News Release

Title

Plasma-activated medium promotes autophagic cell death along with alteration of the mTOR pathway.

Key Points

・Inhibition of endometrial cancer cell growth and cell death were induced by using a plasma activation solution prepared by irradiating the culture solution with atmospheric pressure low-temperature plasma.

・The underlying mechanism was suggested to be involved in the induction of autophagy cell death by the plasma activation solution.

・Plasma activated solution can be an effective treatment option for peritoneal dissemination.

Summary

The biological function of non-thermal atmospheric pressure plasma has been widely accepted in several types of cancer. We previously developed plasma-activated medium (PAM) for clinical use, and demonstrated that PAM exhibits a metastasis-inhibitory effect on ovarian cancer through reduced MMP-9 secretion. However, the anti-tumor effects of PAM on endometrial cancer remain unknown. In this study, we investigated the inhibitory effect of PAM on endometrial cancer cell viability in vitro. Our results demonstrated that endometrial cancer cell viabilities were reduced by PAM at a certain PAM ratio, and PAM treatment effectively increased autophagic cell death in a concentration dependent manner. In addition, we evaluated the molecular mechanism of PAM activity and found that authophagy-related proteins were changed and the mTOR pathway was inactivated by PAM. Moreover, our results demonstrated that the autophagy inhibitor MHY1485 partially inhibited the autophagic cell death induced by PAM treatment. These findings indicate that PAM decreases the viability of endometrial cancer cells along with alteration of the mTOR pathway, which is critical for cancer cell viability. Collectively, our data suggest that PAM inhibits cell viability while inducing autophagic cell death in endometrial cancer cells, representing a potential novel treatment for endometrial cancer.

Research Background

A frequent pattern of progression and recurrence of endometrial cancer is peritoneal metastasis, which is often resistant to systemic chemotherapy. Therefore, there is an increasing demand for novel approaches to peritoneal dissemination of endometrial cancer. Recent studies have revealed that in addition to the direct irradiation of nonequilibrium atmospheric pressure plasma (NEAPP) to bacteria or tissues, indirect plasma treatment with PAM and plasma-activated lactate (PAL), which are activated by NEAPP, exhibit anti-tumor activity in several types of cancer. Despite extensive studies regarding NEAPP and PAM, their anti-tumor effects against endometrial cancer have not been investigated. Furthermore, the mechanism of anti-tumor effect of plasma-activated solution is not well known at this point. The aim of this study was to evaluate the antitumorigenic effects of PAM on endometrial cancer cells and to elucidate the underlying mechanism. To

this end, the suppressive effects of PAM on endometrial cancer cell viability *in vitro* were examined and autophagy was a part of the suppressive effects of PAM (Figure 1).

Research Results

In this study, we investigated the inhibitory effect of PAM on endometrial cancer cell viability *in vitro*. Our results demonstrated that endometrial cancer cell viabilities were reduced by PAM at a certain PAM ratio, and PAM treatment effectively increased autophagic cell death in a concentration dependent manner (Figure 2). In addition, we evaluated the molecular mechanism of PAM activity and found that authophagy-related proteins were changed and the mTOR pathway was inactivated by PAM (Figure 3). Moreover, our results demonstrated that the autophagy inhibitor MHY1485 partially inhibited the autophagic cell death induced by PAM treatment.

Figure 1.

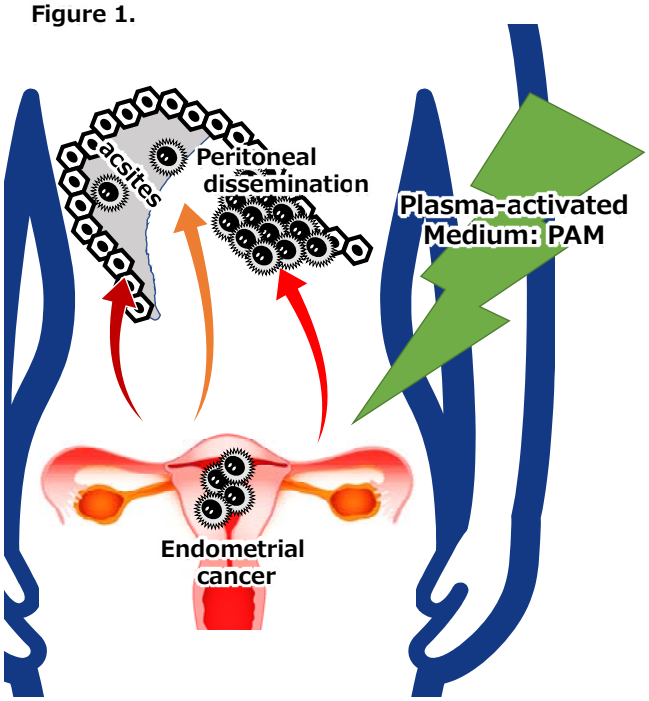


Figure 2.

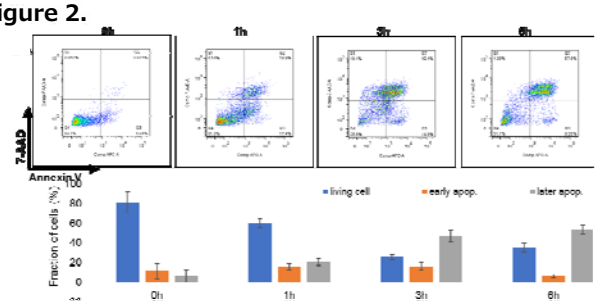
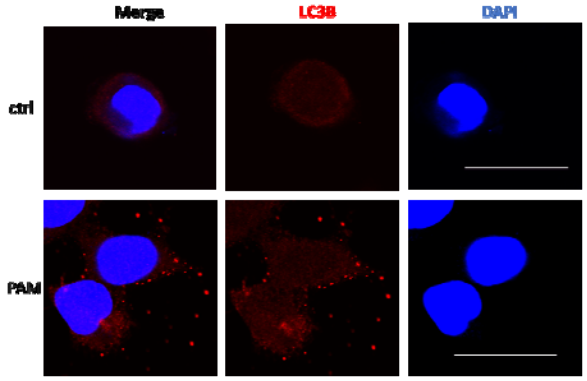


Figure 3.



Research Summary and Future Perspective

The results of our study have shown a novel possibility of plasma-activated solution for the treatment of endometrial cancer. In order to apply this for clinical use, it is necessary to further improve the therapeutic effect and evaluate safety of plasma-activated solution. In the future, our research group will develop a better plasma-active solution that replaces the culture medium used in this study.

Publication

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