Research breakthrough could halt melanoma metastasis

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In laboratory experiments, scientists have eliminated metastasis, the spread of cancer from the original tumor to other parts of the body, in melanoma by inhibiting a protein known as melanoma differentiation associated gene-9 (mda-9)/syntenin. More than 1 million cases of skin cancer are diagnosed each year in the U.S., and melanoma is the deadliest form. With further research, the approach used by the scientists could lead to targeted therapies that stop metastasis in melanoma and potentially a broad range of additional cancers.

The study published online in the journal Cancer Research was led by Paul B. Fisher, M.Ph., Ph.D., Thelma Newmeyer Corman Endowed Chair in Cancer Research and program co-leader of Cancer Molecular Genetics at Virginia Commonwealth University Massey Cancer Center, chairman of VCU's Department of Human and Molecular Genetics and director of the VCU Institute of Molecular Medicine. Fisher and his colleagues found that Raf kinase inhibitor protein (RKIP) interacted with and suppressed mda-9/syntenin. Mda-9/syntenin was originally cloned in Fisher's laboratory, and was shown in previous studies to interact with another protein, c-Src, to start a series of chemical reactions that lead to increased metastasis.

"Prior research suggests that RKIP plays a seminal role in inhibiting cancer metastasis, but, until now, the mechanisms underlying this activity were not clear," says Fisher. "In addition to providing a new target for future therapies, there is potential for using these two genes as biomarkers for monitoring melanoma development and progression."

Through their experiments, the scientists discovered that RKIP physically binds with mda-9/syntenin, and this physical interaction inhibits mda-9/syntenin expression. This finding opens the possibility of developing small molecules that mimic RKIP to be used as drugs to treat metastasis in melanoma and other cancers.

Additionally, the team found that levels of mda-9/syntenin were higher than levels of RKIP in malignant and metastatic melanoma cells while levels of RKIP were higher than levels of mda-9/syntenin in healthy melanocytes, which are the cells that produce pigment in the skin, eyes and hair. The inverse relationship between the two proteins suggests that changes in their levels of expression could be used as a diagnostic tool, enabling clinicians to track the development of the disease or gauge a patient's response to treatments.

"Our findings represent a major breakthrough in understanding the genetic mechanisms that lead to metastasis in melanoma. Prior studies have shown that levels of mda-9/syntenin are elevated in a majority of cancers, including melanoma, suggesting that our findings could be applicable for a wide range of diseases," says Fisher.

Now that the researchers have demonstrated the ability of RKIP to inhibit mda-9/syntenin-mediated metastasis, they are focusing their attention on developing small molecules imitating RKIP that could be used as new treatments for melanoma.

More information:
cancerres.aacrjournals.org/con …
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