New therapeutic target for melanoma identified

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A protein called Mcl-1 plays a critical role in melanoma cell resistance to a form of apoptosis called anoikis, according to research published this week in *Molecular Cancer Research*.

The presence of Mcl-1 causes cell resistance to anoikis. This resistance to anoikis enables the melanoma cells to metastasize and survive at sites distant from the primary tumor, according to Andrew Aplin, Ph.D., an associate professor of Cancer Biology at Jefferson Medical College of Thomas Jefferson University, and a member of the Kimmel Cancer Center at Jefferson. The research was conducted at Albany Medical College in New York by Dr. Aplin and colleagues.

Mcl-1 is part of the Bcl-2 protein family, and is regulated by B-RAF proteins, which are mutated in approximately 60 percent of all human melanomas. The Bcl-2 family includes several prosurvival proteins that are associated with the resistance of cancer cells to apoptosis, or cell death. Dr. Aplin and colleagues analyzed three candidate Bcl-2 proteins: Mcl-1, Bcl-2 and Bcl-XL.

"When we depleted Mcl-1 from the tumor cells, they were susceptible to cell death," Dr. Aplin said. "Mcl-1 showed dramatic results compared to Bcl-2 and Bcl-XL, which was a surprise. Our findings show that targeting Mcl-1, which is upregulated in a majority of melanoma cells, could be a viable treatment strategy."

Dr. Aplin said there are therapeutic agents in development to target this

protein family, but most specifically target Bcl-2 and Bcl-XL. There is one agent in development by Gemin X Biotech that targets Mcl-1. This agent, called obatoclax, is currently in phase I/II trials.

Source: Thomas Jefferson University (news : web)