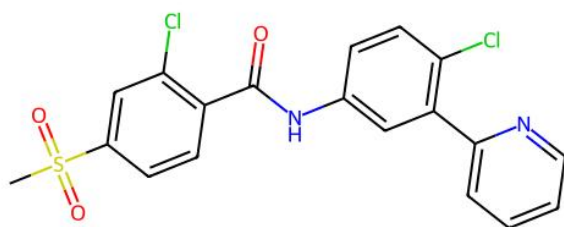


Hedgehog Signaling

The Hedgehog (Hh) signaling pathway is one of the core pathways regulating embryonic development in animals. Initially discovered in *Drosophila*, it plays a decisive role in embryogenesis and metamorphosis. In mammals, this pathway involves three homologous ligands: Sonic Hedgehog (SHH), Desert Hedgehog (DHH), and Indian Hedgehog (IHH), with SHH being the most extensively studied in terms of its functional mechanisms.

When SHH binds to the transmembrane receptor Patched-1 (PTCH1), it relieves the inhibition on the adjacent protein Smoothened (Smo), thereby activating downstream signaling. Activated Smo facilitates the translocation of GLI family transcription factors (including activators Gli1/Gli2 and repressor Gli3) into the nucleus, where they regulate the expression of target genes involved in processes such as embryonic development, limb formation, maintenance of adult stem cells, and hair follicle growth.

Abnormalities in this pathway are linked to various diseases. For example, disruption of Hh signaling during embryogenesis can lead to holoprosencephaly, with severe cases resulting in cyclopia. On the other hand, excessive activation of the pathway may drive the transformation of adult stem cells into cancer stem cells, promoting the development of various cancers. Additionally, Hh signaling may also play a role in tumor angiogenesis and metastasis. Currently, specific inhibitors targeting this pathway are under development and hold promise as novel therapeutic strategies for a range of malignant tumors.



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Figure 1 Chemical structure of Vismodegib (GDC-0449)

Aladdin Smoothened modulators:

Berberine Hydrochloride Hydrate [B139120](#)、[B408884](#)

Cyclopamine [C276580](#)、[C125994](#)

Vismodegib (GDC-0449) [V127477](#)、[V408303](#)

Itraconazole [I426206](#)、[I129771](#)

Jervine [J664401](#)、[J424100](#)、[J135916](#)

NVP-LDE225 Diphosphate [S649283](#)、[S655786](#)

Purmorphamine [P424198](#)、[P1371723](#)、[P126030](#)

Aladdin Hedgehog signaling inhibitors:

Calcitriol [C120126](#)、[C409109](#)

Curcumin [C400271](#)、[C140600](#)、[C110685](#)、[C395975](#)、[C477437](#)、[C400222](#)、[C463317](#)、[C408195](#)

Forskolin [F127328](#)、[C409070](#)

Genistein [G106673](#)、[G106672](#)、[G408928](#)

Imiquimod [I427215](#)、[I129798](#)

trans-Retinoic acid [R1371648](#)、[R106321](#)、[R106320](#)、[T409019](#)

Veratramine [V425030](#)、[V274917](#)

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