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Melanoma uses body's immune system to spread to lungs

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(PhysOrg.com) -- The way melanoma cells use the immune system to spread and develop into lung tumors may lead to a therapy to decrease development of these tumors, according to Penn State researchers.

“Melanoma is the most aggressive and metastatic form of skin cancer,” said Gavin Robertson, professor of pharmacology, pathology, dermatology and surgery in the Penn State College of Medicine. “Therefore, identifying proteins and molecular mechanisms that regulate metastasis is important for developing drugs to treat this disease.”

Metastasis is a complex process in which cancer cells detach from the primary tumor and migrate to other sites in the body by traveling through the lymphatic or blood circulatory systems. Researchers in the Foreman Foundation Melanoma Research Laboratory at Penn State developed a model to determine why the roughly one million tumor cells shed daily from a 1-gram melanoma tumor do not form more metastases in the lungs.

After intravenously injecting 1 million human melanoma cells in a mouse, Robertson and colleagues observed entrapment of many of these cells in the lung vessels. Within 24 hours, however, few cells were still present in the lungs.

“In this study, we show that entrapped, circulating melanoma cells can use a person’s own immune cells—specifically a type of white blood cell called neutrophils—to control lung metastasis development,” Robertson

said. After injecting the mice with neutrophils an hour after the melanoma cell injection, cancer cell retention was increased in the lung by about three times.

Melanoma cells produce and secrete high levels of a protein called IL-8, which is used to attract neutrophils.

“For patients, this is important because a therapy preventing circulating melanoma cells from secreting IL-8 would have the potential to decrease lung metastasis development by about 50 percent by disrupting interaction of the cancer cells with neutrophils,” Robertson said. “Metastases form by proteins on the melanoma and neutrophils interacting and forming physical connections. These connections promote anchoring of the melanoma cells to the lung vessel walls, enabling the cancer cells to migrate through the wall to form lung metastases.”

Decreasing the secretion of IL-8 limits the interaction of melanoma cells with neutrophils, dropping the number of melanoma cells retained in the lungs by about half.

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