ANTIGEN PRESENTATION

Cross-dress to impress

The presentation of MHC class I-bound antigen to $CD8^+$ T cells by professional antigen-presenting cells (APCs) can occur through two mechanisms: direct presentation of antigen by infected APCs; and cross-presentation of antigen that is acquired by phagocytosis of infected cells and then processed and presented by MHC class I molecules. A third mechanism termed 'cross-dressing' has been proposed, which involves the transfer of preformed peptide–MHC class I complexes from the surface of infected cells to uninfected APCs without the need for further antigen processing. Now, a study published in *Nature* shows that cross-dressing does indeed occur and is important for boosting memory $CD8^+$ T cell responses *in vivo*.

To determine whether cross-dressed dendritic cells (DCs) can activate $CD8^+$ T cells *in vitro*, the authors pulsed bone marrow-derived DCs with antigen. These cells were then co-cultured for 4 hours with DCs expressing a mutant MHC class I molecule that is not recognized by $CD8^+$ T cells specific for the antigen. The DCs were then separated into their original populations and cultured with the antigen-specific $CD8^+$ T cells. Both DC populations induced $CD8^+$ T cell proliferation (although the recipient DCs were approximately three orders of magnitude less effective), suggesting that the recipient DCs received preformed peptide–MHC class I complexes from the donor DCs during the co-culture.

So, what is the mechanism of this peptide–MHC class I exchange? Exosomes released by donor DCs were shown not to be the source of the loaded MHC class I molecules. However, cell contact was needed for peptide–MHC class I transfer, suggesting that trogocytosis (the rapid transfer of intact cell-surface proteins between cells that are in contact with each other) might be the mechanism involved.

Next, the authors sought to determine whether cross-dressing occurs *in vivo* during viral infection. They generated bone marrow chimeric mice — in which parenchymal cells expressed both $H2^b$ and $H2^d$ MHC molecules, whereas bone marrow-derived cells expressed green fluorescent protein (GFP) and only $H2^b$ MHC molecules — and these mice were infected with lymphocyte choriomeningitis virus (LCMV). Isolated $CD11c^+GFP^+$ cells were then cultured with T cells specific for an H2-L^d-restricted LCMV epitope, and this resulted in the induction of interleukin-2 production by the T cells. These data indicate that the $CD11c^+$ cells had acquired peptide–MHC class I complexes from the parenchymal cells. Further analysis showed that $CD8\alpha^-$ DCs are more efficient than $CD8\alpha^+$ DCs at antigen presentation through cross-dressing.

Finally, by creating an *in vivo* system that enables the ablation of APCs that, following viral infection, can present antigen only through cross-dressing, the authors found that cross-dressed APCs induced the proliferation of memory $CD8^+$ T cells but not naive $CD8^+$ T cells.

So, cross-dressing is an additional mechanism used by APCs to present viral antigen derived from infected cells to memory $CD8^+$ T cells and is required for an effective antiviral immune response. The mechanism of the selective activation of memory $CD8^+$ T cells by cross-dressed DCs requires further study.

Olive Leavy

ORIGINAL RESEARCH PAPER Wakim, L. M. & Bevan, M. J. Cross-dressed dendritic cells drive memory $CD8^+$ T-cell activation after viral infection. *Nature* **471**, 629–632 (2011)