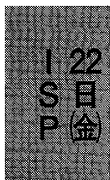


ISP-1-7 Contribution of STAT3 to the resistance of TRAIL-induced apoptosis in cervical cancer

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[Objective] The sensitivity of TNF-related apoptosis inducing ligand (TRAIL)-induced apoptosis differs among various cells including cervical cancer cell lines. The aim of this study is to investigate the potential pathways to improve the sensitivity and seek out the potential therapeutics for cervical cancer, focusing on Stat3 which is a novel target of cancer therapy. [Methods] Expressions of death receptor (DR) 5 and survivin of CaSki and SiHa were measured using RT-qPCR. Then the pSTAT3 level was analyzed using Western blotting. The effect of STAT3 inhibitor on TRAIL-induced apoptosis of SiHa was assessed by Annexin V. After pretreatment of resveratrol (RVT), which is a natural product to suppress STAT3 pathway, TRAIL-induced apoptosis of SiHa was assessed by Annexin V. [Results] SiHa was resistant to TRAIL-induced apoptosis. There was no significant difference between CaSki and SiHa regarding the expression of DR5 and survivin although pSTAT3 expressed higher in SiHa. Inhibition of STAT3 by STAT3 inhibitor and RVT both dramatically enhanced TRAIL-induced apoptosis of SiHa suppressing pSTAT3. [Conclusion] It is suggested that STAT3 would play a central role in resisting the TRAIL-induced apoptosis of cervical cancer. The therapeutics like RVT which can suppress STAT3 activation could be promising strategies for the treatment of cervical cancer.

ISP-1-8 Regeneration of Cervical Reserve Cell-like Cells from Human Induced Pluripotent Stem Cells (iPSCs) : A Novel Method in the Field of Gynecologic Research

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[Objective] Cervical reserve cells are the origin of cervical cancer and investigating the characteristics of cervical reserve cells can be of help to understand cervical cancer stem cells (CSC) s features. In this study, we developed a method for regeneration of cervical reserve cell-like properties from human induced pluripotent stem cells (iPSCs) (induced reserve cell-like cells ; iRCs). [Methods] Using human iPS cells (201B7 ; kindly provided from Dr. Shinya Yamanaka), we induced intermediate mesodermal cells and cultured these cells on collagen IV-coated plates. P63, CK17, CK8 and CK5 were used as reserve cell markers by immunofluorescence. CK7, AGR2, CD63, MMP7 and GDA were used as squamocolumnar junction (SC junction) markers by RT-PCR. ER α , ER β and CA125 were used as Mullerian duct -derived cell markers by RT-PCR. For confirming the pluripotency of iRCs as epithelial progenitor cells, we applied air-liquid interface and 3D-embedded culture method. [Results] About 70% of iRCs are positive for reserve cell markers. iRCs also expressed SC junction markers. iRCs expressed CA125. iRCs formed glandular epithelial-like cells in 3D-embedded culture and got rather pseudostratified than properly stratified in air-liquid interface culture. [Conclusion] We proposed a new method for gynecologic research by generating cervical reserve cell-like cells from iPSCs.

ISP-2-1 Mixed Endometrial Stromal and Smooth Muscle Tumors of the Uterus Associated with Uterine Tumor Resembling Ovarian Sex-cord Tumor

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[Introduction] Mixed endometrial stromal (ES) and smooth muscle (SM) tumor is composed of a prominent component of smooth muscle and endometrial stroma. We report here a case of mixed ES and SM tumor which was composed of leiomyoma, low-grade ES sarcoma (ESS) with sex-cord like differentiation, and uterine tumor resembling ovarian sex-cord tumor (UTROSCT). [Case] A 63-years-old multiparous Japanese woman was referred to our institution complaining of recurrent atypical genital bleeding, anemia, and pointed out intrauterine tumor detected by hysteroscopy. Endometrial Pap smear was negative and tumor markers were within normal range. Magnetic resonance imaging demonstrated a 3.4 cm diameter solid tumor in her uterine cavity. Subsequently, she underwent abdominal total hysterectomy and bilateral adnexectomy. Pathologically, the tumor was consisted of leiomyoma with necrosis, CD10-positive low-grade ESS, and CD10-negative UTROSCT. The component of ESS has extensive necrosis and the mitosis of 20/10 high power fields. She undergoes routine post-treatment surveillance without adjuvant therapy. [Discussion] Mixed ES and SM tumors should be distinguished from leiomyoma, ESS, and UTROSCT. At present, standard treatment protocol is not determined because natural behavior of this tumor is unclear. Careful follow-up is necessary for the possibility of recurrence.