Regulation of the Hedgehog signaling pathway in medulloblastoma

Tamara Scheidt
Oliver Alka
Humberto Gonczarowska-Jorge
Wolfgang Gruber
Florian Rathje
Margherita Dell'Aica
Marc Rurik
Oliver Kohlbacher
René P. Zahedi
Fritz Aberger
Christian G. Huber

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Abstract

Medulloblastoma is the most common brain tumor of childhood. Precisely targeting the signaling pathways involved in medulloblastoma is needed to increase treatment efficacy. One promising treatment, inhibiting the protein Smoothed (SMO), downregulates the Hedgehog signaling pathway, but treatment resistance and severe side effects such as muscle spasms remain a concern for SMO inhibitors. In a new study, researchers sought to better understand Hedgehog signaling pathway regulation in medulloblastoma. Using quantitative phosphoproteomics to evaluate human medulloblastoma cells, they found that Hedgehog signaling via SMO affected ciliary assembly, trafficking, and signal transduction. Several signaling pathways were differentially regulated by SMO inhibitors, including ERK/MAPK, Protein Kinase A, and mTOR. These results help to elucidate the downstream signaling pathways triggered by SMO inhibitor treatment, providing important insight to help prevent adverse effects and therapeutic resistance.