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## GPCR-Like signaling mediated by smoothened contributes to acquired chemoresistance through activating Gli

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**Background:** Smoothened (Smo), which possesses a structural similarity with classic G-protein coupled receptors (GPCR), is the most important molecular target in Hedgehog (Hh) signaling system for developing anticancer drugs; however, whether Smo may transmit GPCR-like signaling to activate the canonical transcriptional factor Gli of Hh signaling system and consequently to be involved in the Gli-dependent biological events remains controversial.

**Results:** In this study, using the acquired chemoresistant cancer cell lines and their respective parental cells, we found that Smo may activate Gli through Gai, Gby-JNK signaling axis, thereby promoting the Gli-dependent acquired chemoresistance. These observations were further complementarily strengthened by data obtained from chemosensitive cancer cells with artificially elevated Hh pathway activity.

**Conclusions:** Hence, our data demonstrate that GPCR-like signaling mediated by Smo contributes to the acquired chemoresistance through activating the canonical Hh transcriptional factor Gli; therefore improving our knowledge of the nature of the signal transduction of Smo and the molecular mechanisms responsible for the acquired chemoresistance maintained by Hh pathway. Moreover, our data that JNK after activated by Smo-Gby signaling axis may stimulate the Gli activity and consequently promotes acquired chemoresistance expose a promising and potential target for developing anti-cancer drugs aimed at Hh pathway and for combating the acquired resistance raised by using of anti-cancer drugs targeting Smo.

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