Immunoreceptor Signaling

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T cells and B cells are stimulated when antigens bind to T-cell receptors (TCRs) and B-cell receptors (BCRs) in their respective plasma membranes (Fig. 1). The antigens presented to T cells are in the form of short peptides that have been processed in infected cells and are displayed on the surface bound to major histocompatibility complex (MHC) class I or class II molecules. BCRs, in contrast, recognize free antigens in their native form present in the extracellular milieu or on cell surfaces.

Despite superficial differences, the responses in the two cell types are remarkably similar. For both, signaling begins with engagement of a complex receptor composed

of antigen receptor subunits with immunoglobulin or immunoglobulin-like domains. Both receptors also contain non-polymorphic subunits, the TCR ζ chain and CD3 subunits (γ , δ , and ϵ) for the TCR, and the α and β chains of the BCR (Reth 1995; Wucherpfennig et al. 2010). Co-receptors are important in both T cells (CD4 for helper T cells; CD8 for cytotoxic T cells) and B cells (CD19). For both receptors, members of two protein tyrosine kinase (PTK) families, Src (Lck for T cells and Lyn for B cells) and Syk (Zap-70 for T cells and Syk for B cells) (Bradshaw 2010; Liu et al. 2010; Wang et al. 2010), are critical signaling molecules closely associated with the receptors and

Figure 1. Early events in T cell and B cell receptor signaling.

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Following antigen engagement, activated tyrosine kinases phosphorylate several adapter proteins and signaling enzymes, which then interact. For T cells, this is exemplified by the phosphorylation of the adapters LAT and SLP-76 (Fig. 2), the formation of multiprotein complexes nucleated at these adapters, and the inclusion of such enzymes as phospholipase C γ (PLC γ 1) and VAV in the protein assemblies (Balagopalan et al. 2010; Jordan and

Downstream from these initial events, a number of other protein complexes are formed, and various signaling

pathways are activated. Many of these involve activation of protein serine kinases (Finlay and Cantrell 2010). In T cells and B cells, activation of protein kinase C (PKC) leads to formation and activation of the CARMA1–Bcl10–MALT1 complex (Thome et al. 2010). Stimulation of PI3K leads to activation of the kinase Akt (Huang and Sauer 2010). Downstream from the TCR and BCR, one also observes activation of small G proteins such as Ras, which, in turn, leads to activation of the Raf/MEK and ERK kinases. Finally, in both cell types, these various events lead to cytoskeletal changes and gene expression induced by transcriptional activators such as NF-AT and NF- κ B. T cells and B cells thus activated can proliferate, differentiate, and synthesize the cytokines and effector molecules that allow them to fulfill their roles in the adaptive immune response.

(Figures adapted with kind permission of Cell Signaling Technology (<http://cellsignal.com>.)

REFERENCES

- Andreotti AH, Schwartzberg PL, Joseph RE, Berg LJ. 2010. T-cell signaling regulated by the Tec family kinase, Itk. *Cold Spring Harb Perspect Biol* 2: a002287.
- Balogopalan L, Coussens NP, Sherman E, Samelson LE, Sommers CL. 2010. The LAT story: A tale of cooperativity, coordination, and choreography. *Cold Spring Harb Perspect Biol* 2: a005512.
- Bradshaw JM. 2010. The Src, Syk, and Tec family kinases: Distinct types of molecular switches. *Cell Signal* 22: 1175–1184.
- Finlay D, Cantrell D. 2010. The coordination of T-cell function by serine/threonine kinases. *Cold Spring Harb Perspect Biol* 3: a002261.
- Huang YH, Sauer K. 2010. Lipid signaling in T-cell development and function. *Cold Spring Harb Perspect Biol* 2: a002428.
- Jordan MS, Koretzky GA. 2010. Coordination of receptor signaling in multiple hematopoietic cell lineages by the adaptor protein SLP-76. *Cold Spring Harb Perspect Biol* 2: a002501.
- Liu W, Sohn HW, Tolar P, Pierce SK. 2010. It's all about change: The antigen-driven initiation of B-cell receptor signaling. *Cold Spring Harb Perspect Biol* 2: a002295.
- Reth M. 1995. The B-cell antigen receptor complex and co-receptors. *Immunol Today* 16: 310–313.
- Thome M, Charton JE, Pelzer C, Hailfinger S. 2010. Antigen receptor signaling to NF- κ B via CARMA1, BCL10, and MALT1. *Cold Spring Harb Perspect Biol* 2: a003044.
- Wang H, Kadlec TA, Au-Yeung BB, Goodfellow HE, Hsu LY, Freedman TS, Weiss A. 2010. ZAP-70: An essential kinase in T-cell signaling. *Cold Spring Harb Perspect Biol* 2: a002279.
- Wucherpfennig KW, Gagnon E, Call MJ, Huseby ES, Call ME. 2010. Structural biology of the T-cell receptor: Insights into receptor assembly, ligand recognition, and initiation of signaling. *Cold Spring Harb Perspect Biol* 2: a005140.

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