Cancer-causing virus exploits key cell-survival proteins

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A cancer-causing retrovirus exploits key proteins in its host cells to extend the life of those cells, thereby prolonging its own survival and ability to spread, according to a new study by researchers at The Ohio State University Comprehensive Cancer Center – Arthur G. James Cancer Hospital and Richard J. Solove Research Institute (OSUCCC – James) and Ohio State's College of Veterinary Medicine.

The human T-lymphotropic virus type-1 (HTLV-1), which causes adult T-cell leukemia and lymphoma, produces a protein called p30 that is essential for the retrovirus to establish an infection. This study found that this viral protein targets two important cell proteins: ATM, a key player in a cell's response to DNA damage, and REG-gamma, which marks proteins within the cell for destruction.

"Our findings suggest that the p30 viral protein prolongs the survival of host cells through this interaction with ATM and REG-gamma, and the longer a virus-infected cell survives, the better chance the virus has to spread, " says principal investigator Michael Lairmore, DVM, PhD, professor of veterinary biosciences and associate director for shared resources at the OSUCCC – James.

The findings were published recently in the *Journal of Biological Chemistry*.

An estimated 20 million people worldwide are infected by HTLV-1, and about five percent of them will develop adult T-cell leukemia or

lymphoma, or one of a variety of inflammatory disorders.

Lairmore and his colleagues used cell lines and a variety of biochemical assays to identify cellular binding partners of p30. They discovered the following:

- p30 specifically binds to cellular ATM (ataxia-telangiectasia mutated), a key regulator of DNA damage responses and cell cycle control, and to REG-gamma, a nuclear proteasome activator.
- Under stressful conditions, p30 levels are associated with lower ATM levels and increased cell survival.
- The expression of p30 changes in concert with expression of REG-gamma, suggesting that overexpression of REG-gamma enhances levels of p30.
- p30 forms a complex with ATM and REG-gamma.

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