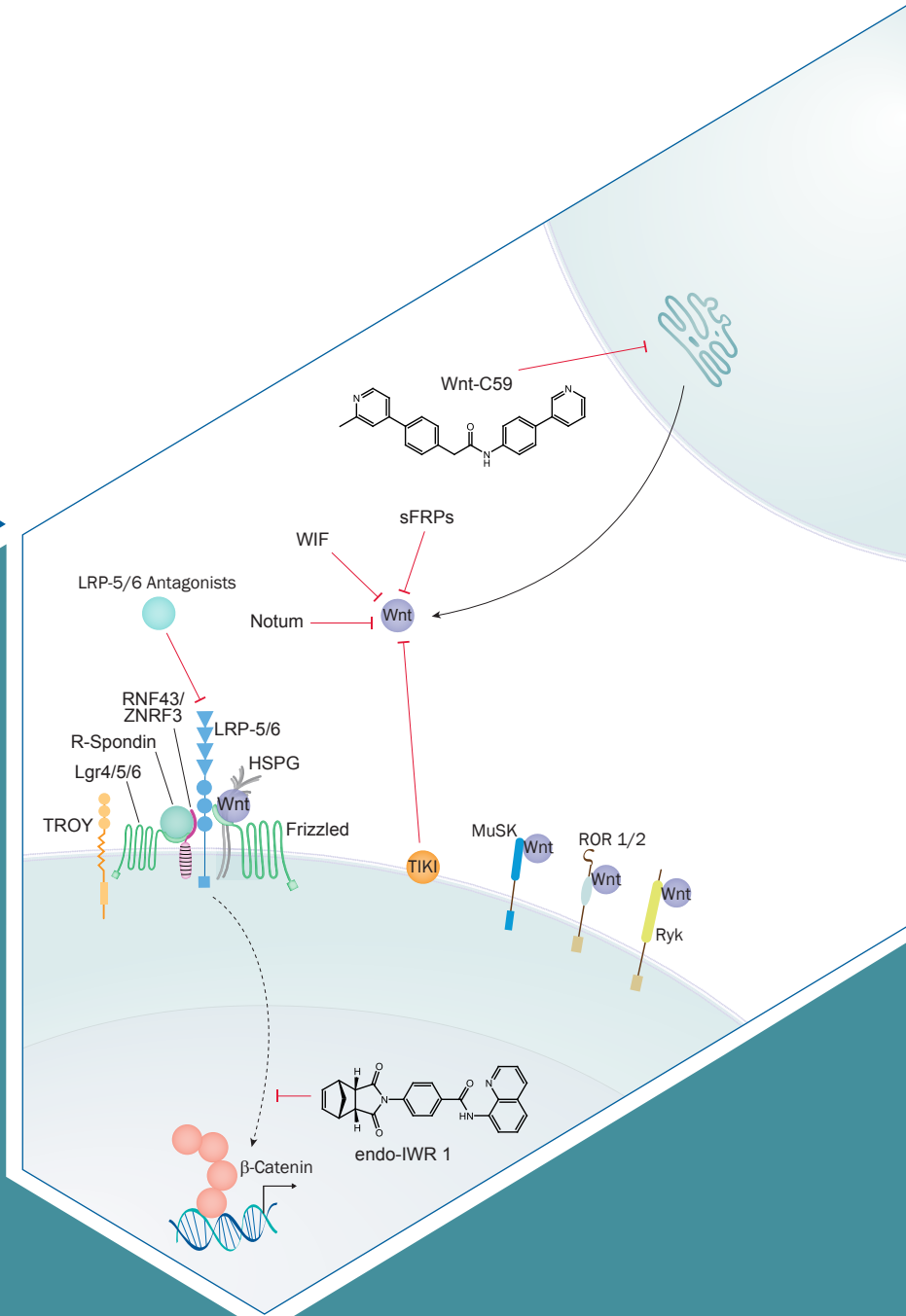


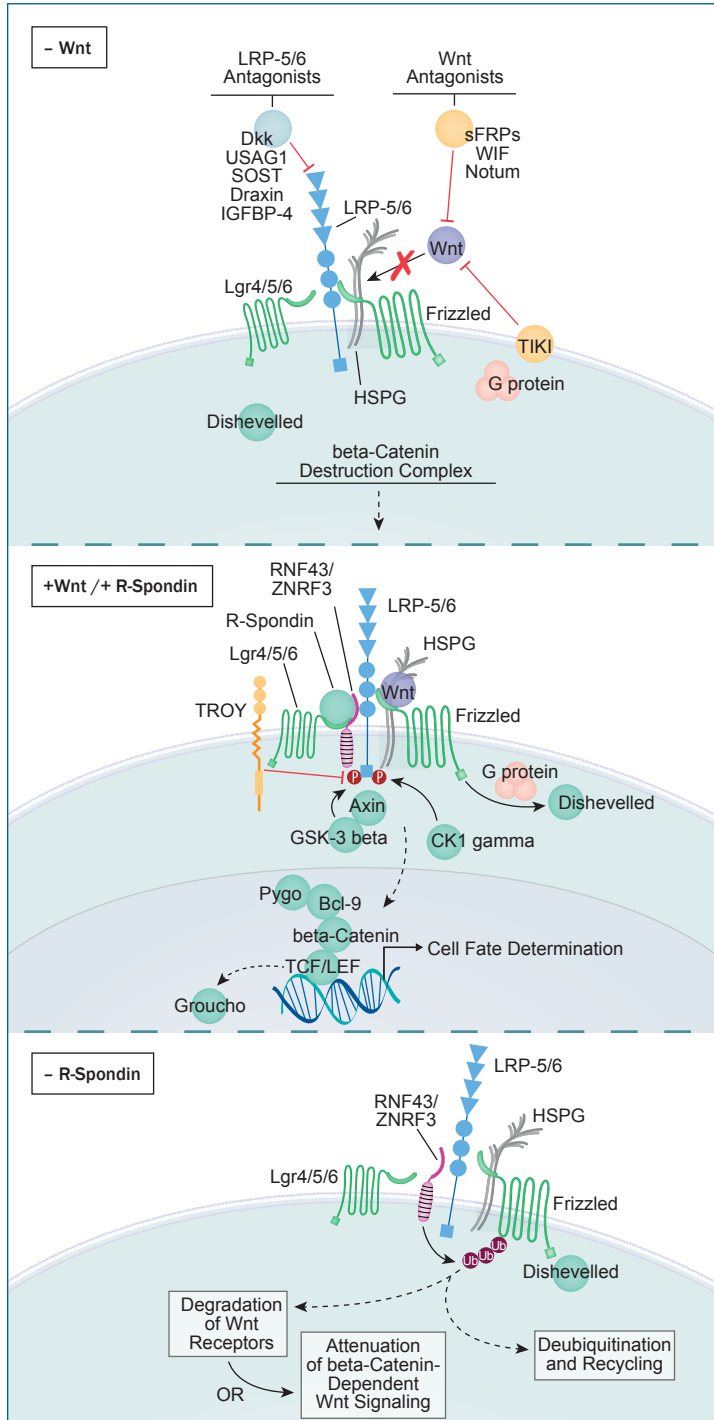
Products for Wnt Research



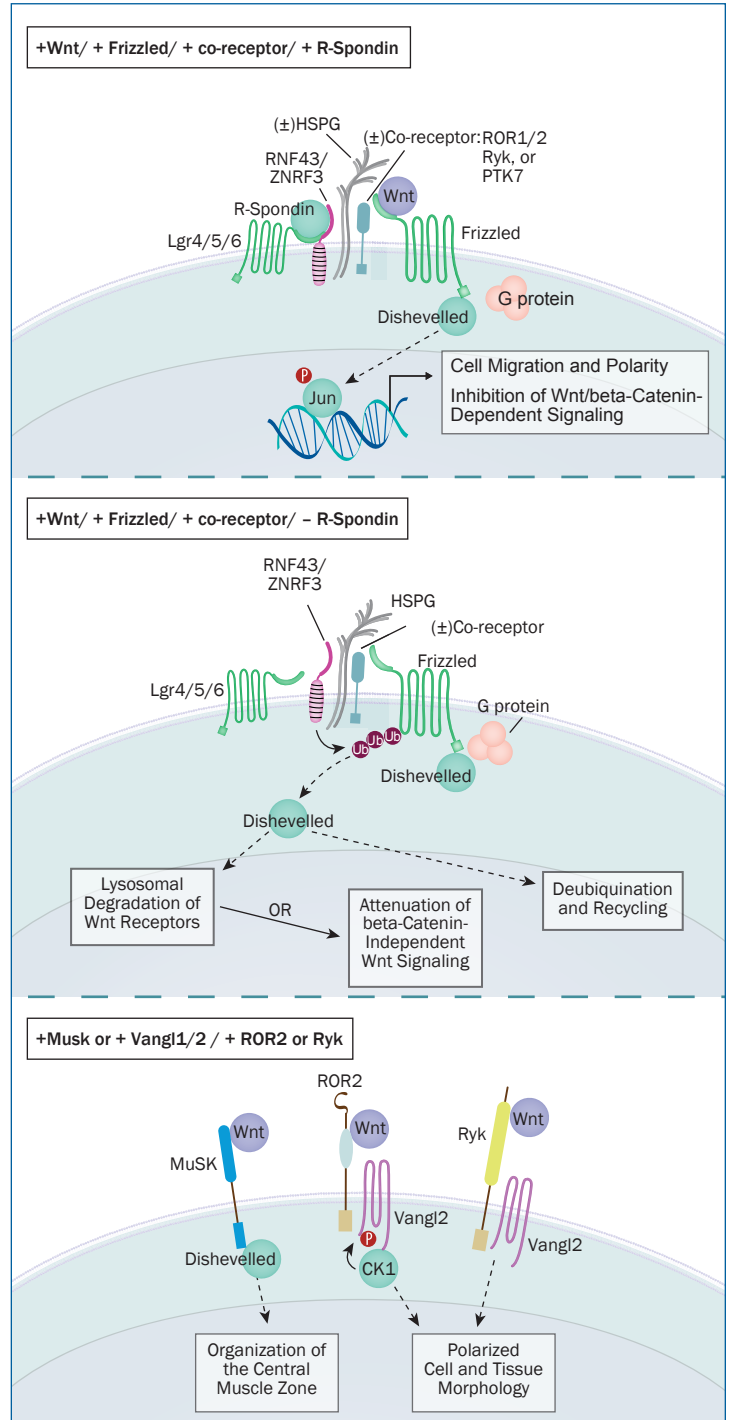
Wnt Signaling Pathways

Wnt ligands are a large family of secreted glycoproteins that have a central role in many processes involved in embryonic development and adult tissue homeostasis. The biological effects of Wnt ligands are mediated through an increasingly complex interplay of Wnt receptors, transmembrane regulators, and soluble inhibitors. The combination of these proteins are critical in determining whether a particular Wnt ligand will initiate β -Catenin-dependent or β -Catenin-independent signaling cascades. R&D Systems is globally recognized as providing the highest quality and