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INNATE IMMUNITY

T cells calm the storm

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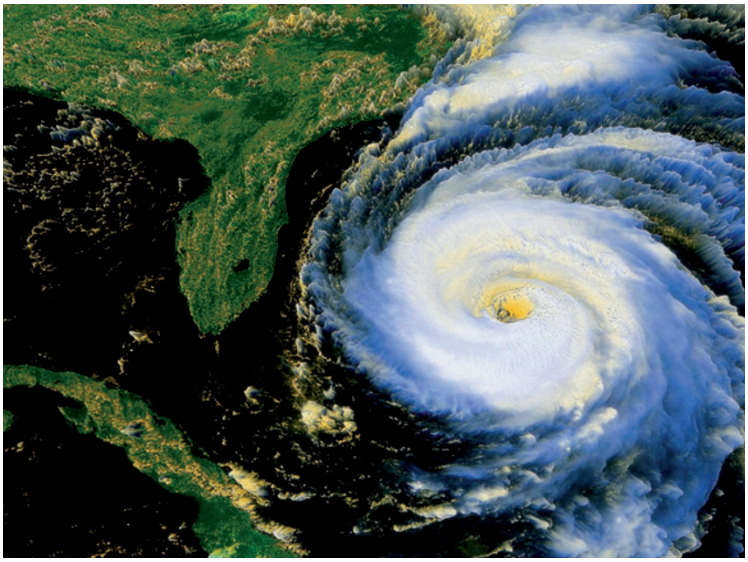
Hosts that lack adaptive immune cells often die of acute infection and it has been presumed that this is due to the lack of an effective adaptive immune response to clear the pathogen. However, in this study the authors show that, following infection, the uncontrolled innate immune response that stems from a lack of T cells may also be the cause of death in immunocompromised hosts.



While studying the early innate immune response the authors found that the infection of nude mice (which lack mature T cells) with a supposedly sublethal dose of the coronavirus MHV-A59 resulted in their death. Surprisingly the lack of T cells did not lead to enhanced viral titres, but instead resulted in an increase in the production of the pro-inflammatory cytokines tumour-necrosis factor (TNF) and interferon-γ (IFNγ), suggesting that an unrestrained early innate immune reponse might be behind the cause of death. Similarly, treatment of nude mice and RAG1 (recombination-activating gene 1)-deficient mice (which have defective lymphocytes) with the polyI:C (polyinosinic–polycytidylic acid) compound, a non-infectious ligand for Toll-like receptor 3 (TLR3), also led to a cytokine storm and death. T cells were sufficient to control this cytokine response, as shown by the adoptive transfer of T cells prior to polyI:C treatment of *Rag1*-knockout mice, which resulted in lower pro-inflammatory cytokine production.

To determine whether one particular subset of T cells was implicated in the control of the cytokine storm, the authors separated T cells into $CD4^+$, $CD8^+$ and regulatory T-cell populations. They found that the three groups of T cells were individually and equally capable of reducing cytokine production and tempering the early innate immune response. These results suggest that a large number of T cells (naive and regulatory) might be required to calm the cytokine surge that occurs during the early innate immune response. The T-cell control of innate immune cells was also shown to be mediated by cell–cell contact and dependent on the recognition of MHC complexes.

This study suggests that the adaptive immune response functions as a negative regulator of the early innate immune response rather than as a positive reinforcer. Therefore, the defective regulation of innate immune cells by T cells might be the cause of death of immunocompromised hosts during the initial phase of infection.

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ORIGINAL RESEARCH PAPER Kim, K. D. *et al.* Adaptive immune cells temper initial innate responses. *Nature Med.* 23 September 2007 (doi:10.1038/nm1633)