ISP-4-1  Tumor-associated Lymphocytes Attenuate Tumor Immunity to Promote Progression of Serous Endometrial Cancer via STAT1 Pathway

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[Objective] Serous papillary endometrial cancers (SPEC) are highly progressive. Tumor infiltrated immune cells (TIi) is frequently observed in SPEC. TIi was initially regarded as an attempt by the host organism to combat malignancy, but it has been revealed to promote tumor growth, tumor survival, & tumor migration. Precise mechanism of TIi in SPEC is still unclear, genetic analysis for SPEC was performed in the aspect of tumor immunity. [Methods] A microarray expression of endometrial cancers, GSE2109, was analyzed to detect a SPEC-specific pathway with putative downstream TIi-correlating genes, which expression was further examined under protocols approved by the Kyoto University Institutional Review Board. Using a SPEC cell line, SPAC-1L, cellular proliferation, migration, & invasion were assessed with or without manipulation of the pathway genes. [Results] Microarray analysis revealed STAT1 pathway was highly activated in SPECs. STAT1 downstream genes, ICAM-1 & PD-L1, co-localized with tumor-associated lymphocytes at the frontier site of invading tumor cells. The expression of ICAM-1 & PD-L1 were induced in SPAC-1L cells by IFN-γ and it was associated with the capability of cellular migration and invasion (p<0.05). [Conclusion] These results indicate that both ICAM-1 & PD-L1 play a certain role in association with the tumor-associated lymphocytes in endometrial cancer progression.

ISP-4-2  Angiotensin II type I receptor and miR-155 in endometrial cancers: Synergistic antiproliferative effects of anti-miR-155 and losartan on endometrial cancer cells

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Purpose: MicroRNA-155 (miR-155) is one of the micro RNAs most consistently involved in neoplastic diseases, and it is known to repress the angiotensin II type I receptor (AGTR1). The aim of the present study was to evaluate the expressions of miR-155 and AGTR1 and to clarify the potential efficacy of anti-miR-155, alone and in combination with AGTR1 blocker losartan in endometrial cancers. 

Experimental Design: Expressions of miR-155 and AGTR1 were evaluated using real-time PCR and immunohistochemistry. An MT assay was performed in endometrial cancer cells following anti-miR-155 and treatment with losartan, individually and in combination.

Results: miR-155 was over-expressed and AGTR1 was underexpressed in endometrial carcinoma tissues. AGTR1 immunoreactivity was found in six of ten (60.0%) normal endometrial samples, 11 of 14 (78.6%) endometrial hyperplasias, and 27 of 62 (43.5%) endometrial carcinoma tissues (P=0.051), and patients with AGTR1 expression showed longer disease-free survival (P=0.019). Abolishing the function of miR-155 and AGTR1 by anti-miR-155 or losartan inhibited cell survival of endometrial carcinoma cells; furthermore, combined treatment showed synergistic effects.

Conclusions: These results demonstrate that miR-155 and AGTR1 may be novel therapeutic targets in the treatment of endometrial cancers.

Keywords: miR-155; AGTR1; losartan; endometrial carcinoma

ISP-4-3  Benefit of adjuvant chemotherapy combined to postoperative radiotherapy for high-risk endometrial cancer: A meta-analysis

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Objective: The standard treatment of high-risk endometrial cancer was a staging operation followed by pelvic radiotherapy. The purpose of this study was to determine whether adjuvant chemotherapy combined to the standard treatment would have benefits for the total recurrence and 5-year overall survival.

Methods: Electronic searches for studies of adjuvant chemotherapy combined to postoperative radiotherapy in endometrial cancer patients between July 1976 and July 2011 were made on MEDLINE, SCOPUS, Web of Knowledge and EMBASE. A meta-analysis of literature was performed and pooled odds ratios (OR) of total recurrence count on observation and 5-year overall survival count by Caplan-Meier methods were appropriately derived from fixed effects model. 

Result: Three case-control studies and 3 randomised clinical trials were included in the final analysis. There was a significant difference between patients whose adjuvant chemotherapy combined to postoperative radiotherapy (CRTx group) and patients with postoperative radiotherapy only (RTx group) in total recurrence count on observation [odds ratio (OR) = 0.72, 95% CI 0.55 to 0.95; p=0.02]. However, no significant difference in 5-year overall survival count between 2 groups was observed [odds ratio (OR) = 1.26, 95% CI 0.93 to 1.70; p=0.14].

Conclusion: This meta-analysis revealed that adjuvant chemotherapy combined to postoperative radiotherapy could significantly reduce the recurrence rate in patients with high-risk endometrial cancer, but would not have an additional benefit in terms of 5-year overall survival when compared with postoperative radiotherapy only. Prospective multicenter studies are required to verify benefit of adjuvant chemotherapy combined to postoperative radiotherapy for high-risk endometrial cancer.