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Inhibition of reovirus-stimulated murine natural killer cell cytotoxicity by cyclosporine

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Abstract: Reovirus type 3 is a double-stranded RNA virus that is a potent inducer of murine natural killer (NK) cell cytotoxicity, most likely as a result of virus-induced interferon production. We determined that reovirus was an effective inducer of high levels of NK cytotoxicity. A single injection of cyclosporine (CS), administered concurrently with reovirus or delayed until three days after injecting CS, significantly inhibited NK cytotoxicity. CS significantly suppressed reovirus-induced NK cytotoxicity when added directly to the chromium-release assay. We determined that CS inhibited the ability of murine spleen cells to form conjugates with YAC-1 tumor target cells. Finally, CS was shown to directly inhibit reovirus replication in vitro. Our results demonstrate that CS is an effective inhibitor of reovirus-induced NK cytotoxicity and suggest that inhibition occurs through multiple mechanisms including direct effects on the NK cells and direct inhibition of virus replication.