

## BACKGROUND

Insulin receptor substrate (IRS) proteins play a central role in maintaining basic cellular functions such as growth and metabolism. IRS proteins act as an interface between multiple growth factor receptors possessing tyrosine kinase activity, such as the insulin receptor, and a complex network of intracellular signaling molecules containing Src homology 2 (SH2) domains. Four members (IRS-1, IRS-2, IRS-3, IRS-4) of this family have been identified which differ in their subcellular distribution and interaction with SH2 domain proteins.<sup>1</sup> Insulin receptor substrate-1 (IRS-1) is a major substrate of insulin and insulin-like growth factor-I receptors. The activated insulin receptor phosphorylates the intracellular substrate IRS-1, which then binds various signaling molecules that contain SH2 domains, thereby propagating the insulin signal. Among these IRS-1-binding proteins, the Grb2-Sos complex and the protein tyrosine phosphatase SHP-2 transmit mitogenic signals through the activation of Ras, and phosphoinositide 3-kinase is implicated in the major metabolic actions of insulin.<sup>2</sup> Insulin also activates several kinases that induce the phosphorylation of IRS-1 on specific serine/threonine sites and inhibit its functions. This is part of the negative-feedback control mechanism induced by insulin that leads to termination of its action.<sup>3</sup> Agents which induce insulin resistance, such as free fatty acids, cytokines, angiotensin II, endothelin-1, amino acids, cellular stress and hyperinsulinemia, also lead to activation of several serine/threonine kinases and phosphorylation of IRS-1. These agents negatively regulate IRS-1 function by phosphorylation and other molecular mechanisms (SOCS expression, IRS degradation, O-linked glycosylation).<sup>4</sup> IRS-1 mediates the control of various cellular processes by insulin. Serine hyperphosphorylation of IRS1 may lead to insulin resistance. Ser307 in rat IRS-1 or Ser312 in human IRS-1 is phosphorylated via several mechanisms, including insulin-stimulated kinases or stress-activated kinases like JNK1.<sup>5</sup>

### References:

1. Yenush, L. & White, M.F.: Bioessays 19:491, 1997.
2. Ogawa, W., Matozaki, T., & Kasuga, M.: Mol. Cell. Biochem. 182:13, 1998.
3. Sesti, G.: Best Pract Res Clin Endocrinol Metab. 20:665, 2006.
4. Gual, P. et al.: Biochimie 87:99, 2005.
5. Aqurrie, V. et al: J. Biol. Chem. 277:1531-7, 2002.

## TECHNICAL INFORMATION

### Source:

Affinity purified Phospho-IRS-1 (Ser307) antibody is a rabbit polyclonal antibody raised against the epitope surrounding and including Ser307 of human IRS-1.

### Specificity and Sensitivity:

This antibody detects endogenous phospho-IRS-1 in 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.

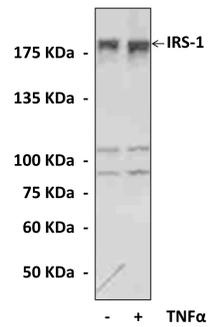
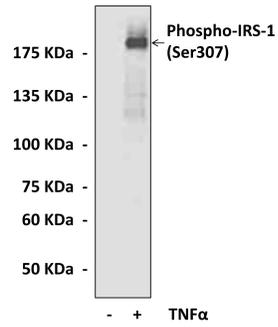
## APPLICATIONS

| 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



The C2C12 cells were treated with TNF-alpha and subjected to Western Blot analysis using Phospho-IRS-1 (Ser307) antibody. (**top**), or IRS-1 antibody (**bottom**).

