway turned on is an important next step in the development of their compound because it would help them determine which patients would benefit the most.

"The effect of our compounds on turning off this melanoma cell growth and progression is much stronger when the pathway is activated," she said. "We could look for the activation of the MRTF proteins as a biomarker to determine risk, especially for those in early-stage melanoma."

According to Neubig, if the disease is caught early, chance of death is only 2 percent. If caught late, that figure rises to 84 percent.

"The majority of people die from melanoma because of the disease

spreading," he said. "Our compounds can block cancer migration and potentially increase patient survival."

Provided by Michigan State University