7-Dehydrocholesterol reductase

7-Dehydrocholesterol reductase, often abbreviated as DHCR7, is an enzyme involved in the biosynthesis of cholesterol. This enzyme plays a crucial role in the conversion of 7-dehydrocholesterol to cholesterol, a key step in the synthesis of this essential lipid.

Here's a brief overview of the process:

Substrate: 7-Dehydrocholesterol is a compound that is produced in the skin in response to ultraviolet (UV) light exposure.

Enzyme Action: DHCR7, or 7-dehydrocholesterol reductase, facilitates the reduction of 7-dehydrocholesterol to cholesterol.

Cholesterol Synthesis: Cholesterol is an essential component of cell membranes and is a precursor for the synthesis of various hormones, bile acids, and vitamin D. It is crucial for the normal functioning of cells and the body.

Genetic Implications: Mutations in the DHCR7 gene can lead to a rare genetic disorder known as Smith-Lemli-Opitz syndrome (SLOS). Individuals with SLOS have impaired DHCR7 activity, resulting in decreased cholesterol production and a range of developmental and physical abnormalities.

Understanding the role of DHCR7 is not only important in the context of cholesterol metabolism but also in the study of genetic disorders associated with its dysfunction. Researchers and healthcare professionals investigate the enzyme and its related pathways to gain insights into both normal physiology and pathological conditions.

RNA sequencing data analysis and sterolomics analysis revealed that vitamin D3 inhibits cholesterol synthesis and cholesterol homeostasis by inhibiting the expression level of 7-dehydrocholesterol reductase, which leads to the accumulation of 7-dehydrocholesterol and other sterol intermediates. In conclusion, our results suggest that vitamin D3, rather than calcitriol, inhibits the growth of patient-derived glioma cell lines via inhibition of the cholesterol homeostasis pathway [1)].

Dong et al. found that cholesterol levels in GBM tissues are abnormally high, and glioma-supportive macrophages (GSMs), an essential “cholesterol factory”, demonstrated aberrantly hyperactive cholesterol metabolism and efflux, providing cholesterol to fuel GBM growth and induce CD8+ T cells exhaustion. Subsequent bioinformatics analysis confirmed that high 7-Dehydrocholesterol reductase (DHCR7) level in GBM tissues was concomitant with increased cholesterol biosynthesis, suppressed tumoricidal immune response, and poor patient survival and DHCR7 expression level was significantly elevated in GSMs. Therefore, they reported an intracavitary sprayable nanoregulator-encased hydrogel system to modulate the cholesterol metabolism of GSMs. The degradable nanoregulator-mediated ablation of DHCR7 in GSMs effectively suppressed cholesterol supply and activated T-cell immunity. Moreover, the combination of Toll-like receptor 7/8 (TLR7/8) agonists significantly promoted GSM polarization to antitumor phenotypes and ameliorated the immunosuppressive TME. Treatment with the hybrid system exhibited superior antitumor effects in the orthotopic GBM tumor model and postsurgical recurrence model. Altogether, the findings unravel the role of GSMs DHCR7/cholesterol

signaling in the regulation of immunosuppressive TME, presenting a potential glioblastoma treatment strategy that warrants further clinical trials [2].

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Yuan R, Zhang W, You YP, Cui G, Gao Z, Wang X, Chen J. Vitamin D3 suppresses the cholesterol homeostasis pathway in patient-derived glioma cell lines. FEBS Open Bio. 2023 Sep;13(9):1789-1806. doi: 10.1002/2211-5463.13679. Epub 2023 Jul 31. PMID: 37489660; PMCID: PMC10476568.
2)
Dong Y, Zhang J, Wang Y, Zhang Y, Rappaport D, Yang Z, Han M, Liu Y, Fu Z, Zhao X, Tang C, Shi C, Zhang D, Li D, Ni S, Li A, Cui J, Li T, Sun P, Benny O, Zhang C, Zhao K, Chen C, Jiang X. Intracavitary Spraying of Nanoregulator-Encased Hydrogel Modulates Cholesterol Metabolism of Glioma-Supportive Macrophage for Postoperative Glioblastoma Immunotherapy. Adv Mater. 2023 Dec 21:e2311109. doi: 10.1002/adma.202311109. Epub ahead of print. PMID: 38127403.