Silibinin suppresses the maintenance of colorectal cancer stem-like cells by inhibiting PP2A/AKT/mTOR pathways.


Source

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Abstract

Silibinin, an effective chemo-preventive agent in various cancer types, suppresses cancer cell growth, but its effects on cancer stem-like cells (CSLCs) remain unclear. This study aimed to examine whether silibinin inhibited the development of CSLCs and disclose the underlying signaling. The colorectal cancer spheroid culture system was used for enriching CSLCs. The effects of silibinin on CSLCs were evaluated by counting sphere numbers, and calculating the percentage of CD133+ cells by flow cytometry and immunofluorescence both in the absence and presence of different concentrations of silibinin. The results showed the sphere number of CCS was 36 ± 9.6 after 15 days of CSLC enrichment in spheroid culture, and the percentage of CD133+ cells increased to 18 ± 6.4% compared to 3 ± 0.8% before enrichment. Treatment with silibinin reduced the sphere formation to 5 ± 3.3 and decreased the CD133+ percentage to 8 ± 2.3%. Interestingly, treatment of silibinin suppressed the activation of the AKT Ser473/mTOR pathway in spheroid culture through suppressing the activity of protein phosphatase 2Ac subunit (PP2Ac). In a xenograft tumor model, treatment with silibinin also inhibited tumor formation rate and tumor growth. Silibinin, which inhibits colon CSLCs self-renewal and sphere formation by suppressing the PP2Ac/AKT Ser473/mTOR pathway, may be a compound for developing new strategies in modulating CSLCs in cancer therapy.

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