RPRD1B is a potentially molecular target for diagnosis and prevention of human papillomavirus E6/E7 infection-induced cervical cancer: A case-control study.

Related Articles

**RPRD1B is a potentially molecular target for diagnosis and prevention of human papillomavirus E6/E7 infection-induced cervical cancer: A case-control study.**

Asia Pac J Clin Oncol. 2020 Aug 31;
Authors: Wen N, Bian L, Gon J, Meng Y

Abstract

**BACKGROUND:** The objective of the study is to investigate the biomarkers for diagnosis and prevention of human papillomavirus (HPV) infection-induced cervical cancer.

**METHODS:** Cervical cancer tissues were collected from patients with cervical cancer, while noncancer tissues were collected from patients diagnosed with cervical lesions or uterine fibroids at the Chinese PLA General Hospital 301 and 309, China from December 2017 to June 2018. The cancer tissues were collected from the site of lesion, while the noncancer tissues were collected from similar anatomical locations. Quantitative real-time PCR, Western blot (WB), and immunohistochemistry (IHC) were used to detect the mRNA and protein levels of HPV E6/E7, RPRD1B (regulation of nuclear pre-mRNA domain containing 1B), cyclin D1, and transcription factor 4 (TCF4) between cervical cancer tissues and noncancer tissues. The correlation of HPV E6/E7, RPRD1B, cyclin D1, and TCF4 expressions was analyzed.

**RESULTS:** Twenty patients with cervical cancer and 27 controls without cervical cancer were included in this study. The mRNA expression of HPV E6/E7 and RPRD1B was significantly higher in patients with cervical cancer than controls, while cyclin D1 mRNA expression was significantly lower in patients with cervical carcinoma in situ stage, compared with controls. RPRD1B protein expression was significantly higher in patients compared to controls when analyzed by IHC. TCF4 was significantly lower in clinical stage I and Ib of cervical cancer when analyzed by WB. The mRNA and protein expressions of RPRD1B and cyclin D1 were significantly different between patients younger than 50 years old, compared to patients 50 years and older.

**CONCLUSIONS:** HPV E6/E7 expression was associated with RPRD1B level in cervical cancer. The expression of RPRD1B and cyclin D1 in patients with cervical cancer might be affected by age.

PMID: 32866332 [PubMed — as supplied by publisher]
Roles of long non-coding RNAs in cervical cancer.

Related Articles

Roles of long non-coding RNAs in cervical cancer.

Luo F, Wen Y, Zhou H, Li Z.

Cervical cancer (CC) is regarded as the second serious threat to women’s health worldwide; it’s associated with certain viruses that are transmitted through sexual intercourse. Therefore, the pathogenesis of CC remains to be studied. The identified long non-coding RNAs (lncRNAs) as a key genomic product were found to be commonly dysregulated in CC and to exert significant effects in the initiation, migration, invasion and therapeutic response of CC. Therefore lncRNAs may be used as tumor suppressor genes or oncogenes to interact with DNA, RNA or proteins for the regulation of gene expression and cell signaling pathways. The relationship between single lncRNA and CC has been discovered. However, full-scale reviews on the lncRNAs function in CC are deficiency. In this review, we describe the recent reports on the dysregulated patterns regulation of lncRNAs in CC. We also conclude the recent advances on biologic functions and molecular regulation mechanism and potential clinical application of lncRNAs in CC.

PMID: 32561395 [PubMed — indexed for MEDLINE]

Increased risk of cervical dysplasia in females with autoimmune conditions-Results from an Australia database linkage study.


BACKGROUND: Autoimmune conditions (AICs) and/or their treatment may alter risk of human papilloma virus (HPV) infection and females with AICs are therefore at an increased risk of cervical dysplasia. However, inclusion of these at-risk populations in cervical cancer screening and HPV-vaccination guidelines, are mostly lacking. This study aimed to determine the prevalence of cervical dysplasia in a wide range of AICs and compare that to HIV and immunocompetent controls to support the optimisation of cervical cancer preventive health measures.

METHODS: Data linkage was used to match cervical screening episodes to emergency department records of females with AICs or HIV to immunocompetent controls over a 14-year period. The primary outcome was histologically confirmed high-grade cervical disease. Results, measured as rates by cytology and histology classification per 1,000 females screened, were analysed per disease group, and intergroup comparisons were performed.

