DENDRITIC CELLS

A new role for pDCs

Plasmacytoid dendritic cells (pDCs) are a subset of DCs that are morphologically similar to plasma cells and can rapidly produce large amounts of type I interferons (IFNs) after exposure to viruses. Most studies on pDCs have focused on their ability to stimulate T-cell responses, but a new study from Jacques Banchereau's group shows that pDCs have a role in inducing virus-specific antibodies.

When peripheral-blood mononuclear cells (PBMCs) were depleted of pDCs before being exposed to influenza virus *in vitro*, this resulted in a 90% decrease in IFN-α secretion and virtually no influenza-specific antibodies were detectable by enzyme-linked immunosorbent assay. B cells co-cultured with virus, T cells or a CD40L-transfected cell line, and interleukin-2 (IL-2) produced low levels of virus-specific antibodies, but addition of 5000 pDCs resulted in a marked increase in antibody production.

To investigate the mechanism, they cultured CD40-activated B cells in transwells and showed that plasma-cell differentiation was mediated by soluble factors. These factors were identified as IFN-α/β and IL-6 because neutralization of these factors totally inhibited antibody secretion. Addition of IL-2, IL-6 and IFN-α induced the highest secretion of antibodies.

The authors suggest that when pDCs are exposed to virus, they secrete type I IFNs and become mature, antigen-presenting DCs. T cells respond by secreting IL-2 and expressing CD40L, which stimulates the pDCs to secrete IL-6 and activates B cells. Type I IFNs from the pDCs induce B cells to become plasmablasts, whereas IL-6 promotes the transition of plasmablasts into antibody-secreting plasma cells.

This study shows that in addition to their role in triggering T-cell responses, pDCs are important for generating antibody-secreting plasma cells during virus infection.

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References and links

ORIGINAL RESEARCH PAPER Jego, G. *et al.* Plasmacytoid dendritic cells induce plasma cell differentiation through type I interferon and interleukin 6. *Immunity* **19**, 225–234 (2003)

MUCOSAL IMMUNITY

A shock to the system

The non-polymorphic MHC class-I-like molecule CD1d is highly expressed on both the apical and basolateral surfaces of intestinal epithelial cells where it is thought to regulate the inflammatory state of the intestine. Despite these *in situ* observations epithelium-derived cell lines express low levels of CD1d, making *in vitro* observations hard to correlate with *in vivo* studies. Insight into these differences and understanding of the mechanisms that govern CD1d expression levels has now been provided by a study from Richard Blumberg's group in which they identify heat shock protein 110 (Hsp110) as the main component of lumenal contents responsible for regulating cell-surface expression of CD1d.

Cell-surface levels of CD1d were observed to increase markedly on epithelial cell lines cultured in the presence of solubilized lumenal contents, with the increase being greater when the lumenal contents were applied to the apical surface than to the basolateral membrane. This upregulation was specific to epithelium-derived cell lines and was at least in part a result of increased CD1d transcription.

The CD1d-inducing activity was shown not to be of microbial origin, as upregulation of CD1d expression was observed on epithelium-derived cell lines exposed to lumenal contents isolated from mice bred under germ-free conditions but not to lipopolysaccharide (LPS). However, after fractionation and analysis of the lumenal contents, the CD1d-inducing activity was identified by peptide microsequencing as Hsp110. This was further confirmed by showing that antibodies specific for Hsp110 inhibited the upregulation of CD1d expression by intestinal epithelial cell lines in the presence of solubilized lumenal contents, and that recombinant Hsp110 had the same CD1d-inducing activity as solubilized lumenal contents.

Interestingly, high levels of Hsp110 were detected in the epithelium of the small intestine, indicating the existence of an autocrine positive-feedback loop. Therefore, these studies define one mechanism by which CD1d expression levels can be regulated in the intestine, and given the data indicating that CD1d ligation might negatively regulate mucosal inflammation this might be important in understanding the biology of chronic inflammatory diseases.

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References and links

ORIGINAL RESEARCH PAPER Colgan, S. *et al.* Intestinal heat shock protein 110 regulates expression of CD1d on intestinal epithelial cells. *J. Clin. Invest.* **112**, 745–754 (2003)