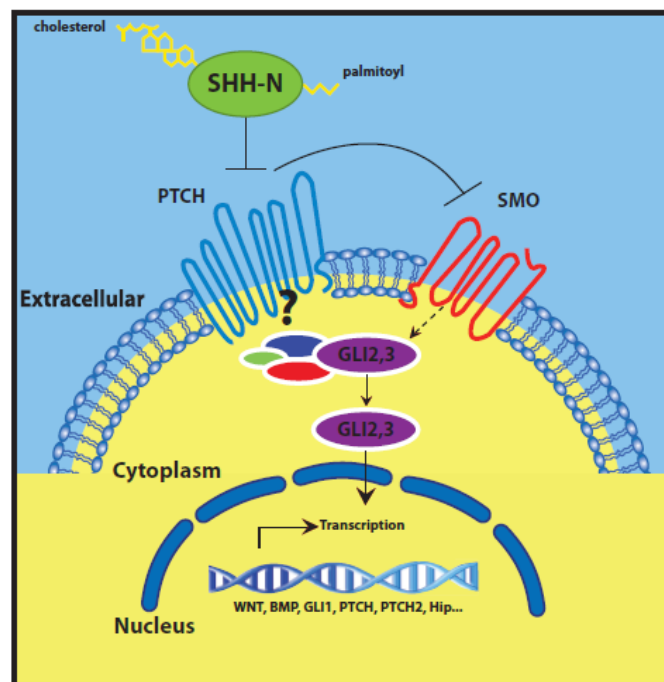


# Sonic Hedgehog Pathway

Mammals have three Hedgehog homologues, of which Sonic hedgehog is the best studied: Desert hedgehog (Dhh), Indian hedgehog (Ihh) and Sonic hedgehog (Shh). The original hedgehog gene was identified in *Drosophila* and is named since the embryo phenotype resembles a hedgehog (covered with pointy denticles). Two vertebrate genes are named after species of hedgehogs (Dhh, Ihh) and shh after a video game character. Shh is involved in a wide variety of embryonic events and can act as both a short-range, contact-dependent factor and as a long-range, diffusible morphogen. Shh genes are highly conserved and have been identified within a variety of species, including human, mouse, frog, fish, and chicken. Mouse and human Shh proteins are 92% identical. In the human embryo, Shh is expressed in the notochord, the floor plate of the neural tube, the gut, and in the developing limbs.

Shh is translated as a ~ 45 kDa precursor and undergoes autocatalytic processing to produce a ~ 20 kDa N-terminal signaling domain (referred to as Shh-N) and a ~ 25 kDa C-terminal domain with no known signaling role. During the cleavage, a cholesterol molecule is added to the carboxyl end of the N-terminal domain, which is involved in trafficking, secretion and receptor interaction of the ligand. The hydrophobicity of the signal peptide due to the cholesterol moiety is further increased by lipid modification; (a palmitoylation of the highly conserved N-terminal cysteine residue (Cys-24) which is dependent on the cholesterol addition). Secretion and consequent paracrine hedgehog signaling require the participation of Dispatched protein. When Shh reaches its target cell, it binds to the Patched-1 (PTCH1) receptor, a 12- pass transmembrane protein. In the absence of ligand, PTCH1 inhibits Smoothed (SMO), a downstream protein in the pathway. PTCH1 has a sterol sensing domain (SSD), which has been shown to be essential for suppression of SMO activity. The binding of Shh relieves SMO inhibition, leading to activation of the Gli transcription factors (activators Gli1 and Gli2 and the repressor Gli3). The sequence of molecular events that connect SMO to Glis is poorly understood. The accumulation of activated Gli in the nucleus controls the transcription of hedgehog target genes. Mammals have another hedgehog receptor PTCH2 whose sequence identity with PTCH1 is 54%. All three mammalian hedgehogs bind both receptors with similar affinity, so PTCH1 and PTCH2 cannot discriminate between the ligands. They do, however, differ in their expression patterns. PTCH2 is expressed at much higher levels in the testis and mediates desert hedgehog signaling there. In the absence of ligand binding PTCH2 has a decreased ability to inhibit the activity of SMO.



