News Release

Title: 9-oxo-ODAs suppresses the proliferation of human cervical cancer cells through the inhibition of CDKs and HPV oncoproteins

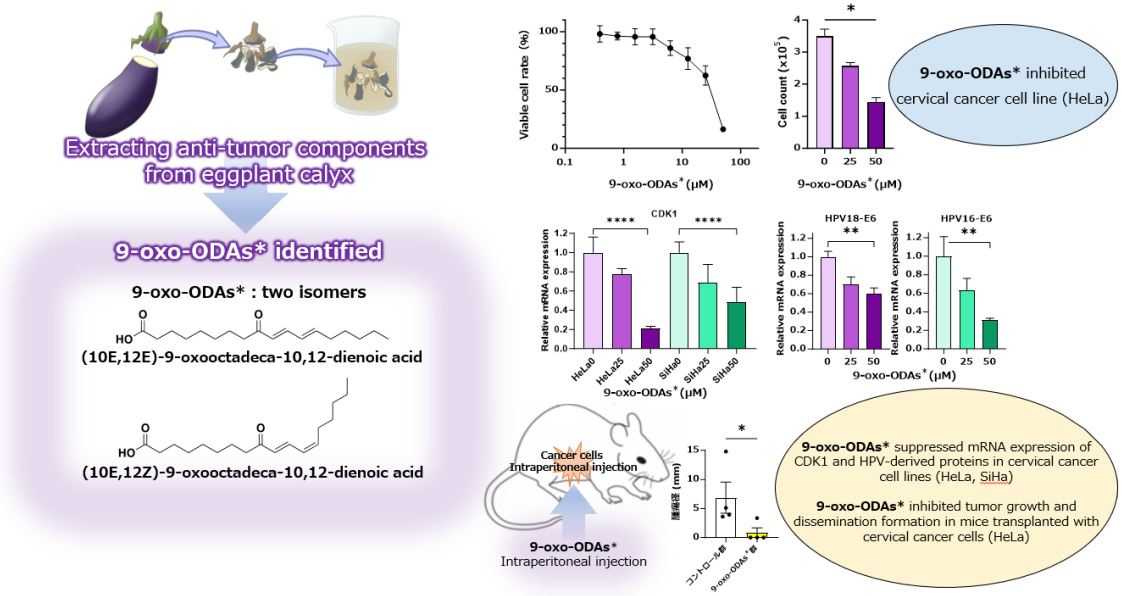
Key Points

•Natural compound 9-oxo-ODAs exhibits antitumor effects on cervical cancer cells

• 9-oxo-ODAs may lead to potential drug candidates for cervical cancer and cervical dysplasia, HPV-related diseases

Summary

The calyx of eggplants has been used as a folk remedy for common warts caused by human papillomavirus (HPV) in Japan. We previously reported that an ethanol extract of dried eggplant calyx reduced ovarian cancer and condyloma and identified 9-oxooctadeca-10,12-dienoic acid (9-oxo-ODAs) as the active ingredient in the extract. In this study, we investigated the antitumor effects of 9-oxo-ODAs on cervical cancer, an HPV-related disease similar to verruca vulgaris and condyloma acuminatum, using human cervical cancer cell lines and mouse models. The results showed that 9-oxo-ODAs suppress the expression of CDK1, which is involved in cell division, and E6 and E7, HPV-derived proteins involved in cervical carcinogenesis, and induce cell cycle arrest and apoptosis in HPV-positive human cervical cancer cells. The anti-tumor effect of 9-oxo-ODAs was also confirmed in a mouse model. This study indicates that 9-oxo-ODAs may be a potential therapeutic candidate for the treatment of HPV-positive diseases.



Research Background

Human papillomavirus (HPV) is the causative virus of cervical cancer, and cervical cancer is one of the leading causes of cancer-related deaths among women worldwide. It has been widely reported that HPV-derived E6 and E7 proteins function in the mechanism of carcinogenesis and progression of cervical cancer. However, therapies targeting these HPV-derived proteins and their oncogenic mechanisms have not yet been clinically applied. We had previously reported that an ethanol extract of eggplant calyx inhibited condyloma acuminatum, an HPV-related disease, and identified 9-oxo-ODAs as the active ingredient in this ethanol extract. In this study, the antitumor effect of 9-oxo-ODAs on human cervical cancer, the same HPV-related disease, was investigated.

Research Results

Administration of 9-oxo-ODAs was found to inhibit cell proliferation in a concentration-dependent manner and induce apoptosis in human cervical cancer cells (HeLa and SiHa). RNAsequence and mass spectrometry analysis of cervical cancer cell lines after treatment with 9-oxo-ODAs revealed that the p53 pathway, which is involved in cell cycle pathways and apoptosis, was altered and cyclin-dependent kinase 1 (CDK1) expression was decreased. Furthermore, 9-oxo-ODAs were found to reduce HPV-derived RNA and protein expression in cervical cancer cell lines. Mice model experiments also confirmed that administration of 9-oxo-ODAs inhibited metastasis formation and proliferation of cervical cancer cells implanted in mice. Based on these results, 9-oxo-ODAs are suggested to induce cell cycle arrest and apoptosis of HPV-positive human cervical cancer cells by suppressing the expression of CDK1 and HPV oncoprotein, thereby exerting an antitumor effect.

Research Summary and Future Perspective

9-oxo-ODAs are potential anti-tumor compounds, and we intend to investigate their mechanism in more detail with the aim of applying them to clinical treatment.

Publication

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