

## BACKGROUND

Interleukin-1 receptor activated kinases (IRAKs) are key mediators in the signaling pathways of TLRs/IL-1Rs. By means of their kinase and adaptor functions, IRAKs initiate a cascade of signaling events eventually leading to induction of inflammatory target gene expression. Due to this pivotal role, IRAK function is also highly regulated via multiple mechanisms. Four IRAK members have been identified in the human genome (IRAK-1, 2, M, and 4), which seem to play distinct roles.<sup>1</sup> IRAK-1 is a highly specific signaling molecule activated by the Toll/IL-1 receptor family. It is a multidomain protein consisting of an N-terminal death domain, a regulatory ProST (proline-, serine-, threonine-rich) region, a conventional serine/threonine protein kinase domain and a large C-terminal rest. After activation of TLR4 or the type 1 IL-1 receptor, MyD88 and IRAK1 are recruited to the activated receptor complex. IRAK1 becomes phosphorylated, dissociates from the receptor complex, and associates with TNF receptor-associated factor 6 (TRAF6). The signal is then distributed to multiple downstream targets, including NF- $\kappa$ B, c-Jun NH2-terminal kinase (JNK), and p38 $\alpha$  MAPK.<sup>2</sup> The signaling function of IRAK-1 is independent of its enzymatic activity. The kinase domain and the ProST region serve as a self-activating kinetic switch module in IRAK-1. Two different phosphorylation events take place in a sequential fashion in IRAK-1.<sup>3</sup> The first is an autophosphorylation of the kinase domain resulting in full enzymatic activity. This is followed by multiple phosphorylations in the ProST region. The introduction of negative charges adjacent to the death domain has two consequences: First hyperphosphorylated IRAK-1 dissociates from the upstream adapter MyD88 and thus leaves the active receptor complex allowing optimal interaction with the downstream adapter TRAF6. Second, hyperphosphorylated IRAK-1 is targeted to the proteasome where it is proteolytically degraded and thus removed out of the signaling chain. This self-limitation guarantees a transient IL-1 signal. This regulatory function is completely dispensable for IRAK-1's adapter function as a signaling molecule.

## References:

- Gottipati S et al.: Cell Signal. 20:269-276, 2008.
- Akira S & Takeda K.: Nature Rev. Immunol. 4:499-511, 2004.
- Neumann D et al.: J. Leuk. Biol. 84:807-813, 2008.

## TECHNICAL INFORMATION

### Source:

IRAK1 is a rabbit polyclonal antibody raised against the epitope near the human IRAK1 carboxyl terminal sequence.

### Specificity and Sensitivity:

This affinity purified antibody detects endogenous IRAK1 proteins in various cell lysates.

**Storage Buffer:** PBS and 30% glycerol

### Storage:

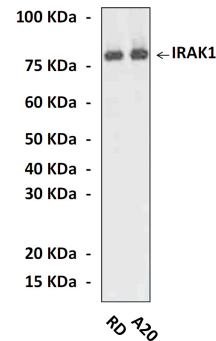
Store at -20°C for at least one year. Store at 4°C for frequent use. Avoid repeated freeze-thaw cycles.

## APPLICATIONS

Application:	*Dilution:
WB	1:1000
IP	n/d
IHC (Paraffin)	n/d
ICC	n/d
FACS	n/d

*\*Optimal dilutions must be determined by end user.*

## QUALITY CONTROL DATA



Various cell lysates were subjected to Western Blot analysis using IRAK1 Antibody.