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## Antibodies

Product Name	Cat. No.	Size
GSK-3 $\alpha$ Antibody	3493	100 $\mu$ g
GSK-3 $\beta$ Antibody	3494	30 $\mu$ g, 100 $\mu$ g
Phospho-GSK-3 $\alpha$ Antibody	3516	100 $\mu$ g
Phospho-GSK-3 $\beta$ Antibody	3495	100 $\mu$ g
PKA Antibody	3115	30 $\mu$ g, 100 $\mu$ g

## Agonists

Product Name	Cat. No.	Size	CAS Number
Purmorphamine	1672	5 mg	483367-10-8
Smo Agonist, SAG	1939	500 $\mu$ g , 1 mg	912545-86-9
Smo agonist, SAG dihydrochloride	2801	1 mg, 5 mg	364590-63-6

## Antagonists

Product Name	Cat. No.	Size	CAS Number
BMS-833923	9547	5 mg, 25 mg	1059734-66-5
BODIPY-Cyclopamine	2160	50 $\mu$ g, 250 $\mu$ g	334658-24-1
CUR-61414	2743	5 mg, 25 mg	334998-36-6
Cyclopamine	1578	5 mg	4449-51-8
Cyclopamine tartrate	2518	1 mg, 5 mg	1178510-81-0
Cyclopamine-KAAD	1910	50 $\mu$ g	306387-90-6
GANT58	1812	5 mg, 25 mg	64048-12-0
GANT61	1892	5 mg	500579-04-4
GDC-0449	1890	5 mg, 25 mg	879085-55-9
DiscoveryPak™ Hedgehog (Hh) Signaling Pathway Inhibitors Set	K868	6 inhibitors	Multiple Inhibitors
Hh Signaling Pathway Antagonist	1659	1 mg	330796-24-2
HPI-1	2410	5 mg, 25 mg	599150-20-6
Itraconazole	1987	50 mg, 100 mg, 500 mg, 1 g	84625-61-6
Jervine	2357	1 mg, 5 mg	469-59-0
JK 184	1726	1 mg	315703-52-7
LDE-225	2892	5 mg, 25 mg	956697-53-3
LDE-225 diphosphate	2893	5 mg, 25 mg	1218778-77-8
LY-2940680	9604	5 mg, 25 mg	1258861-20-9
MK-4101	B1255	5 mg, 25 mg	935273-79-3
Robotnikinin	1923	1 mg	1132653-79-2
SANT-1	1978	1 mg, 5 mg	304909-07-7
SANT-2	1976	1 mg, 5 mg	329196-48-7
Tomatidine hydrochloride	1893	25 mg	6192-62-7

## GSK3 Inhibitors

Product Name	Cat. No.	Size	CAS Number
1-Azakenpauillone	1944	1 mg, 5 mg	676596-65-9
Alsterpauillone	1897	1 mg, 5 mg	237430-03-4
BIO	1673	1 mg	667463-62-9
Bisindolylmaleimide I	1945	1 mg, 5 mg	133052-90-1
Bisindolylmaleimide I hydrochloride	1947	1 mg, 5 mg	176504-36-2
CHIR 99021	1677	5 mg, 25 mg	252917-06-9
EZSolution™ CHIR99021	1748	5 mg	252917-06-9
EZSolution™ CHIR99021, Sterile- Filtered	1991	1 ml	252917-06-9
GSK-3 Inhibitor, AR-A014418	1953	2 mg, 5 mg	487021-52-3
GSK-3β Inhibitor, TWS119	1655	2 mg	601514-19-6
Kenpauillone	1904	1 mg	142273-20-9
Ro 31-8220 methanesulfonate	1946	1 mg, 5 mg	138489-18-6
SB 216763	1769	1 mg, 5 mg	280744-09-4

## Proteins

Product Name	Cat. No.	Size
Active Sonic Hedgehog (SHH), human recombinant	4010	25 µg, 100 µg, 1 mg
Active Sonic Hedgehog (SHH), murine recombinant	4020	25 µg, 100 µg, 1 mg
CK2α1, Active	7738	5 µg
GSK-3α-GST Fusion Protein	7003	100 µg
GSK-3β, human recombinant	7004	10 µg, 100 µg, 1 mg
PKA cy, Active	7728	5 µg
PKAα, Active	7743	5 µg
PKAβ, Active	7744	5 µg
Human CellExp™ SHH, human recombinant	7223	10 µg

## Other Related Inhibitors

Product Name	Cat. No.	Size	CAS Number
D4476	1770	1 mg, 5 mg	301836-43-1
Fasudil, Monohydrochloride	1787	10 mg, 50 mg	105628-07-7
H-89 Dihydrochloride	1768	1 mg, 5 mg	127243-85-0

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