

Elucidation of mechanism of growth inhibition of human colorectal stem cell by dietary polyphenol antioxidant.

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【Background】

Polyphenol compounds in foods contain antioxidants and are known to have effects of liver protection, hypoglycemic, and cholesterol-lowering. Colorectal cancer is one of the most types of cancers and the mortality rate is the second-highest in Japan. Since cancer stem cells are related to drug resistance and recurrence of colorectal cancer, a new remedy that targets cancer stem cells is needed. In the previous study, we established a novel culture method of the human colorectal air-liquid interface (ALI) organoids, which could recapitulate three-dimensional cancer microenvironment including patient-derived cancer stem cells. In this study, we investigated whether polyphenol antioxidants affect the survival rate of human colorectal ALI organoids and analyzed the inhibitory mechanisms.

【Methods and results】

Organoids were treated with polyphenol antioxidants at the dose of 3-100 μ g/ml for 72 hours. The survival rate of organoids was measured by alamarblue assay. Polyphenol antioxidants suppressed survival rate of organoids in a concentration-dependent manner. The expression of marker genes for cancer stem cells, *LGR5* and *PROM1* were drastically decreased by polyphenol antioxidants. Expression of a G₁/S transition-related gene, *CCND1* was also decreased.

【Conclusion】

These results suggest that polyphenol antioxidants inhibit proliferation of human colorectal cancer stem cells via suppression of *LGR5*, *PROM1*, and *CCND1*, which might lead to the development of dietary supplements targeting colorectal cancer stem cells.