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Oncolytic virotherapy for clear cell ovarian carcinoma: A potential treatment strategy

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Ovarian cancer is one of the three leading gynecological malignancies, hardly to be diagnosed at early stages. Mammalian lignans Enterodiol (END) and Enterolactone (ENL) can reduce the risk of various cancers. We have previously reported the production of END and ENL from flaxseeds by human intestinal microbiota through biotransformation (seeds of *Linum usitatissimum* L.) and isolated bacterial strains that produced mammalian lignans. Both END and ENL reduce the risk of various cancers, but their anti-cancer mechanisms in ovarian cancer remain unclear. We used *in vitro* assays on the ES-2 cell line to evaluate the inhibiting effects of END and ENL on ovarian cancer cell proliferation, invasion and migration ability and *in vivo* xenograft experiments on nude mice to validate the anticancer effects of END and ENL. We also sequenced the transcriptomes of high-dose ENL to investigate the possible anticancer mechanisms of ENL. The *in vitro* assays demonstrated that high-doses of END and ENL could obviously inhibit ovarian malignant properties, including cancerous proliferation, invasion and metastasis. Compared to END, ENL behaved in a better time-dose dependent manner on the cancer cells. The *in vivo* experiments showed that END (1 mg/kg), ENL (1 mg/kg) and ENL (0.1 mg/kg) suppressed the tumor markedly with statistically significant differences between the experimental and control groups in tumor weight and volume. Compared to END, which have serious side effects to the animals at high concentration such as 1 mg/kg, ENL had higher anticancer activities and fewer side effects in the animals than END at the same concentrations. GO and KEGG pathway enrichment analysis showed that ENL mainly inhibited the invasion and metastasis of the cancer cells. We further confirmed that the expression levels and activities of MMP-2 and MMP-9 were inhibited by ENL treatments in a dose-dependent manner. ENL had better inhibition effects than END on ovarian cancer. The inhibition was achieved by suppressing the cancer invasion and metastasis pathways and down-regulating the expression of MMP-2 and MMP-9. These results demonstrated possibilities of clinical application of the phytoestrogens in the treatment of ovarian cancer.

Biography

Huidi Liu has received her PhD degree from Harbin Medical University, Harbin, China, with a major in Microbial and Biochemical Pharmacy. She later joined the Genomic Research Center at HMU and worked on genomic research of ovarian cancer and natural anti-cancer drugs. She has an overseas experience at University of Calgary as a Visiting Scholar supported by China Scholar Council (CSC, 2016-2017). She has published more than 10 papers in core international journals on ovarian cancer. Further, he has been appointed as the Project Manager for the Centre for Infection and Genomics, a joint project between HMU and the Faculty of Medicine at the University of Calgary.

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