largest selection of Wnt proteins on the market. This brochure highlights our breadth of Wnt-related reagents including difficult-to-isolate Wnt ligands, our selection of recently discovered transmembrane regulators of Wnt (RNF43, ZNRF3, LGR 4-6, and TROY), our range of Wnt-related antibodies, and Tocris small molecules that target the Wnt pathway.

β -Catenin Dependent



β -Catenin Independent



Proteins for Wnt Research

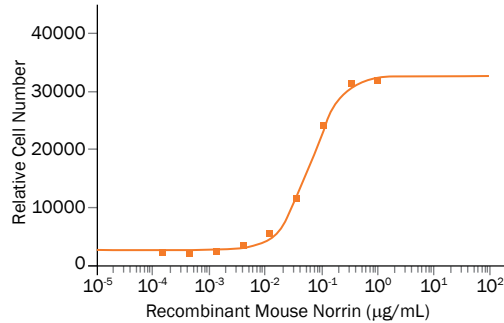
Wnt Ligands: Most Extensive Offering!

Molecule	Species	Catalog #
Wnt-2b	Mouse	3900-WN New!
Wnt-3a	Human	5036-WN GMP
	Mouse	1324-WN
Wnt-3a High Purity	Human	5036-WNP*
	Mouse	1324-WNP
Wnt-4	Human	6074-WN
	Mouse	475-WN

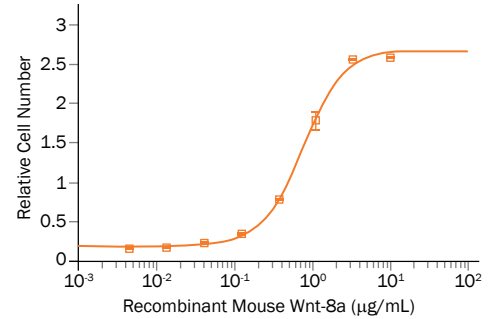
Molecule	Species	Catalog #
