

DESCRIPTION

Species Reactivity	Human
Specificity	Detects human LRP-6 in direct ELISAs and Western blots.
Source	Polyclonal Goat IgG
Purification	Antigen Affinity-purified
Immunogen	Mouse myeloma cell line NS0-derived recombinant human LRP-6 Ala20-Pro1368 Accession # O75581
Formulation	Lyophilized from a 0.2 µm filtered solution in PBS with BSA as a carrier protein. See Certificate of Analysis for details.

APPLICATIONS

Please Note: Optimal dilutions should be determined by each laboratory for each application. *General Protocols* are available in the *Technical Information* section on our website.

	Recommended Concentration	Sample
Western Blot	0.1 µg/mL	Recombinant Human LRP-6 Fc Chimera (Catalog # 1505-LR)

PREPARATION AND STORAGE

Reconstitution	Reconstitute at 0.2 mg/mL in sterile PBS.
Shipping	The product is shipped at ambient temperature. Upon receipt, store it immediately at the temperature recommended below.
Stability & Storage	<p>Use a manual defrost freezer and avoid repeated freeze-thaw cycles.</p> <ul style="list-style-type: none"> • 12 months from date of receipt, -20 to -70 °C as supplied. • 1 month, 2 to 8 °C under sterile conditions after reconstitution. • 6 months, -20 to -70 °C under sterile conditions after reconstitution.

BACKGROUND

The low-density lipoprotein (LDL) receptor-related protein 5 (LRP-5) and LRP-6 constitute a distinct subgroup of the LDL receptor family. Both LRP-5 and LRP-6 are type I transmembrane proteins that function as co-receptors with Frizzled (FZD) in the canonical Wnt signaling pathway (1, 2). LRP-6 cDNA encodes a 1613 amino acid residue (aa) precursor with a 19 aa signal sequence, a 1353 aa extracellular region, a 23 aa transmembrane (TM) segment and a 218 aa cytoplasmic domain (3). The extracellular region contains four N-terminal cysteine-rich EGF-like repeats, followed by three cysteine-rich LDLR repeats. This pattern of the EGF and LDLR repeat arrangement is different than that typically found in other LDL receptor family proteins. The intracellular region of LRP6 contains protein-protein interaction motifs and is required for canonical Wnt signal transduction (4). Human LRP-6 shares 98% and 74% aa sequence identity with mouse LRP-6 and human LRP-5, respectively. Based on the current model, canonical Wnt signaling requires the interaction of Wnt with FZD and LRP to form a trimeric complex which signals downstream to stabilize cytoplasmic β-catenin. The stabilized β-catenin is then translocated to the nucleus where it complexes with the transcription factor LEF/TCF to regulate the transcription of target genes (5). LRP-6 has also been shown to interact with the Dickkopf proteins (DKKs), which are modulators of Wnt signaling (6-8). Binding of DKK-1 to LRP-6 dissociates LRP-6 from FZD, and antagonizes the formation of the functional receptor complex. On cells where the transmembrane proteins Kremen are also present, a ternary complex of LRP-6, DKK-1 and Kremen is formed to trigger the internalization of the complex and removal LRP6 from the cell surface. Thus, DKK-1 and Kremen function synergistically to antagonize LRP-6-mediated Wnt activity. Although DKK-2 also functions as a Wnt antagonist on cells that express Kremen, DKK-2 binding to LRP-6 in the absence of Kremen activates rather than inhibits LRP mediated β-catenin signaling (9, 10).

References:

1. Howell, B.W. and J. Herz (2001) *Curr. Op. Neurobiology* **11**:74.
2. Pinson, K.I. *et al.* (2000) *Nature* **407**:535.
3. Brown, S.D. *et al.* (1998) *Biochem. Biophys. Res. Commun.* **248**:879.
4. Tamai, K. *et al.* (2000) *Nature* **407**:530.
5. Schweizer, L. and H. Varmus (2003) *BMC Cell Biology* **4**:4.
6. Mao, B. *et al.* (2001) *Nature* **411**:321.
7. Semenov, M.V. *et al.* (2001) *Curr. Biol.* **11**:951.
8. Bafico, A. *et al.* (2001) *Nature Cell Biol.* **3**:683.
9. Zorn, A.M. (2001) *Curr. Biol.* **11**:R592.
10. Mao, B. *et al.* (2002) *Nature* **417**:664.