BACKGROUND

Nuclear Receptor Corepressor (NCoR, also known as NCOR1) and silencing mediator of retinoid and thyroid hormone receptors (SMRT, also known as NCOR2) were initially identified based on their ability to bind unliganded retinoic acid and thyroid hormone receptors and to mediate active repression of their respective target genes through the recruitment of additional corepressor molecules that include histone deacetylases (HDACs). In addition to nuclear receptors, NCoR and SMRT can exert repressive effects via interactions with numerous other transcription factors, including AP-1 proteins, ETO-1/2, NF-kappaB, and Ets proteins.

In absence of ligands, thyroid hormone (TR) and retinoic acid receptor (RAR) isoforms recruited at least NCOR1 and SMRT, which, in turn, recruit a multiprotein complex with histone deacetylase activity that appears to modify chromatin to prevent transcription. In the presence of their cognate ligands, the TR and RAR isoforms release the nuclear corepressors and recruit members of the coactivator family, which include the p160 family members [steroid receptor coactivator-1 (SRC-1), TIF II, and ACTR], CREB-binding protein (CBP) and p300, pCAF, and other coactivators such as p120. Unlike the nuclear corepressors, the coactivator complex possesses histone acetyl transferase activity, which allows for transcriptional activation. In addition, NcoR1 complexes are also essential for ligand-dependent transrepression of at least some of these genes by the nuclear receptors PPARgamma and liver X receptors (LXRs). Inhibition of lipopolysaccharide (LPS) activation of the *iNOS* gene by PPARgamma and LXR agonists in macrophages and inhibition of IL1beta activation of the *CRP* gene in hepatocytes by LXR agonists was found to result from their ability to prevent signal-dependent clearance of NCoR complexes from the promoters of these genes.

Although NCoR1 and SMRT share a common molecular architecture and form similar complexes, it was shown that they cannot fully compensate for each other during development. In addition, SMRT and NCoR1 also differ in their response to kinase pathways that regulate their function. SMRT is regulated by MEKK1 and IKKalpha, leading to its redistribution from the nuclear to the cytoplasmic compartment. In contrast, NCoR1 can be negatively regulated by the Akt and MEKK1/TAB2 pathways. However, the combinatorial roles of NCoR1 and SMRT were discovered in the regulation of broad sets of inflammatory response genes in macrophages and it was demonstrated that they are required for nearly all of the transrepression activities of LXRs. Moreover, both NCoR1 and SMRT are required to establish stable corepressor complexes on a large subset of these genes. As a consequence, both NCoR1 and SMRT are required for LXR transrepression of these genes. Conversely, this class of genes can also be derepressed by signals that selectively target NCoR1 or SMRT. Combinatorial interactions between NCoR1 and SMRT thus provide a widely used corepressor-based strategy for integration of inflammatory and anti-inflammatory signaling pathways.

References:

1. Underhill, C. et al: J. Biol. Chem. 275: 40463-70, 2000
2. Li, J. et al: EMBO J. 19: 4342-50, 2000
3. Jepsen, K & Rpsemfeld, M. G. J. Cell Sci. 115: 689-98, 2002

TECHNICAL INFORMATION

Source:
NcoR1 antibody is a mouse monoclonal antibody raised against purified recombinant human NcoR1 fragments expressed in *E. coli*.

Specificity and Sensitivity:
This antibody detects NcoR1 proteins without cross-reactivity with other family members.

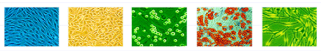
Storage Buffer: PBS and 30% glycerol

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	1:200
ICC	n/d
FACS	n/d

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

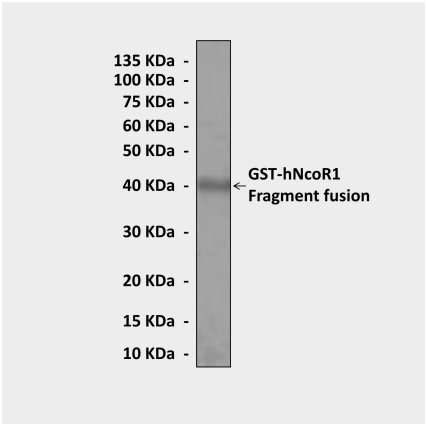


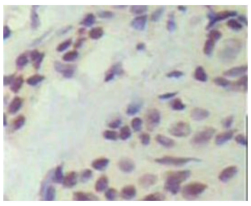
NcoR1 Antibody

Cat. No. CP10182

Applications:	**WB, IHC**
Detected MW:	**250 kDa**
Species & Reactivity:	**Human**
Isotype:	**Mouse IgG1**

QUALITY CONTROL DATA





Top: Western Blot detection of NcoR1 proteins in bacterial lysate containing GST-hNcoR1 (1-150aa) fusion proteins (predicted MW: 40kDa) using NcoR1 Antibody. **Bottom:** This antibody stains paraffin-embedded human breast cancer tissue in immunohistochemical analysis.