RESULTS: Females with inflammatory bowel disease (2,683), psoriatic and enteropathic arthropathies (1,848), multiple sclerosis (MS) (1,426), rheumatoid arthritis (1,246), systemic lupus erythematosus and/or mixed connective tissue disease (SLE/MCTD) (702), HIV (44), and 985,383 immunocompetent controls were included. SLE/MCTD and HIV groups had greater abnormality rates compared to controls. Increased rates of high-grade histological and cytological abnormalities compared to controls. Increased rates of low-grade cytological abnormalities were detected in all females with AICs, with the exception of the MS group.

CONCLUSIONS: Females with SLE/MCTD or HIV have increased rates of high-grade cervical abnormalities. The increased low-grade dysplasia rate seen in most females with AICs is consistent with increased HPV infection. These findings support expansion of cervical cancer preventative programs to include these at-risk females.

PMID: 32555638 [PubMed — indexed for MEDLINE]
MicroRNA-455-5p exerts inhibitory effect in cervical carcinoma through targeting S1PR1 and blocking mTOR pathway.

Related Articles

MicroRNA-455-5p exerts inhibitory effect in cervical carcinoma through targeting S1PR1 and blocking mTOR pathway.

Arch Gynecol Obstet. 2020 05;301(5):1307–1315

Authors: Hu D, Sun S, Wang Y

Abstract

BACKGROUND: MicroRNAs (miRNAs) have been increasingly exploited in human malignancies. The regulation of microRNA-455-5p (miR-455-5p) has been shown in several cancers, except for cervical carcinoma. Therefore, the role of miR-455-5p was exploited in cervical carcinoma.

METHODS: The qRT-PCR experiment was used to assess miR-455-5p and S1PR1 expression levels. We explored the function of miR-455-5p through MTT and Transwell assays. The mTOR pathway and cell apoptosis were detected by Western blot assays. The relationship between miR-455-5p and S1PR1 was testified by dual-luciferase reporter assay.

RESULTS: MiR-455-5p expression was decreased in cervical carcinoma, which was related to poor clinical outcome in cervical carcinoma patients. MiR-455-5p inhibited cell viability and metastasis in cervical carcinoma. Further, S1PR1 is a direct target of miR-455-5p. S1PR1 recovered the inhibition of cell viability and metastasis induced by miR-455-5p in cervical carcinoma. In addition, miR-455-5p induced cell apoptosis and inactivated the mTOR pathway in cervical carcinoma.

CONCLUSION: MiR-455-5p exerts inhibitory effect in cervical carcinoma through targeting S1PR1 and blocking the mTOR pathway.

PMID: 32303890 [PubMed — indexed for MEDLINE]

The impact of age and high-risk human papillomavirus (hrHPV) status on the prevalence of high-grade cervical intraepithelial neoplasia (CIN2+) in women with persistent hrHPV-positive, cytology-negative screening samples: a prospective cohort study.

BJOG. 2020 09;127(10):1260–1267

Authors: Tidy JA, Lyon R, Ellis K, Macdonald M, Palmer JE

Abstract

OBJECTIVE: To establish the prevalence of high-grade cervical intraepithelial neoplasia (CIN2+) in women referred to colposcopy with persistent high-risk human papillomavirus (hrHPV) cytology-negative screening sample according to hrHPV genotype, age at referral and colposcopic performance.

SETTING: Single colposcopy clinic linked to a population-based screening programme.

POPULATION: Women referred with persistent hrHPV cytology-negative routine screening samples.

METHODS: Prospective study with descriptive statistics from a single colposcopy unit between June 2014 and July 2019.

MAIN OUTCOME MEASURES: Prevalence of hrHPV genotypes and CIN2+, positive predictive value for colposcopic impression, and inadequate colposcopic examinations.

RESULTS: A total of 3107 women were referred. Prevalence of CIN2+ was highest for persistent HPV16 infections (10.7%) compared with HPV18 (3.6%) or HPV16O (4.7%). Prevalence of CIN2+ declined with age (25–34 years 14.2% to 55–64 years 1.1%) whereas the percentage of women with an inadequate colposcopic examination increased (25–34 years 0.9% to 55–64 years 29.5%). High-grade colposcopic impression fell over time during the study from 16.1 to 5.1%. The positive predictive value for colposcopic impression of CIN2+ was affected by hrHPV genotype (57.3% for HPV16 versus 32.1% for nonHPV16). The adjunctive use of electrical impedance spectroscopy detected an extra 42 cases of CIN2+, which was irrespective of hrHPV genotype.

CONCLUSIONS: Primary hrHPV cervical screening increases detection of CIN2+; however, low specificity results in more women being referred to colposcopy with a low prevalence of CIN2+. Colposcopy performs poorly in some groups, particularly with HPV16O infections and women over 50 years of age. An appropriate threshold for referral to colposcopy in primary hrHPV screening has not been established.

