968 PUBLICATION

Expression of syndecan-1 in endometrial cancers and its functions

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Syndecan-1 is one of major proteoglycans on cell membrane. It has been reported that syndecan-1 plays critical parts in a plethora of cell functions, including embryogenesis, cell migration, wound healing, and cancer progression. Often it is believed that the loss of syndecan-1 is correlated with aggressive phenotypes of cancer cells and poor prognosis. However, there have been contradictory reports regarding the correlation between level of syndecan-1 expression and cancer phenotype in other cancer cases, notably in breast cancer. Therefore, the expression and the loss of syndecan-1 may be tissue specific and thus display different functions of syndecan-1. In cases of endometrial cancer, there have been only two reports about syndecan-1 expression in the cancer tissue, which characterized the cancer with the loss of syndecan-1 in higher cancer grade without mentioning molecular and cellular functions of syndecan-1. Nevertheless, we report the contradictory results after examining 43 different tissue samples against syndecan-1 collected from 1995 to 2003. Our findings support significant close relationships of the syndecan-1 overexpression to the higher tumor grade ($p \leqslant 0.043$) and surgical grade ($p \leqslant 0.039$) along with increased myometrium invasion depth ($p \leqslant 0.012$), and lymphatic invasion ($p \leqslant 0.009$). In order to support the results, we have set an In-Vitro model with a well-differentiated endometrial cancer cell line HEC-1A, expressing syndecan-1 at a low level. Treatment of small hairpin antisense RNA (shRNAi) against syndecan-1 down-regulated the growth of HEC-1A dramatically while the overexpression of syndecan-1 caused more rapid growth of the cancer cells in both 96 well plates and agarose suspension culture.
In addition, the silencing of syndecan-1 decreased the cell invasiveness by half into matrigel in the Boyden chamber compared to the cells transfected with control shRNAi. Moreover, we have found after running a nano 2-D chromatography analysis of the whole cell protein extracts that the silencing caused different profiles of expressed proteins in the cancer.
In conclusion, it is thought that the syndecan-1 expression in the endometrial cancer cells has a linear correlation to the progression of carcinogenesis, and roles of syndecan-1 are thought to help cells survive and proliferate by regulating its down stream gene expressions.
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969 PUBLICATION

CYP2E1 polymorphism and susceptibility to cervical cancer

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Background: Cervical cancer (CC) causes about 190.000 deaths annually, being one of the most common causes of death in women. Among the risk factors for CC, both genetic and environmental factors have an important role. In fact, infection with HPV is the major factor of risk in the development of CC, although other co-factors (with genetic, environmental or immunological origin) may interfere in the multi-stage process that leads to the disease. There is commonly accepted that this is a continuum process, beginning with the infection with HPV in normal cervix, passing for a stage of low grade lesions (LSIL) and high grade lesions (HSIL) and ending in an invasive carcinoma. Some of these co-factors are the tobacco smoke, dietary factors and other sexually transmitted diseases.
CYP2E1 interferes in the metabolism of several exogenous and endogenous factors, such as N-nitrosamines and alcohol, promoting the formation of DNA adducts. The role of tobacco smoke is well documented in the aetiology of CC. The enzyme activity is also described as being modulated by several immunological factors, whose importance in the CC development and progression is under investigation.
Methods: There were analysed a total of 207 cases of women with pathologies of the uterine cervix (59 presented LSIL or HSIL lesions, 122 invasive squamous cell carcinoma (ICC) and 8 presented adenocarcinoma. In the other cases it was not possible to determine the histological status) and 273 healthy controls. The genotypic analysis was performed using PCR-RFLP technique.
Results: We observed that the presence of C allele (genotype CC/CD) is higher in cases (27%) than in controls (18%) and this different was statistically significant ($p = 0.029$). Although we did not find any statistical differences between controls and women with ICC, we observed that the C allele may have a protective role in the development of cervical lesions, that may lead to invasive carcinoma (OR = 0.08, 95% IC 0.012–0.65; $p = 0.001$). The analysis was stratified according to patient's median age.
Conclusions: The allele C may have an important role in the development of the initial lesions of the uterine cervix. This may be important due to its interference in the metabolization of compounds of the tobacco smoke and dietary factors.

970 PUBLICATION

High cyclooxygenase-2 expression is related with local recurrence in cervical cancer treated with postoperative radiotherapy

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Background: The purpose of this study was to examine the relationship between local recurrence or distant metastasis and COX-2 expression in cervical cancer patients treated with postoperative radiotherapy. A clinicopathologic study was performed on 56 patients.
Methods and Material: Formalin-fixed, paraffin-embedded tumor biopsies were stained for Cyclooxygenase-2 (COX-2). COX-2 expression was evaluated by a semiquantitative score and by calculating the labelling index, i.e. defining the ratio between stained and negative cells, for each sample. Clinical factors such as stage, grade, tumor size and radiotherapy dose were also evaluated.
Results: The median COX-2 labelling index (LI) was 58.8%. In terms of local tumor control none of the 28 patients with COX-2 LI below the median developed a local recurrence, whereas in 3 patients (out of 27) with COX-2 LI above the median a local recurrence war observed ($p = 0.07$). Although a high percentage of distant metastases was observed (21%) in this relatively small patient cohort, no relationship according to high COX-2 expression could be demonstrated. Among the clinicopathologic factors stage and grade were found to closely correlate with COX-2 expression.
Conclusion: These findings indicate that increased expression of COX-2 portends an increased local treatment failure in patients with invasive carcinoma of the cervix treated with postoperative radiotherapy. Because COX-2 is an early-response gene involved in angiogenesis and inducible by different stimuli, these data my indicate opportunity to intervene with specific inhibitors of COX-2 in carcinoma of the cervix.

Haematological Malignancies

Oral presentations (Thu, 3 Nov, 8.30–10.30)

Treatment of malignancies in children and adults – long term side effects

971 ORAL

Adolescent cancer survival in France

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To study survival of adolescents diagnosed with cancer in France.
Patients and methods: Data from the FRANCIM network of French population-based cancer registries covering 10% of French population were used to examine patterns of survival of adolescents diagnosed with a cancer (excluding basal cell carcinoma). Data of all the patients aged 15 to 19 recorded in these registries over a 10-year period, (1988 to 1997) were studied. Follow-up information (cancer recurrence or progression, death from treatment side effects or from the cancer itself) became available after actively searching the medical records of each hospital in which patients had been treated.
Results: Five-year OS and DFS for all cancers pooled ($n = 648$) was respectively 74.2% (95% CI: 70.8–77.6) and 68.9% (95% CI: 65.3–72.5). OS and DFS at 5 years were respectively 100% and 100% for thyroid carcinoma (35pts), 85% and 90% for Hodgkin disease (98pts), 95% and 89% for melanoma (63 pts), 89% and 82% for germ-cell tumors (89 pts), 69% and 68.5% for soft-tissue sarcoma (49 pts), 64% and 60.9% for NHL (49pts), 63% and 55.9% for CNS tumors (67pts), 56% and 47.6% for malignant bone tumors (68pts), 45% and 45% for ANLL (20pts), and 42% and 33.8% for ALL (47pts).