Wnt-5a	Human	645-WN
	Mouse	645-WN
Wnt-5b	Human	7347-WN
	Mouse	3006-WN
Wnt-7a	Human	3008-WN
Wnt-8a	Human	8419-WN New!
Wnt-9a	Mouse	8148-WN

Molecule	Species	Catalog #
Wnt-9b	Mouse	3669-WN
Wnt-10b	Human	7196-WN
	Mouse	2110-WN
Wnt-11	Human	6179-WN
Wnt-16b	Human	7790-WN
Norrin	Human	3014-NR
	Mouse	3497-NR

GMP Available as GMP-Grade



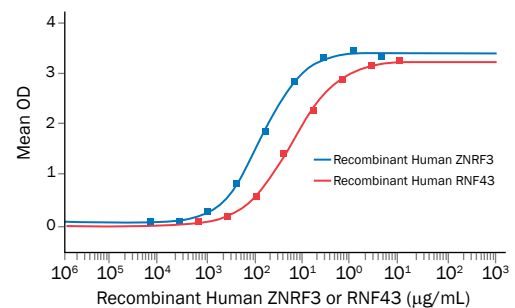
Recombinant Mouse Norrin Activates β -Catenin/TCF Through Frizzled-4 and LRP-5. The β -catenin/TCF reporter activity (RFU) in HEK293 human embryonic kidney cells overexpressing human Frizzled-4 and human LRP-5 was dose-dependently increased by Recombinant Mouse (rm)Norrin (Catalog # 3497-NR). In this assay the typical ED_{50} for rmNorrin ranges from 40–200 ng/mL.



