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PATTERN RECOGNITION RECEPTORS

Picking LOX to find antibodies

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Reporting in *Immunity*, Joo *et al.* describe a new role for the pattern recognition receptor lectin-like oxidized low-density lipoprotein 1 (LOX1; also known as OLR1) in promoting humoral immune responses.

LOX1 is expressed on the surface of endothelial cells, smooth muscle cells and immune cells; it recognizes both endogenous and exogenous ligands, including modified lipoproteins and bacterial components. Ligation of LOX1 has been shown to promote dendritic cell (DC) activation and $CD8^+$ T cell responses. However, its wide pattern of expression suggested it may have additional immune functions. The authors generated a monoclonal antibody specific for the extracellular domain of human LOX1. In histological analyses of human spleens, they used this antibody to identify $LOX1^+CD11c^+$ cells interacting with IgD^+ B cells in the marginal zone, suggesting that LOX1-expressing DCs may support B cell responses.

To explore this, they co-cultured B cells with monocyte-derived DCs that had been pre-treated with the LOX1-specific antibody or a control antibody. Compared with controls, B cells cultured with DCs that had been pre-treated with LOX1-specific antibody showed increased proliferation and plasmablast differentiation and secreted greater amounts of antibody. Long-term co-cultures showed that DCs treated with LOX1-specific antibody also promoted class-switching responses in B cells. Consistent with this, DCs treated with LOX1-specific antibody produced a proliferation-inducing ligand (APRIL) and B cell-activating factor (BAFF), and B cells co-cultured with these DCs showed increased expression of the transcription factors STAT3 and BLIMP1, which promote plasma cell differentiation.

> “LOX1 targeting could be used to improve the efficacy of new vaccines”

As B cells also express LOX1, the authors examined the functional significance of this. They found that LOX1 is expressed by naive and memory B cells, but is downregulated following the activation of these cells. Treatment of B cells with LOX1-specific antibody did not promote their differentiation into plasmablasts, and although it did promote antibody production, the levels observed were much lower than those seen in the DC co-culture experiments. Interestingly, B cells treated with LOX1-specific antibody upregulated expression of CC-chemokine receptor 6 (CCR6), CCR7 and CXC-chemokine receptor 5 (CXCR5), which are involved in homing to lymphoid tissues. By contrast, B cells co-cultured with DCs that had been pre-treated with LOX1-specific antibody downregulated CXCR5 and upregulated expression of CCR10, which promotes plasmablast homing to non-lymphoid tissues, such as the skin and intestinal mucosa.

Finally, the authors examined whether targeting LOX1 could be effective for vaccination purposes. They fused influenza virus haemagglutinin 1 (HA1) to LOX1-specific antibody and immunized rhesus macaques with these constructs. Compared with animals that were immunized with an inactivated influenza virus containing equivalent amounts of HA1, animals immunized with the fusion protein produced higher levels of HA1-specific neutralizing antibodies and had reduced viral titres following subsequent infection with influenza virus. Based on these findings, the authors propose that LOX1 targeting could be used to improve the efficacy of new vaccines.

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ORIGINAL RESEARCH PAPER Joo, H. *et al.* C-type lectin-like receptor LOX-1 promotes dendritic cell-mediated class-switched B cell responses. *Immunity* http://dx.doi.org/10.1016/j.immuni.2014.09.009 (2014)