

BACKGROUND

BMPR2 is a ubiquitously expressed receptor member of TGF- β receptor family of transmembrane serine/threonine kinases. These receptors mediate cellular responses to TGF-beta superfamily members, including TGF-beta, activins, inhibins, and the bone morphogenetic proteins (BMPs). Bone morphogenetic proteins (BMPs) are a large family of secreted molecules that belong to the TGF- β superfamily. BMPs regulate a wide range of developmental functions, as well as more complicated roles in cell homeostasis not limited to migration, apoptosis, proliferation, and differentiation. BMP ligands, when they have been processed into mature forms and secreted, bind to type I and II serine/threonine kinase receptors (BMPR1 and BMPR2) and induce heteromeric assembly of type I and type II receptors. Seven members of the type I and five members of the type II receptor are identified in mammals. The type II receptor functions to activate the type I receptor by phosphorylation of its glycine-serine rich (GS) domain. Subsequently, the type I receptor binds and phosphorylates members of the Smad family of transcription factors. The type II receptor BMPR2 associates principally with BMPR1A, BMPR1B and ACVR1 which all target SMAD1/5/8. However, BMPR2 can signal through many additional pathways of which the best characterised downstream signaling molecules are p38, pERK, JNK, and Akt/PI3K.¹ In particular, BMPR2 is unique among the five type II receptors in having a long C-terminal tail domain shown to be important for the regulation of cytoskeletal protein function.² Unlike the TGF β type II receptor, which has a high affinity for TGF- β 1, BMPR2 does not have a high affinity for BMP-2, BMP-7 and BMP-4, unless it is co-expressed with a type I BMP receptor. In TGF beta signaling all of the receptors exist in homodimers before ligand binding. In the case of BMP receptors only a small fraction of the receptors exist in homomeric forms before ligand binding. Once a ligand has bound to a receptor, the amount of homomeric receptor oligomers increase, suggesting that the equilibrium shifts towards the homodimeric form. The low affinity for ligands suggests that BMPR2 may differ in the from other type II TGF beta receptors in that the ligand may bind the type I receptor first.³ Currently, there are more than 20 known BMP ligands and at least 10 antagonists, which operate with varied duration, distance, and affinity.

Mutations in BMPR2 are a cause of pulmonary arterial hypertension, a rare autosomal dominant disorder characterized by plexiform lesions of proliferating endothelial cells in pulmonary arterioles. Eventually these lesions lead to elevated pulmonary arterial pressure, right ventricular failure, and death.⁴ Mutations in BMPR2 cause a loss of function or dominant negative effect and can be found in the extracellular ligand-

binding domain, in the kinase domain, or in the long cytoplasmic tail, all of which can affect the signaling mechanism as well as interaction of the receptor with the cytoskeleton. The disease phenotype can be mimicked in heterozygous mutant mice which develop increased arterial pressure and pulmonary vascular resistance compared with their wild-type littermates. However, homozygous knockout mice die at the gastrulation stage of embryogenesis consistent with a critical role for BMPR2 in development. Loss of BMPR2 is also associated with some cancer types and is linked to a 5-year survival rate in human prostate cancer.⁵ Overexpression of a dominant negative form of BMPR2 has been shown to inhibit growth of human breast cancer cells. Finally, in mice conditional inactivation of BMPR2 in the stroma leads to epithelial hyperplasia throughout the colon with increased epithelial cell proliferation and polyp formation.

References:

1. Sebald, W. et al: *Biol. Chem.* 385:697-710, 2004
2. Hassel, S. et al: *Proteomics* 4:1346-58, 2004
3. Feng, X.H. et al: *Annu Rev Cell Dev Biol* 21:659-93, 2005
4. Morrell, N.W.: *Proc. Am. Thoracic Soc.* 3:680-6, 2006
5. Owens, P. et al: *Proc. Natl. Acad. Sci. USA* 2011 : 1101139108v1-201101139.

TECHNICAL INFORMATION

Source:

BMPR2 antibody is a mouse monoclonal antibody raised against purified recombinant fragments of human BMPR2 expressed in *E. Coli*.

Specificity and Sensitivity:

This antibody detects BMPR2 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.

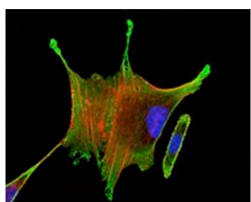
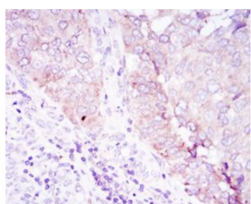
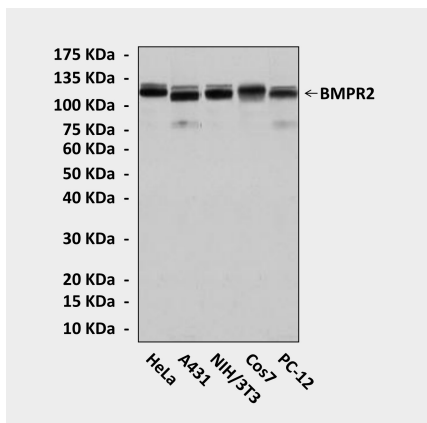
APPLICATIONS

Application:	*Dilution:
WB	1:1000
IP	n/d
IHC	1:50-200
ICC	1:50-200
FACS	n/d

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



QUALITY CONTROL DATA



Top: Western Blot detection of BMPR2 proteins in various cell lysates using BMPR2 Antibody. **Middle:** This antibody stains paraffin-embedded human kidney cancer tissue in immunohistochemical analysis. **Bottom:** It also stains Eca109 cells in confocal immunofluorescent assay (BMPR2 Antibody: Green; Actin filament: Red; DRAQ5 DNA Dye: Blue).