Recombinant Mouse Wnt-8a Activates Osteoblast Differentiation of Mouse Mesenchymal Stem Cells. Addition of Recombinant Mouse (m)Wnt-8a (Catalog # 8419-WN) to C3H10T1/2 mouse mesenchymal stem cells induced osteoblast differentiation as quantified with a dose responsive increase in alkaline phosphatase production. In this assay the typical ED_{50} for mWnt-8a ranges from 0.5–2.5 μ g/mL.

Regulators of Wnt Signaling: New and Emerging Proteins

Molecule	Species	Catalog #
ZNRF3	Human	7994-RF New!
	Mouse	8328-RF New!
RNF43	Human	7964-RN New!
TROY/TNFRSF19	Human	1548-TR New!
	Mouse	723-TR New!
LRP-4	Human	5948-LR New!
LRP-5	Mouse	7344-LR New!
LRP-6	Human	1505-LR New!
	Mouse	2960-LR New!
ROR2	Human	8609-RO New!

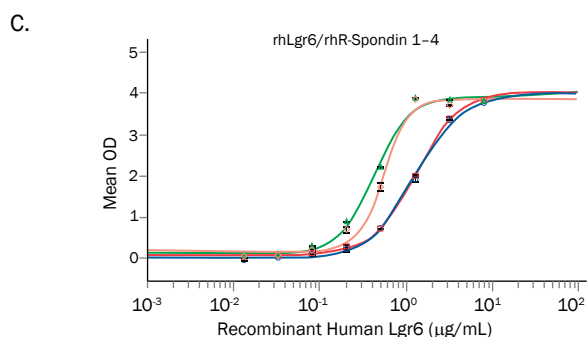
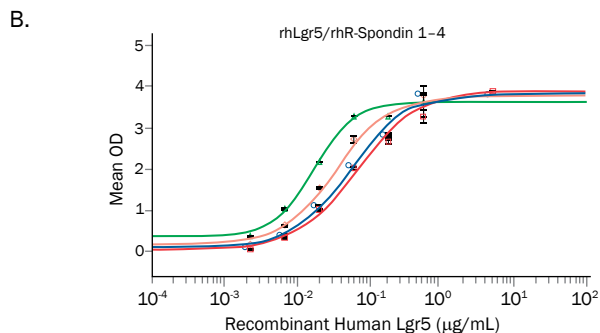
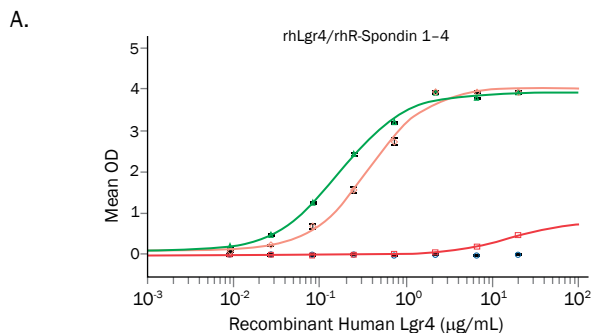


Robust Binding Activity for Recombinant Human ZNRF3 and RNF43. Binding activity of Recombinant Human (rh)ZNRF3 and rhRNF43 for rhR-Spondin 3 (Catalog # 4575-RS) was analyzed using ELISA. rhZNRF3 binds to rhR-Spondin 3 with a $K_d = 0.2$ nM (blue line). rhRNF43 binds to rhR-Spondin 3 with a $K_d = 0.1$ nM.

Cutting Edge Research from R&D Systems

R&D Systems takes pride in being the leading manufacturer of Wnt family proteins as well as an incubator for scientists to perform cutting edge research to advance our knowledge of Wnt signaling.

