ISP-5-10 The BMP signaling pathway leads to enhanced proliferation in serous ovarian cancer—A potential therapeutic target

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[Objective] Bone morphogenetic proteins (BMPs) have gained increasing interest in cancer research, and current evidence suggests that it participates in various biological processes of cells such as proliferation, and differentiation. We investigated possible roles of BMP function in ovarian serous carcinoma. [Methods] We analyzed the publicly available microarray dataset (GSE2109) using binary regression. Using sk-ov-3 (ovarian serous carcinoma cell line), and immortalized OSE (IOSE), we investigated (1) mRNA expression of BMPs, receptors, and Smads by qRT-PCR, (2) phospho-Smad5 protein expression by western blotting, and (3) cell proliferation analysis. We employed recombinant BMP2 protein (rBMP2) and Dorsomorphin, small molecular inhibitor of BMP signaling, in these assay. [Results] Microaray analysis showed the upregulation of Smad5 associated with poor overall-survival rate in ovarian serous carcinoma ($p = 0.005$). BMP2 mRNA was increased in sk-ov-3 compared to IOSE. pSmad5 protein translocation from cytoplasm to nucleus by BMP2 is dramatically induced in sk-ov-3 compared to IOSE. BMP treatment promoted sk-ov3 proliferation compared to dorsomorphin-treated cells. [Conclusion] BMP signaling possibly control the proliferation in ovarian serous carcinoma with induced translocation of pSmad5 to nucleus, then it could be the potential therapeutic target of ovarian serous carcinoma.

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ISP-6-1 Prevalence and incidence of perioperative venous thromboembolism in gynecologic malignancy patients—Strategies for prevention—

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[Objective] Venous thromboembolism (VTE) is a severe complication in surgical patients with gynecologic malignancy. We investigated the prevalence of preoperative VTE and risk factors. We also conducted a preliminary study on postoperative VTE. [Methods] In our institution, gynecologic malignancy patients are screened for VTE by D-dimer before operation. Those with D-dimer $>1\mu g/mL$ are examined by enhanced CT. Patients are also screened for VTE by enhanced CT postoperatively. Surgical patients with gynecologic malignancy from Jan to Sep 2011 with informed consent were enrolled, and their medical records were reviewed. The preliminary study on postoperative VTE only targeted the patients from Jan to Mar 2011, when intermittent pneumatic compression (IPC), elastic stocking, and early ambulation were used as prophylaxes. [Results] 14% of the patients had preoperative VTE. The prevalence was not different by cancer types or histological subtypes. Advanced FIGO stage was the only significant risk factor ($p<0.001$). D-dimer had a moderate accuracy (AUC = 0.89). Anticoagulants and/or IVC filter were used for those with VTE. In the study on postoperative VTE, 50% developed VTE after operation. [Conclusion] Perioperative VTE is common. We are conducting a RCT of enoxaparin vs. strict use of IPC until full ambulation to develop solid evidence for VTE prevention. This study obtained IRB approval.

ISP-6-2 Recombinant H2 relaxin inhibits apoptosis with induction of cell proliferation in human uterine leiomyoma

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[Objective] The present study was conducted to evaluate the effects of human relaxin on proliferation and apoptosis in cultured human uterine leiomyoma cells and normal myometrial cells. [Methods] Nine samples were obtained from Japanese women with regular menstrual cycles who underwent hysterectomy for uterine leiomyoma. Informed consent was obtained from each patient before surgery. LGR7 expressions in cultured leiomyoma and myometrial cells were evaluated by immunocytochemical staining. Cell proliferation, PCNA-positive rate, and TUNEL-positive rate were assessed by MTS assay, immunocytochemistry, and TUNEL assay, respectively. The caspase-3 expression was evaluated by Western blot analysis. [Results] LGR7 expression was observed both in cultured human leiomyoma cells and myometrial cells. Compared with untreated control cultures, treatment with human recombinant (rH2) relaxin increased the number of viable cultured leiomyoma cells and the PCNA-positive rate, but decreased the TUNEL-positive rate in cultured leiomyoma cells. Similarly, Western blot analysis revealed that treatment with rH2 relaxin decreased the expression of caspase-3 in cultured leiomyoma cells. [Conclusion] These results suggest that rH2 relaxin selectively inhibits apoptosis by down regulating caspse-3 expression and induces proliferation in cultured human leiomyoma cells.