Function-specific variations in the immunological synapses formed by cytotoxic T cells

Darrell J. Irvine*

Biological Engineering Division/Department of Materials Science and Engineering, Massachusetts Institute of Technology, Cambridge, MA 02139

CD8⁺ cytotoxic T lymphocytes (CTLs) provide defense against intracellular pathogens and tumors by recognizing and subsequently destroying infected or transformed cells. Recognition is achieved by T cell receptors (TCRs) on the CTL binding to non-self-peptide fragments presented in the cleft of class I MHC molecules (peptide–MHC complexes) on the surface of the target cell. TCR ligation triggers target cell destruction by the CTL through several mechanisms, including the delivery to target cells of a pore-forming protein that penetrate the target cell membrane (perforin) and specialized proteases (granzymes). It has been known for some time that the density of peptide–MHC (pMHC) complexes on the surface of target cells required to stimulate cytotoxic functions in CTLs is dramatically lower than that required to stimulate cytokine production or proliferation. 

In this issue of PNAS, Faroudi et al. (4) now report a minimal lytic synapse formed by recruitment of components required for cell lysis but lacking features present in the mature IS.

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*E-mail: djirvine@mit.edu.

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nal cytotoxicity (peptide–MHC complexes generated by incubating target cells with 1 nM peptide), to that observed at a very high pMHC density (target cells pulsed with 10 μM peptide) that promotes full cytokine production, and found significant differences in the accumulation of molecules at the T cell–target cell interface under these two conditions. They found that CTLs still assemble some (but not all) of the components of their IS in response to the very low number of pMHC complexes formed by pulsing target cells with the low peptide concentration. Under these conditions, CTLs polarized the microtubule-organizing center (MTOC) and perforin to the cell interface. Under these conditions, CTLs polarized the microtubule-organizing center (MTOC) and perforin to the cell interface. Under these conditions, CTLs polarized the microtubule-organizing center (MTOC) and perforin to the cell interface. Under these conditions, CTLs polarized the microtubule-organizing center (MTOC) and perforin to the cell interface. Under these conditions, CTLs polarized the microtubule-organizing center (MTOC) and perforin to the cell interface. Under these conditions, CTLs polarized the microtubule-organizing center (MTOC) and perforin to the cell interface. Under these conditions, CTLs polarized the microtubule-organizing center (MTOC) and perforin to the cell interface.