Lgr4-6 Show Different R-Spondin Binding Preferences and Affinities



D.

		rhLgr4	rhLgr5	rhLgr6
rhR-Spondin 1	—	No binding	2.1 nM	21.9 nM
rhR-Spondin 2	—	No binding	2.6 nM	22.0 nM
rhR-Spondin 3	—	6.6 nM	0.66 nM	5.8 nM
rhR-Spondin 4	—	14.5 nM	1.4 nM	7.7 nM

Analysis of Lgr Receptor Affinity for R-Spondin. Binding Activity of Recombinant Human (rh)Lgr4, rhLgr5, and rhLgr6 to rhR-Spondin 1 (blue), rhR-Spondin 2 (red), rhR-Spondin 3 (green), and rhR-Spondin 4 (peach) was analyzed using ELISA. **(A)** Binding curves of rhLgr4 with rhR-Spondins 1-4. **(B)** Binding curves of Lgr5 with rhR-Spondins 1-4. **(C)** Binding curves of Lgr6 with rhR-Spondins 1-4. **(D)** Table of dissociation constants (Kd) for all Lgr/R-Spondin combinations tested.

Use These Proteins in Your Research

Molecule	Species	Human
Lgr4	Human	7750-GP New!
	Mouse	8077-GP New!
Lgr5	Human	8078-GP New!
Lgr6	Human	8470-GP New!
	Mouse	8029-GP New!

Exclusively Available at R&D Systems!

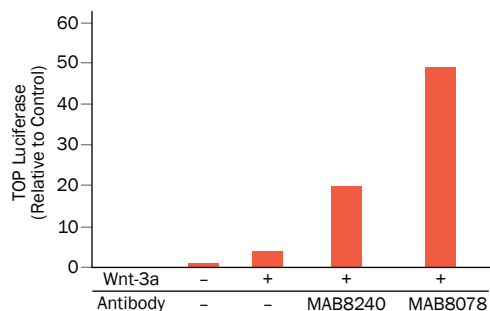
Molecule	Species	Human
R-Spondin 1	Human	4645-RS
	Mouse	8029-GP New!
R-Spondin 2	Human	3266-RS
	Mouse	8029-GP New!
R-Spondin 3	Human	3500-RS
	Mouse	4120-RS
R-Spondin 4	Human	4575-RS
	Mouse	4106-RS

Antibodies for Wnt Research

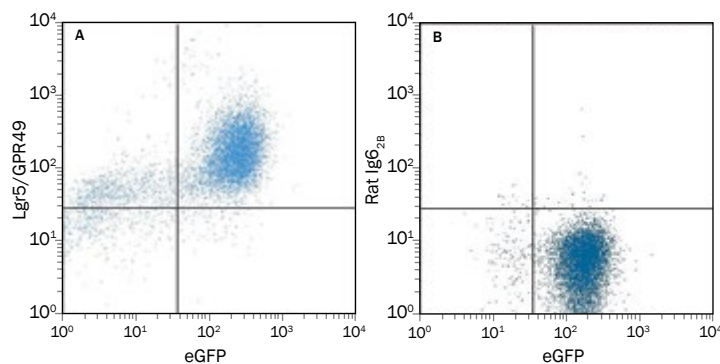
Lgr5/GPR49 Antibodies: Qualified by Application

Molecule	Species	Catalog #	Application	Conjugates
Lgr5/GPR49	Mouse	FAB82401A	FC	APC
		FAB8240P	FC	PE
		MAB82401	FC	-
		MAB8240	FA, FC, ICC	-
	Human	FAB8078	FC	APC, PE
		MAB8078	FA, FC, ICC	-

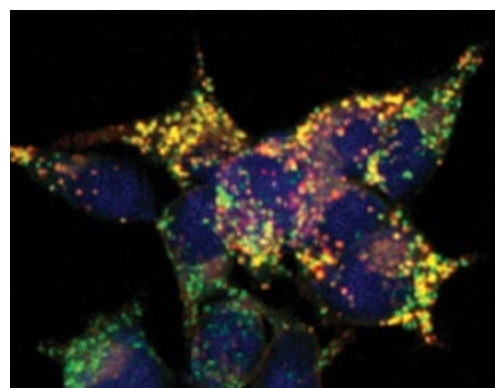
FA Functional Assay FC Flow Cytometry ICC Immunocytochemistry



Human Lgr5/GPR49 Antibody Promotes Canonical Wnt Signaling. Stimulation of Lgr5-expressing HEK293 human embryonic kidney cells with Wnt-3a induced TOPflash Luciferase activity, indicating increased β -Catenin-dependent Wnt signaling. Both Rat Anti-Mouse Lgr5/GPR49 Monoclonal Antibody (Catalog # MAB8240; published as clone RD20) and Mouse Anti-Human Lgr5/GPR49 Monoclonal Antibody (Catalog # MAB8078; published as clone RD42) enhanced Wnt-3a-induced TOPflash Luciferase activity (Data courtesy of Dr. Wim de Lau and Dr. Hans Clevers, Hubrecht Institute, The Netherlands). See also Peng *et al.* (2013) Cell Rep. 3(6):1885.



