Study reveals how a common virus eludes the immune system

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Viruses have numerous tricks for dodging the immune system. In the September 7, 2009 issue of the *Journal of Cell Biology*, Stagg et al. reveal a key detail in one of these stratagems, identifying a protein that enables cyto-megalovirus to shut down an antiviral defense (online August 31).

Cytomegalovirus, which most people contract at some point in their lives, eludes immune system surveillance by targeting the protein MHC I. When we're sick, MHC I captures bits of viral proteins and presents them to cytotoxic T cells, which respond by killing cells that harbor the virus, stanching the infection. However, two cytomegalovirus genes dupe cells into ubiquitinating MHC I and demolishing it in the proteasome, the cellular garbage disposal. To trigger MHC I ubiquitination, the genes co-opt a cellular protein called the E3 ligase. Researchers haven't been able to pin down the identity of this protein, which could be one of several hundred enzymes.

Stagg et al. sifted 373 candidates by depleting them one by one with RNAi. Knocking down a ligase called TRC8 spared MHC I from destruction, the team found. Mutant versions of TRC8 that curtail ubiquitination allow MHC I to return to duty. Researchers know little about the function of the protein except that it is mutated in some rare hereditary and sporadic kidney tumors. That result suggests that one of the normal targets of TRC8 helps spur cancer.

More information: Stagg, H.R., et al. 2009. *J. Cell Biol.*

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