RESEARCH HIGHLIGHTS

ANTIGEN PRESENTATION

DCs spot the difference

A question that has puzzled immunologists for many decades is how the immune system discriminates between self- and non-self-antigens. Although this puzzle remains far from being solved, a recent paper published in Nature indicates that dendritic cells (DCs) can distinguish antigens taken up in the presence of Toll-like receptor (TLR) ligands from those taken up in the absence of such ligands.

During an infection, DCs efficiently phagocytose microorganisms, leading to DC activation (for example, through microbial ligation of their TLRs) and presentation of microbial peptides to CD4⁺ T cells, thereby initiating an immune response. At the same time, these DCs are surrounded by large amounts of self-antigen (for example, apoptotic cells).

66 DCs can distinguish antigens taken up in the presence of TLR ligands from those taken up in the absence of such ligands

So, Blander et al. set out to investi-

mechanisms that prevent DCs from

these self-antigens during an infec-

lbumin (OVA) and bacteria express-

ing H2-E α , it was shown that ~60%

derived DCs or splenic DCs) that

gate whether there are regulatory

initiating an immune response to

tion. Using fluorescently labelled

apoptotic cells expressing ova-

of DCs (either bone-marrow-

had taken up the fluorescently

labelled apoptotic cells had also

taken up bacteria. However, only

MHC class II molecules; this was

indicated by the observation that

CD4⁺ T cells specific for an H2-Eα

peptide were induced to proliferate,

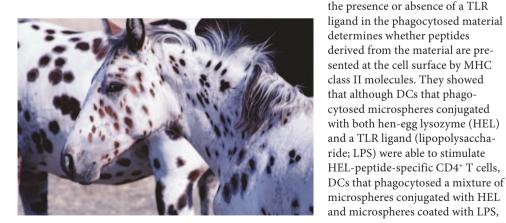
whereas CD4+ T cells specific for an

OVA peptide were not. The authors

then provided further evidence that

peptides derived from the bacteria

were presented at the cell surface by



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and DCs that had phagocytosed microspheres conjugated with HEL and were stimulated by exogenous LPS, were not.

Isolated phagosomes from DCs that had phagocytosed a mixture of microspheres conjugated with only HEL and microspheres conjugated with both HEL and LPS were separated and biochemically characterized. In phagosomes containing the microspheres conjugated with HEL and LPS, the invariant chain (Ii) — a chaperone molecule that assists in the assembly of nascent MHC class II molecules and whose degradation is required for the peptide-binding groove of MHC class II molecules to become available for peptide loading — was degraded, whereas in phagosomes containing the microspheres conjugated with only HEL, Ii degradation was not observed. Consistent with this, HEL-peptide-MHC-class-II complexes were only observed in phagosomes that contained microspheres conjugated with both HEL and LPS.

These data indicate that DC presentation of cell-surface peptide-MHC-class-II complexes is regulated in a TLR-dependent phagosome-autonomous manner, providing details of one mechanism to ensure that self-antigens that are phagocytosed by DCs during an infection are not presented to CD4⁺ T cells.

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ORIGINAL RESEARCH PAPER Blander, I. M. & Medzhitov, R. Toll-dependent selection of microbial antigens for presentation by dendritic cells. Nature 19 Feb 2006 (doi:10.1038/ nature04596)

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