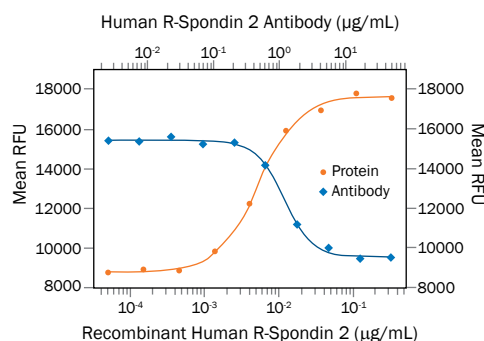
Detection of Lgr5/GPR49 by Flow Cytometry. The HEK293 human embryonic kidney cell line was transfected with eGFP-tagged mouse Lgr5/GPR49 and stained with either (A) Rat Anti-Mouse Lgr5/GPR49 PE-conjugated Monoclonal Antibody (Catalog # FAB8240P) or (B) Rat IgG_{2b} PE-conjugated Isotype Control (Catalog # IC013P). (A) Cells in the upper right quadrant are double-positive for eGFP and Lgr5/GPR49.



Lgr5/GPR49 is Localized to the Cell Surface and Cytoplasm. The HEK293 human embryonic kidney cell line was transfected with GFP-tagged mouse Lgr5/GPR49 (green). Cells were immersion fixed and stained with Rat Anti-Mouse Lgr5/GPR49 Monoclonal Antibody (red; Catalog # MAB8240) followed by NorthernLights™ 557-conjugated Anti-Rat IgG Secondary Antibody (Catalog # NL013). The LGR5/GPR49 antibody and the GFP-tagged Lgr5/GPR49 colocalized (yellow) at the cell surface and within the cytoplasm. The cells were counterstained with DAPI (blue).

R-Spondin Neutralizing Antibodies: Modulate Wnt Signaling

Molecule	Species	Catalog #
R-Spondin 1	Human	AF4645
	Mouse	MAB3474
R-Spondin 2	Human	MAB3266
R-Spondin 3	Human	AF35001
R-Spondin 4	Mouse	AF4106

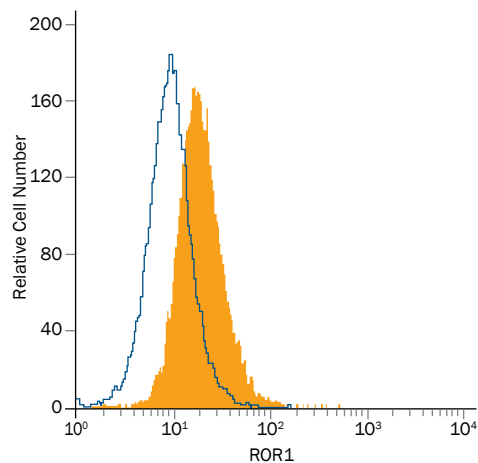


Human R-Spondin 2 Antibody Neutralizes the β -Catenin Response Induced by Recombinant R-Spondin 2. Recombinant Human (rh)R-Spondin 2 (30 ng/mL; Catalog # 3266RS) potentiates Wnt-3a (5 ng/mL; Catalog #1324-WN) induced β -catenin activation in HEK293T human embryonic kidney cells (orange line). Rat Anti-Human R-Spondin 2 Monoclonal Antibody (Catalog # MAB3266) neutralized this response in a dose-dependent manner. The ND₅₀ for this assay is typically 0.4–2 μ g/mL.

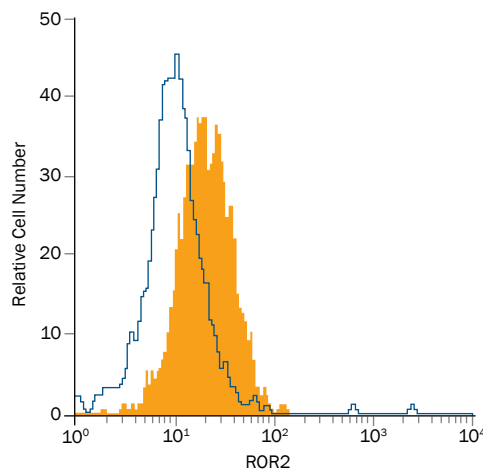
Antibodies for Wnt Research

ROR1 and ROR2: Now Detectable by Flow Cytometry!

