

BACKGROUND

The family of estrogen receptor-related receptors (ERRs) is a subfamily of the orphan nuclear receptors, which is closely related to the estrogen receptor (ER) family. The ERRs, comprising ERR α (NR3B1), ERR β (NR3B2) and ERR γ (NR3B3), bind and regulate transcription via estrogen response elements (EREs) and extended ERE half-sites termed ERR response elements (ERREs), but do not bind endogenous estrogens. ERRs seem to interfere with the classic ER-mediated estrogen responsive signaling in various ways. ERR α , ERR β and ERR γ possess the typical structural features of NRs: a central zinc finger DNA-binding domain that is highly conserved among the three members and enables recognition of DNA sites bearing specific sequences; a conserved C-terminal domain with a putative ligand binding domain (LBD) and interaction surfaces for coactivators and corepressors; and a less conserved N-terminal region. ERRs attain active LBD conformations in the absence of ligand, consistent with the notion that these receptors are constitutively active. Analyses of genetically modified mice have shown that the three ERRs display stricter specificity in their primary biological functions. Nonetheless, genetic redundancy between receptor isoforms was also evident. ERRs regulate vast gene networks involved in a wide range of bioenergetic processes. In particular, the ERRs can now be considered as essential factors for normal mitochondrial biogenesis and function. Mechanistically, the ERRs appear to be the major conduits for the action of PGC-1 α and related isoforms in the control of energy metabolism. Apart from energy metabolism, ERRs are involved in modulating cell fate decisions and the development of cancer. Given their extended roles in the transcriptional control of energy homeostasis, the ERRs represent leading targets for therapeutic interventions of metabolic diseases such as obesity, diabetes, and heart failure, as well as cancer.¹

Estrogen-related receptor β (ERR β) was one of the first two orphan nuclear receptors reported and is believed to play important roles in estrogen-regulated pathways. Embryo lethality of ERR β -null mice indicated that ERR β is essential for embryo development. Studies grouped ERR β and ERR γ with steroid hormone receptor (SHR) receptors involved in circadian and basic metabolic functions and shown that in the mouse highest levels of expression of ERR β mRNA could be detected in the eye, kidney and heart with lower concentrations in testis, thyroid and parts of the brain. Moreover, it was shown that ERR β is selectively expressed in rod photoreceptors and coordinates expression of multiple genes that are rate-limiting regulators of ATP generation and consumption in photoreceptors. ERR β is a critical regulator of rod photoreceptor function and survival.² Furthermore, an essential role for ERR β in placental development and proliferation of primordial germ

cells has been revealed by studies in ERR β null mice. Recent data has also implicated ERR β in regulating genes critical for the formation and function of the inner ear where it is believed to regulate cell fate decisions. Studies in the human have demonstrated immunoeexpression of ERR β in the cochlea and missense mutations in the ESRRB 5 gene have been detected in affected families diagnosed with nonsyndromic hearing impairment. Studies using cells from the mouse have suggested that ERR β may function in conjunction with OCT4 and SOX-2 to promote expression of genes involved in self-renewal and pluripotency.^{3,4} The full-length human ERR β gene contains 12 exons and three ERR β mRNA splice variants have been identified in human tissues; a short form (exons 1-9), a long form (exons 1-12) and a Δ 10 form that results in a shift in the reading frame and a protein with an altered C terminus. Genomic sequence alignment suggests that only the short form exists in species other than primates.

References:

1. Hartman, J. et al: Steroids. 74:635-41, 2009
2. Onishi, A. et al: Proc. Natl. Acad. Sci. USA 107:11579-84, 2010
3. Zhang, X. et al: J. Biol. Chem. 283:35825-33, 2008
4. van den Berg, D.L.C. et al: Mol. Cell. Biol. 28: 5986-5995, 2008

TECHNICAL INFORMATION

Source:

ERR-beta Antibody is a rabbit antibody raised against a short peptide from human ERR-beta sequence.

Specificity and Sensitivity:

This antibody detects endogenous levels of ERR-beta proteins without cross-reactivity with other related proteins.

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.

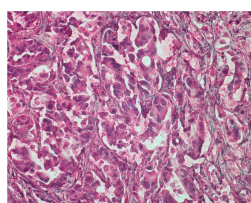
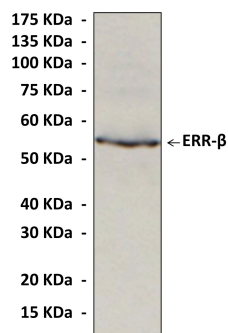
APPLICATIONS

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

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



QUALITY CONTROL DATA



Top: Western Blot detection of ERR-beta proteins in mouse liver tissue lysate using ERR-beta Antibody.
Bottom: This antibody also stains paraffin-embedded human hepatoma tissue in immunohistochemical analysis.