TWEETABLE ABSTRACT: Low prevalence of CIN2+ in HPV-positive negative cytology samples. HPV genotype, age and prevalence of CIN2+ affect colposcopic performance.

PMID: 32279427 [PubMed — indexed for MEDLINE]
A 10-gene prognostic methylation signature for stage I-III cervical cancer.

Related Articles

A 10-gene prognostic methylation signature for stage I-III cervical cancer.
Arch Gynecol Obstet. 2020 05;301(5):1275–1287
Authors: Cai S, Yu X, Gu Z, Yang Q, Wen B, Sheng J, Guan R

Abstract
PURPOSE: Cervical cancer (CC) patients usually have poor prognosis. The present study aims to find a DNA methylation signature for predicting survival of CC patients.
METHODS: We selected CC patients at pathological stage I-III with corresponding information on radiotherapy and overall survival (OS) from TCGA. Differential expression and methylation analysis was done between patients with and without radiotherapy. We selected feature genes using recursive feature elimination algorithm to build a support vector machine classifier. DNA methylation biomarkers predictive of prognosis were identified using a LASSO Cox-Proportional Hazards model to construct a prognostic scoring model. The classifier and the prognostic model were tested on the training set and the validation set. Nomogram combining risk score and prognostic clinical factors were used.
RESULTS: We obtained 497 differentially expressed genes (DEGs) and 865 differentially methylated genes (DMGs). Fifteen feature genes were selected from the 292 common genes between the DEGs and the DMGs to construct a classification model for radiotherapy. A DNA methylation signature including 10 genes was identified and used to establish a prognostic scoring model. The 10-gene methylation signature could effectively separate patients into two risk groups with markedly different OS time. Predictive capability of the methylation signature was successfully confirmed on the validation set. A nomogram comprised of risk score, radiotherapy, and recurrence was applied, with calibration plots displaying good concordance between predicted and actual OS. The DEGs were involved in 12 KEGG pathways most of which were correlated with metastasis and proliferation of various cancers, such as pathways in cancer, basal cell carcinoma, transcriptional misregulation in cancer and ECM-receptor interaction.
CONCLUSION: We identified a 10-gene methylation signature for risk stratification of CC patients at pathological stages I-III, and ten methylation biomarkers might be novel therapeutic targets for CC.
PMID: 32274635 [PubMed — indexed for MEDLINE]

Piperlongumine increases the apoptotic effect of doxorubicin and paclitaxel in a cervical cancer cell line.

Related Articles

Piperlongumine increases the apoptotic effect of doxorubicin and paclitaxel in a cervical cancer cell line.
Authors: Seber S, Sirin DY, Yetisyigit T, Bilgen T

Abstract
Objective: Piperlongumine (PL) is an alkaloid derived from the edible pepper (Piper longum L) and it has been described to have various biologic activities including anticancer effects. Our aim in this study was to assess the cytotoxic role of PL on a cervical cancer cell line (HeLa) and to evaluate the effects of PL/doxorubicin and PL/paclitaxel combination therapies on apoptotic cancer cell death.
Material and Methods: The cytotoxicity, IC50 doses by MTT assay confirmed by fluorescent imaging, and apoptotic cell rates by Annexin V staining using flow cytometry were determined for PL, doxorubicin, paclitaxel, and for their combinations.
Results: It was shown that the PL by itself induced the apoptosis in HeLa cells. PL in combination with doxorubicin and paclitaxel increased apoptotic cell death compared to either chemotherapeutic agent alone.
Conclusion: We conclude that the PL inhibits cancer cell growth by inducing apoptosis and has a potential anticancer activity in cervical cancer, especially when combined with doxorubicin and paclitaxel.
PMID: 32134040 [PubMed — indexed for MEDLINE]

Use of bowel preparation does not reduce postoperative infectious morbidity following minimally invasive or open hysterectomies.

Related Articles

Use of bowel preparation does not reduce postoperative infectious morbidity following minimally invasive or open hysterectomies.
Am J Obstet Gynecol. 2020 08;223(2):231.e1-231.e12
Authors: Kalogera E, Van Houten HK, Sangaralingham LR, Borah BJ, Dowdy SC

Abstract
BACKGROUND: Literature on the use of bowel preparation in gynecologic surgery is scarce and limited to minimally invasive
Value of indocyanine green pelvic lymph node mapping in the surgical approach of cervical cancer.

Related Articles

Value of indocyanine green pelvic lymph node mapping in the surgical approach of cervical cancer.