Molecule	Species	Catalog #	Conjugate	Additional Conjugates Available
ROR1	Human	FAB2000G	Alexa Fluor® 488	PE, PerCP, APC
ROR2	Human	FAB20641P	PE	APC, Alexa Fluor® 488



Detection of Human ROR1 by Flow Cytometry. MDA MB 231 human breast cancer cell line was stained with Goat Anti-Human ROR1 Alexa Fluor® 488-conjugated Antigen Affinity-purified Polyclonal Antibody (filled histogram; Catalog # FAB2000G) or Alexa Fluor 488-conjugated Goat IgG Isotype Control Antibody (open; Catalog # IC108G).

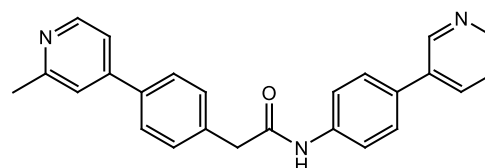


Detection of Human ROR2 by Flow Cytometry. SH SY5Y human neuroblastoma cell line was stained with Mouse Anti-Human ROR2 PE-conjugated Monoclonal Antibody (filled histogram; Catalog # FAB20641P) or PE-conjugated Mouse IgG2A Isotype Control Antibody (open histogram; Catalog # IC003P).

Tocris Small Molecules for Wnt Signaling

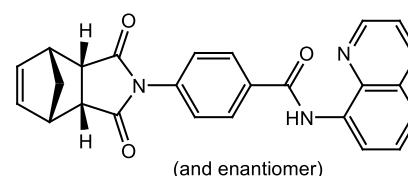
Selectively Target Wnt Signaling Pathways

Product name	Catalog #	Product Description
BIO	3194	Potent and selective GSK-3 inhibitor
CHIR 99021	4423	Highly selective GSK-3 inhibitor
endo-IWR 1	3532	Wnt/ β -catenin signaling pathway inhibitor
EHT 1864	3872	Potent inhibitor of Rac family GTPases
Foxy 5	5461	Wnt-5a peptide mimetic
iCRT 14	4299	Inhibits β -catenin-responsive transcription
IWP 2	3533	PORCN inhibitor; inhibits Wnt processing and secretion
IWP 12	5279	Potent PORCN inhibitor; active <i>in vivo</i>
JW 55	4514	Tankyrase inhibitor; inhibits canonical Wnt signaling
JW 74	5653	Wnt pathway inhibitor; induces degradation of active β -catenin
LH 846	4896	Selective CK1 δ inhibitor
NSC 23766	2161	Selective inhibitor of Rac1-GEF interaction
PF 670462	3316	Potent and selective CK1 ϵ and CK1 δ inhibitor
PP 2	1407	Potent, selective Src family kinase inhibitor
SB 216763	1616	Potent and selective GSK-3 inhibitor; induces β -catenin-dependent gene transcription
U 73122	1268	Phospholipase C inhibitor
Wnt-C59	5148	Potent PORCN inhibitor
XAV 939	3748	Tankyrase inhibitor; inhibits Wnt signaling



Wnt-C59 - Catalog # 5148

Wnt-C59 is a highly potent Porcupine (PORCN) inhibitor (IC_{50} = 74 pM). The compound downregulates Wnt/ β -catenin target genes and blocks progression of mammary tumors in MMTV-WNT1 transgenic mice. Wnt-C59 also induces cardiomyocyte differentiation from human iPSCs following culture with CHIR 99021 (Catalog # 4423). The compound is cell permeable and orally bioavailable.



endo-IWR 1 - Catalog #3532

endo-IWR 1 is an inhibitor of the Wnt/ β -catenin signaling pathway. The compound increases Axin-2 protein levels and promotes β -catenin phosphorylation by stabilizing Axin-scaffolded destruction complexes. Its negative control, exo-IWR (Catalog # 3947), is also available.

Full Wnt Family Product Listing

Wnt Ligands			
Molecule	Proteins and Enzymes	Antibodies	ELISAs
Wnt-1		M	
Wnt-2		H	
Wnt-2b	M New!	H M	
Wnt-3a GMP	H M	H M	
Wnt-4	H M	H M	
Wnt-5a	H M	H M R	
Wnt-5b	H M	M	
Wnt-6		H	
Wnt-7a	H	H	
Wnt-7a/b		H	
Wnt-7b		H	
Wnt-8a	M New!	M	
Wnt-8b		H M	
Wnt-9a	M	H	
Wnt-9b	M	H M	
Wnt-10a		H M	
Wnt-10b	H M	H M	
Wnt-11	H	H M	
Wnt-16b	H		
Norrin	H M	H M	

