Hedgehog Signaling

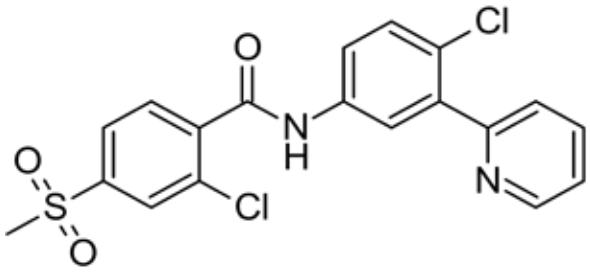
The hedgehog (Hh) signaling pathway is a key regulator of embryonic development in all animals. Hh signaling was first studied in *Drosophila*, where it is necessary in embryogenesis and metamorphosis. Mammals have three Hh homolog proteins: sonic hedgehog (SHH), desert hedgehog (DHH) and Indian hedgehog (IHH).

Out of these three homologs, SHH is the best studied. SHH binds Patched-1, a transmembrane receptor, allowing activation of Smoothened (Smo), a nearby protein. Without SHH, Patched-1 inhibits Smo activity. Activation of Smo results in activation of GLI transcription factors Gli1 and Gli2 (activators) and Gli3 (a repressor). Activated GLI accumulates in the nucleus where it regulates transcription of genes involved in embryogenesis, limb development, adult stem cell proliferation, and hair follicle growth[1].

Alterations in Hh signaling are linked to a variety of diseases. Inhibition of Hh signaling during fetal development causes holoprosencephaly, potentially resulting in cyclopia[2]. Aberrant activation of this pathway is implicated in the development of various cancers likely through transformation of adult stem cells into cancer stem cells[3]. Hh signaling may also play a role in angiogenesis and metastasis[4]. New inhibitors of Hh signaling pathway components are in development as chemotherapeutics to treat a wide range of malignancies.

Hedgehog signaling inhibitors:
C0145 Calcitriol
C8069 Curcumin
C8070 Curcumin (high purity)
F5668 Forskolin
G1652 Genistein
I5034 Imiquimod
R1780 trans-Retinoic acid
V1868 Veratramine

Smoothened modulators:
B1870 Berberine Hydrochloride Hydrate
C9710 Cyclopamine
G1408 GDC-0449 (Vismodegib)
I7870 Itraconazole
J1870 Jervine
N8663 NVP-LDE225 Diphosphate
P8370 Purmorphamine



G1408 GDC-0449 (Vismodegib)

References:
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3. Shimizu T, Nakagawa K. Nihon Rinsho. 2015 Aug;73(8):1342-8.
4. Velcheti V. Med Hypotheses. 2007;69(4):948-9.