Arch Gynecol Obstet. 2020 03;301(3):787-792


Abstract

PURPOSE: Lymph node metastasis is a significant predictive factor for disease recurrence and survival in cervical cancer patients and
relevant for therapeutic strategies. We evaluated the clinical value of indocyanine green (ICG) by measuring the sensitivity and negative predictive value of sentinel lymph node mapping compared with the gold standard of complete lymphadenectomy in detecting lymph node metastases for cervical cancer.

METHODS: We utilized the near-infrared imaging agent ICG to detect tumor-infested lymph nodes in the pelvis analogue to a classical sentinel lymph node procedure by analyzing data from 20 patients who had undergone surgery for cervical cancer at our institution. A laparoscopic lymph node mapping procedure by means of ICG, followed by a complete pelvic lymphadenectomy with or without paraaortic lymphadenectomy was done in all patients.

RESULTS: Histological examination identified seven patients with tumor-positive pelvic nodes, whereas mapping with ICG identified only five of these patients. Detection rate of positive nodes by ICG mapping and false negative rate was 71.4% and 28.6%, respectively; bilateral detection rate was 83.3%. One of the two false negative patients additionally suffered from deep infiltrating endometriosis.

CONCLUSIONS: Our results indicate that ICG can identify the relevant pelvic nodes independent of tumor size, provided bilateral detection is achieved and additional, related diseases are excluded.

TRIAL REGISTRATION: This trial is registered within the German Clinical Trial Register (DRKS-ID: DRKS00014692).

PMID: 32048031 [PubMed — indexed for MEDLINE]

Factors predicting recurrence in patients with stage IA endometrioid endometrial cancer: what is the importance of LVSI?

**Abstract**

**PURPOSE:** The aim of this study is to define the clinical and pathological prognostic factors for recurrence and to evaluate the recurrence patterns and adjuvant therapies used in this group of patients with stage IA endometrioid type endometrial cancer (FIGO 2009-International Federation of Gynecology and Obstetrics).

**METHODS:** Among the patients with epithelial endometrial cancer operated between January 1993 and May 2013 in a single institution, 720 patients with stage IA endometrioid endometrial cancer were included. Patients with a tumor type of serous, clear cell, mucinous, undifferentiated, and mixed type and with a tumor containing sarcomatous component and the patients with a secondary primer cancer were excluded from the study.

**RESULTS:** Lympho-vascular space invasion (LVSI) was present in 60 (8.3%) patients. Pelvic and para-aortic lymphadenectomy was performed in 266 (36.9%) patients. Median follow-up time was 48 months (range 3-240). Recurrence occurred in 23 (3.4%) patients and 6 (0.9%) died of disease. The median time-to recurrence (TTR) was 24 months (range 4-52 months) in the patients with recurrence. LVSI was associated with recurrence in the univariate analysis. Five-year disease-free survival (DFS) decreased from 96.8 to 80.1% in the presence of LVSI (p CONCLUSIONS: Only LVSI and tumor grade were associated with DFS and disease-specific survival (DSS), respectively, in the 686 patients with stage IA endometrial cancer in the univariate analysis, since these associations could not be shown in multivariate analysis.

**PMID:** 31883046 [PubMed — indexed for MEDLINE]

Analysis of HPV genotype-specific concordance between EUROArray HPV and HPV 3.5 LCD-Array Kit in cervical samples of 163 patients.

**Related Articles**

**Analysis of HPV genotype-specific concordance between EUROArray HPV and HPV 3.5 LCD-Array Kit in cervical samples of 163 patients.**

Arch Gynecol Obstet. 2020 03;301(3):745–751

Authors: Bräutigam K, Ehret C, Schillinger V, Baum S, Klar M, Köster F, Rody A, Panning M

**Abstract**

**PURPOSE:** Human papilloma virus (HPV) as the most common viral infection of the anogenital tract is highly associated with intraepithelial neoplasia and cancer of the cervix and other anogenital regions. To date, 15 high-risk (HR-) HPV and 3 probably/possibly HR-HPVs have been found to be associated with cervical cancer. Therefore, a screening especially for HR-HPV by appropriate tests is important for detection of precancerous lesions to prevent cancer. The purpose of this study was to analyze prospectively the concordance of the EUROArray HPV genotyping assay (Euroimmun; EUROArray) and the HPV 3.5 LCD-Array Kit (Chipron; LCD-Array).

**METHODS:** Liquid-based, clinician-collected cervical cytology samples (n = 163) from women undergoing cervical inspection at the dysplasia consultation in the colposcopy clinic at the Medical Center-University of Freiburg, Germany were analyzed.

