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Gene inactivation drives spread of melanoma: study

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Why do some cancers spread rapidly to other organs and others don't metastasize? A team of UNC researchers led by Norman Sharpless, MD, have identified a key genetic switch that determines whether melanoma, a lethal skin cancer, spreads by metastasis.

Treating melanoma is extremely challenging. The cancer spreads rapidly and to sites in the body that are remote from the original cancer site. Melanoma is the most deadly form of skin cancer, and advanced melanoma kills more than 8600 Americans each year. It is the most common form of cancer in young adults, aged 25-29 and the incidence of people under 30 developing melanoma is increasing fast – more than 50 percent in young women since 1980.

In a paper published today in the journal *Cancer Cell*, a team from UNC Lineberger Comprehensive Cancer Center demonstrates that inactivating a gene called LKB1 (or STK11) causes non-aggressive melanoma cells to become highly metastatic when tested in a variety of models using tumors from humans and mice. While Sharpless and his colleagues showed a role for LKB1 inactivation in lung cancer metastasis, the effects of LKB1 loss on melanoma spread is even more dramatic.

"Although we are not totally certain how LKB1 loss promotes metastasis in multiple cancer types, one important effect is the loss of LKB1 starts a chain reaction, activating a family of proteins called SRC kinases, which are known to drive metastasis," said Sharpless, who is associate director for translational research at UNC Lineberger.

"Loss of LKB1 occurs in about 30 percent of lung cancer and 10 percent of melanoma, and ongoing studies at UNC and elsewhere will determine if these LKB1 deficient tumors have a worse prognosis. These data suggest LKB1 deficient cancers will be more likely to metastasize, and therefore more likely to be incurable."

"The work is exciting because the laboratory model reliably replicates distant metastases, helping us better understand what treatments may work for melanoma that has spread. While several targeted drugs have recently been approved by the FDA for metastatic disease, these targeted mutations don't indicate whether the disease is likely to metastasize," said Stergios Moschos, MD, clinical associate professor of hematology/oncology. Moschos works in the area of drug development for melanoma but was not involved in this research project.

Provided by University of North Carolina Health Care