Wnt Inhibitors			
Molecule	Proteins and Enzymes	Antibodies	ELISAs
Dkk-1	H M R	H M R	H M
Dkk-2	H M	M	
Dkk-3	H	H M R	H
Dkk-4	H M	H M	H
Draxin	H M	H M R	
IGFBP-4	H M	H	H
sFRP-1	H	H	
sFRP-2	H M	H M	
sFRP-3	H M	H M	H
sFRP-4	H	H	
sFRP-5	H M		H
Soggy-1/DkkL1	H M	H M	M
SOST/Sclerostin	H M	H M	H M R
USAG1	H	H	
WIF-1	H M	H M	H

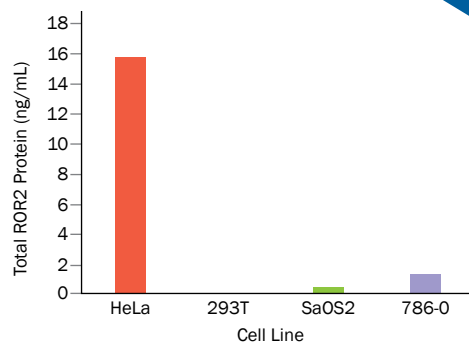
Wnt Signaling Receptors			
Molecule	Proteins and Enzymes	Antibodies	ELISAs
CELSR2		H M	
CELSR3		H	
Cripto	H M	H M	H
Frizzled-1	H M	H M	
Frizzled-2	H M	H M	
Frizzled-3		H M	
Frizzled-4	H M	H M	
Frizzled-5	H	H	
Frizzled-6		H M	
Frizzled-7	H M	H M	
Frizzled-8	H M	M	
Frizzled-9	M	M	
Frizzled-10	H		
LRP-1		H	
LRP-1 Cluster II	H	H	
LRP-1 Cluster III	H	H	
LRP-1 Cluster IV	H		
LRP-1B		H	
LRP-4	H New!	H R	
LRP-5	M New!	H	
LRP-6	H New! M New!	H M	
LRP-11		H	
LRPAP	H M	H M	
MuSK		H R	
PTK7/CCK4		H M R	
ROR1		H	H
ROR2	H New!	H	H
Ryk	H M	H	
ST7/LRP12	H M	H	
VANGL1		H	
VANGL2		H M R	

Wnt Modulators			
Molecule	Proteins and Enzymes	Antibodies	ELISAs
Axin-2		H	
β-TrCP1/BTRC		H	
Biglycan	H M	H	
CYLD	H		
DAB2		H	
DACT3/Dapper 3		H M	
DISC1		H	
ETV2/ER71		M	
FRAT2		H	
Glypican 1	H M	H	
Glypican 2	H M	H M	
Glypican 3	H M	H	H
Glypican 5	H M	H M	
Glypican 6	H	H M	
Kremen-1	M	H M	M
Kremen-2	H M R	H M	
LEF1		H	
Lgr4/GPR48	H New! M New!	H	
Lgr5/GPR49	H New!	H M	
Lgr6	H New! M New!		
LIMD1		H	
LRP-5	M	H	
MESDC2	M	H M	
MFRP	H	H M	
Myocilin		H	
NeuroD1		H M	
Norrin	H M	H M	
Nucleoredoxin		H	
R-Spondin 1	H M	H M	H
R-Spondin 2	H M	H	
R-Spondin 3	H M	H M	H
R-Spondin 4	H M	H M	H
RNF43	H New!		
Shisa-4		H M	
Syndecan-1/CD138	H M	H M	H
Syndecan-2	H M	H M	
Syndecan-3	H M	H M	H
Syndecan-4	H M	H	H
Tiki1/TRABD2A		H	
TROY/TNFRSF19	H New! M New!		
WTX		H	
ZNRF3	H New! M New!		
ZRANB1/Trabid	H		

H Human M Mouse R Rat **GMP** Available as GMP-grade

Select ELISA Assays for Wnt Research

Quantikine®	Species	Catalog #
Dkk-1	Human	DKK100
	Mouse	MKK100
Glypican 3	Human	DGLY30
SOST/Sclerostin	Human	DSST00
	Mouse, Rat	MSST00
DuoSet®	Species	Catalog #
Dkk-1	Human	DY1906
	Mouse	DY1765
IGFBP-4	Human	DY804
WIF-1	Human	DY134
DuoSet® Intracellular	Species	Catalog #
ROR1	Human	DYC2000-2
ROR2	Human	DYC2064-2



Endogenous ROR2 Expression Detected in Established Cell Lines. ROR2 levels were quantified in the HeLa human cervical epithelial carcinoma cell line (HeLa), 293T human embryonic kidney cell line (293T), SaOS2 primary osteosarcoma cell line (SaOS2), and 786-0 human renal cell adenocarcinoma cell line (786-0) using the Total ROR2 DuoSet IC ELISA (Catalog # DYC2064-2). Adapted from Rasmussen N.R., et al. (2014) PLoS ONE 9(12): e116101.

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