

Novel nanoparticles prevent radiation damage (w/ Video)

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Tiny, melanin-covered nanoparticles may protect bone marrow from the harmful effects of radiation therapy, according to scientists at Albert Einstein College of Medicine of Yeshiva University who successfully tested the strategy in mouse models. Infusing these particles into human patients may hold promise in the future. The research is described in the current issue of the *International Journal of Radiation Oncology, Biology and Physics*.

Radiation therapy is used to kill <u>cancer cells</u> and shrink tumors. But because radiation also damages normal cells, doctors must limit the dose. <u>Melanin</u>, the naturally occurring <u>pigment</u> that gives skin and hair its color, helps shield the skin from the damaging effects of sunlight and has been shown to protect against radiation.

"A technique for shielding normal cells from radiation damage would allow doctors to administer higher doses of radiation to tumors, making the treatment more effective," said Ekaterina Dadachova, Ph.D., associate professor of <u>nuclear medicine</u> and of microbiology & immunology and the Sylvia and Robert S. Olnick Faculty Scholar in Cancer Research at Einstein, as well as senior author of the study.

In previously published research, Dr. Dadachova and colleagues showed that melanin protects against radiation by helping prevent the formation of free radicals, which cause DNA damage, and by scavenging the free radicals that do form.



"We wanted to devise a way to provide protective melanin to the <u>bone</u> <u>marrow</u>," said Dr. Dadachova. "That's where blood is formed, and the bone-marrow stem cells that produce blood cells are extremely susceptible to the damaging effects of radiation."

Dr. Dadachova and her colleagues focused on packaging melanin in particles so small that they would not get trapped by the lungs, liver or spleen. They created "melanin <u>nanoparticles</u>" by coating tiny (20 nanometers in diameter) silica (sand) particles with several layers of melanin pigment that they synthesized in their laboratory.

The researchers found that these particles successfully lodged in bone marrow after being injected into mice. Then, in a series of experiments, they investigated whether their nanoparticles would protect the bone marrow of mice treated with two types of radiation.

In the first experiment, one group of mice was injected with nanoparticles and a second group was not. Three hours later, both groups were exposed to whole-body radiation. For the next 30 days, the researchers monitored the blood of the mice, looking for signs of bone marrow damage such as decreased numbers of white blood cells and platelets.

Compared with the control group, those receiving melanin nanoparticles before radiation exposure fared much better; their levels of white cells and platelets dropped much less precipitously. Ten days after irradiation, for example, platelet levels had fallen by only 10 percent in mice that had received nanoparticles compared with a 60 percent decline in untreated mice. Furthermore, levels of white blood cells and platelets returned to normal much more quickly than in the control mice.

A second experiment assessed not only bone-marrow protection but whether the nanoparticles might have the undesirable effect of



infiltrating and protecting tumors being targeted with radiation. Two groups of mice were injected with melanoma cells that formed melanoma tumors. After one group of mice was injected with melanin nanoparticles, both groups received an experimental radiation treatment designed by Dr. Dadachova and her colleagues specifically for treating melanoma.

This treatment uses a radiation-emitting isotope "piggybacked" onto an antibody that binds to melanin. When injected into the bloodstream, the antibodies latch onto the free melanin particles released by cells within melanoma tumors. Their isotopes then emit radiation that kills nearby melanoma tumor cells.

Following the second experiment, the melanoma tumors shrank significantly and to the same extent in both groups of mice - indicating that the melanized nanoparticles did not interfere with the radiation therapy's effectiveness. And once again, the melanized nanoparticles prevented radiation-induced bone-marrow damage: between the third and seventh day after the antibody-isotope radiation therapy was administered, mice injected with nanoparticles experienced a drop in white cells that was significantly less than occurred in mice not pretreated with nanoparticles.

"The ability to protect the bone marrow will allow physicians to use more extensive cancer-killing radiation therapies and this will hopefully translate into greater tumor response rates," said Arturo Casadevall, M.D., Ph.D., professor of medicine and of microbiology & immunology, the Leo and Julia Forchheimer Chair in Microbiology & Immunology, and a co-author of the study.

Some nanoparticles could still be found in bone marrow 24 hours after their injection, which shouldn't pose a problem. "Since the nanoparticles are rapidly removed by phagocytic <u>cells</u>, they're unlikely to damage the



bone marrow," said Dr. Dadachova. "We didn't detect any side effects associated with administering the particles."

"These results are encouraging for other potential applications of melanin, including radioprotection of other radiation-sensitive tissues, such as the gastrointestinal tract," noted Andrew Schweitzer, M.D., formerly a Howard Hughes Medical Institute fellow at Einstein and lead author of the study.

Clinical trials testing whether melanized nanoparticles might protect cancer patients undergoing radiation therapy could begin in two to three years, Dr. Dadachova predicted. She also noted that melanized nanoparticles might also have other applications, such as protecting workers charged with cleaning up nuclear accidents, protecting astronauts against <u>radiation</u> exposure in space, or even protecting people following a nuclear attack.

More information: The paper, "Melanin-covered nanoparticles for protection of bone marrow during radiation therapy of cancer," was published in the April 26 online issue of the International Journal of Radiation Oncology, Biology and Physics.

Provided by Albert Einstein College of Medicine

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