Study links molecule to muscle maturation, muscle cancer

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Denis C. Guttridge, a researcher with Ohio State University's human cancer genetics program. Credit: Ohio State University Medical Center

Researchers at The Ohio State University Comprehensive Cancer Center have discovered that a molecule implicated in leukemia and lung cancer is also important in muscle repair and in a muscle cancer that strikes mainly children.

The study shows that immature muscle cells require the molecule, called miR-29, to become mature, and that the molecule is nearly missing in cells from rhabdomyosarcoma, a cancer caused by the proliferation of immature muscle cells.

Cells from human rhabdomyosarcoma tumors showed levels of the

molecule that were 10 percent or less of those in normal muscle cells. Artificially raising the level of the molecule in the cancer cells cut their growth by half and caused them to begin maturing, slowing down tumor growth.

MiR-29 is a type of microRNA, a family of molecules that helps regulate the proteins cells produce. Researchers say this study is unusual because it also sheds light on the how a microRNA itself is regulated.

"This study shows that there is a connection between this microRNA, muscle development and rhabdomyosarcoma," says principal investigator Denis C. Guttridge, associate professor of molecular virology, immunology and medical genetics and a researcher with Ohio State's human cancer genetics program.

"The findings should give us a better understanding of muscle repair and development, and of rhabdomyosarcoma, and could lead to new treatments for this and other muscle diseases," he says.

The study is published in a recent issue of the journal *Cancer Cell*.

Guttridge and his colleagues discovered that the gene for miR-29 is silenced by the action of a protein, called NF-□B (pronounced, NF kappa B). Their study shows that this protein is present at high levels in rhabdomyosarcoma cells, and that this keeps miR-29 shut off, preventing muscle progenitor cells from maturing.

When they raised the level of the microRNA molecule in the cells, or lowered the level of the NF-□B protein, the cells' growth rate dropped two fold, and they began taking on the appearance of mature muscle cells. The modified cells also formed significantly smaller tumors when transplanted into an animal model than did typical rhabdomyosarcoma cells.

"High levels of the protein silence miR-29, which blocks differentiation, causing muscle cells to remain immature. If we can restore the levels of miR-29 in patients," Guttridge says, "it might provide a new therapy for this childhood cancer and perhaps other muscle diseases."

Source: Ohio State University Medical Center