P Rex-1 protein key to melanoma metastasis

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Researchers from UNC Lineberger Comprehensive Cancer Center are part of a team that has identified a protein, called P-Rex1, that is key to the movement of cells called melanoblasts. When these cells experience uncontrolled growth, melanoma develops.

Melanoma is one of the only forms of cancer that is still on the rise and is one of the most common forms of cancer in young adults. The incidence of melanoma in women under age 30 has increased more than 50 percent since 1980. Metastases are the major cause of death from melanoma.

The team found that mice lacking the P-Rex1 protein are resistant to melanoma metastases. When researchers tested human melanoma cells and tumor tissue for the protein, P-Rex1 was elevated in the majority of cases - a clue that the protein plays an important role in the cancer's spread. Their findings were published today in the journal *Nature Communications*.

"We know that mutations in a gene called BRAF are important for the development of melanoma and several years ago we published a collaborative paper listing 82 proteins that seem to be affected by this genetic pathway. From that list, we focused on P-Rex1 in collaboration with Dr. Nancy Thomas here at UNC and researchers in the United Kingdom," says Channing Der, PhD, a member of the UNC research team. Der is Kenan Professor of pharmacology at UNC-Chapel Hill and member of UNC Lineberger.

A drug approved this summer, vemurafenib, is the first treatment directed at the BRAF mutation. Clinical trials found that the treatment offers a significant survival benefit.

"We think that vemurafenib may work, in part, by blocking the up-regulation of P-Rex1," Der adds.

"As a physician and scientist, I know firsthand the frustration of having very limited therapeutic options to offer to patients with metastatic melanoma," says Nancy Thomas, MD, PhD, whose laboratory analyzed the protein's expression in human cells. "Pinpointing that P-Rex1 plays a key role in metastasis gives us a better understanding of how vemurafenib may work and a target for developing new treatments," she adds.

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