

DESCRIPTION

Source	Mouse myeloma cell line, NS0-derived		
	Mouse ZNRF3 (Lys53-Met216) Accession # Q5SSZ7	IEGRMDP	Mouse IgG _{2a} (Glu98-Lys330)
	N-terminus		C-terminus
N-terminal Sequence Analysis	Lys53		
Structure / Form	Disulfide-linked homodimer		
Predicted Molecular Mass	45 kDa		

SPECIFICATIONS

SDS-PAGE	51-60 kDa, reducing conditions
Activity	Measured by its binding ability in a functional ELISA. When Recombinant Mouse R-Spondin 3 (Catalog # 4120-RS) is coated at 0.25 µg/ml, Recombinant Mouse ZNRF3 Fc Chimera binds with an apparent $K_d < 0.2$ nM.
Endotoxin Level	<0.10 EU per 1 µg of the protein by the LAL method.
Purity	>95%, by SDS-PAGE with silver staining.
Formulation	Lyophilized from a 0.2 µm filtered solution in PBS. See Certificate of Analysis for details.

PREPARATION AND STORAGE

Reconstitution	Reconstitute at 100 µg/mL in PBS.
Shipping	The product is shipped at ambient temperature. Upon receipt, store it immediately at the temperature recommended below.
Stability & Storage	Use a manual defrost freezer and avoid repeated freeze-thaw cycles. <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. • 3 months, -20 to -70 °C under sterile conditions after reconstitution.

DATA

<p>Binding Activity</p> <p>ZNRF3 Binds R-Spondin 3. When Recombinant Mouse R-Spondin 3 (Catalog # 4120-RS) is coated onto a microplate well at 0.25 µg/mL, Recombinant Mouse ZNRF3 Fc Chimera (Catalog # 8328-RF) binds with an apparent $K_d < 0.2$ nM.</p>	<p>SDS-PAGE</p> <p>1 µg/lane of Recombinant Mouse ZNRF3 (Catalog # 8328-RF) was resolved with SDS-PAGE under reducing (R) and non-reducing (NR) conditions and visualized by silver staining, showing bands at 54.7 and 138 kDa, respectively.</p>
----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------	-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------

BACKGROUND

ZNRF3 (zinc/RING finger protein 3) is a member of the ZNRF3 family of type 1 transmembrane ubiquitin ligases (1). Mature mouse ZNRF3 consists of a 163 amino acid (aa) extracellular domain (ECD) with a protease associated (PA) domain fold, a short transmembrane segment, and a 675 aa cytoplasmic tail that contains a RING-type zinc finger with E3 ubiquitin ligase activity. Within the ECD, mouse and human ZNRF3 share 98% sequence identity. ZNRF3 is co-expressed on the cell surface with the homologous protein RNF43. Both proteins serve to inhibit the Wnt signaling pathway through the ubiquitination of LRP6 and a majority of the Frizzled family of Wnt receptors (1, 4, 6). ZNRF3 ubiquitin ligase activity is regulated jointly by R-Spondin and its cell surface receptors, Lgr4, 5, and 6 (2). The R-Spondin-Lgr complex binds to and facilitates the removal of the ZNRF3 from the plasma membrane, resulting in an enhancement of Wnt signaling (3, 4). Conversely, ZNRF3 can antagonize R-Spondin enhanced Wnt signaling (3, 5). ZNRF3 is highly expressed in crypt stem cells of the intestine where it modulates Wnt-induced cell proliferation to control the turnover of intestinal epithelial cells (6). ZNRF3 expression is down-regulated in gastric carcinomas, and ZNRF3 mutations are linked to carcinomas of the gastric tract, pancreas, liver, and ovary (7-10).

References:

1. de Lau, W. *et al.* (2014) *Genes Dev.* **28**:305.
2. Xie, Y. *et al.* (2013) *EMBO Rep.* **14**:1120.
3. Peng, W.C. *et al.* (2013) *PLoS One* **8**:e83110.
4. Hao, H.X. *et al.* (2012) *Nature* **485**:195.
5. Moad, H.E. and A.A. Pioszak (2013) *Biochemistry* **52**:7295.
6. Koo, B.K. *et al.* (2012) *Nature* **488**:665.
7. Ong, C.K. *et al.* (2012) *Nat. Genet.* **44**:690.
8. Zhou, Y. *et al.* (2013) *J. Mol. Histol.* **44**:555.
9. Ryland, G.L. *et al.* (2013) *J. Pathol.* **229**:469.
10. Jiang, X. *et al.* (2013) *Proc. Natl. Acad. Sci. USA* **110**:12649.