**RESULTS:** Seventeen of the HR-HPV genotypes included in both assays were detected in 42.3% and 38% of samples by EUROArray and by LCD-Array, respectively; i.e. an agreement of 92.0% and a kappa value of 0.83 could be proven between the EUROArray and the LCD-Array. In 50 of 72 samples, identical HR-HPV genotypes were analyzed (81.9%, $\kappa = 0.47$) and genotyping for HPV 16
and/or 18 was highly concordant in both tests (relative agreement 96.3%, $k = 0.88$). Detection of any HR-HPV was not significantly different after comparison of EUROArray with LCD-Array.

CONCLUSION: Both of the tests showed comparable results for the detection of HPV in cervical specimens and permit these assays to be suitable for routine diagnostics.

PMID: 31875249 [PubMed — indexed for MEDLINE]

VERU-111 suppresses tumor growth and metastatic phenotypes of cervical cancer cells through the activation of p53 signaling pathway.

Related Articles

VERU-111 suppresses tumor growth and metastatic phenotypes of cervical cancer cells through the activation of p53 signaling pathway.

Cancer Lett. 2020 02 01;470:64–74

Abstract
In this study, we investigated the therapeutic efficacy of VERU-111 in vitro and in vivo model systems of cervical cancer. VERU-111 treatment inhibited cell proliferation and, clonogenic potential, induce accumulation of p53 and down regulated the expression of HPV E6/E7 expression in cervical cancer cells. In addition, VERU-111 treatment also decreased the phosphorylation of Jak2(Tyr1007/1008) and STAT3 at Tyr705 and Ser727. VERU-111 treatment arrested cell cycle in the G2/M phase and modulated cell cycle regulatory proteins (cyclin B1, p21, p34cdc2 and pcdk1). Moreover, VERU-111 treatment induced apoptosis and modulated the expression of Bid, Bcl-xl, Survivin, Bax, Bcl2 and cleavage in PARP. In functional assays, VERU-111 markedly reduced the migratory and invasive potential of cervical cancer cells via modulations of MMPs. VERU-111 treatment also showed significant (P
PMID: 31809801 [PubMed — indexed for MEDLINE]

MBNL1 regulates resistance of HeLa cells to cisplatin via Nrf2.

Related Articles

MBNL1 regulates resistance of HeLa cells to cisplatin via Nrf2.

Biochem Biophys Res Commun. 2020 02 12;522(3):763–769
Authors: Wang T, Liu Q, Duan L

Abstract
Chemotherapy is an important method in the treatment of cervical cancer, but some patients will face drug resistance, which often indicates a poor prognosis. Moreover, there is no complete solution at present. Therefore, it is urgent to study the drug resistance mechanism of cervical cancer. Based on sequencing data mining, we predicted that MBNL1 might be involved in the occurrence and poor prognosis of cervical cancer, and verified that MBNL1 could regulate the resistance of HeLa cells to cisplatin via Nrf2. In addition, we demonstrated that MBNL1 up regulated the degradation of Nrf2 protein by increasing the mRNA stability of Cul3. These results can provide theoretical basis for clinical development of new diagnosis and treatment targets for cisplatin resistance.

PMID: 31791583 [PubMed — indexed for MEDLINE]

Adherence to Cervical Cancer Screening Guidelines Among Women Aged 66–68 Years in a Large Community-Based Practice.

Related Articles

Adherence to Cervical Cancer Screening Guidelines Among Women Aged 66–68 Years in a Large Community-Based Practice.

Authors: Chao CR, Xu L, Lonky NM

Abstract
INTRODUCTION: The 2012 national cervical cancer screening guidelines recommended cessation of screening after age 65 years in women with adequate prior screening. In this retrospective cohort study, adherence to these screening exit guidelines was examined.

METHODS: Women who turned age 66 years in 2012–2013 at Kaiser Permanente Southern California were followed through age 68 years for cervical cancer screening uptake. Adequacy of prior screening was assessed between age 56 and 65 years using electronic medical records. Guideline adherence was determined based on screening pattern between age 66 and 68 years. Patient- and physician-level correlates for guideline adherence were examined using multivariable logistic regression. Data collection and analyses were conducted in 2018.

RESULTS: A total of 14,778 women were included; 24% did not have adequate prior screening by age 65 years. Among those without adequate prior screening, the proportion screened after age 65 years ranged from 71% (177 of 249) in those whose most recent test was abnormal to 3% (34 of 1,330) in those who did not have any testing in 10 years. Prior screening pattern was the only factor associated with screening after age 65 years. Of those with adequate prior screening, 10% (1,135 of 11,295) continued to receive screening after age 65 years. Frequent office visits and having a male primary care physician were associated with continuing screening after age 65 years.

CONCLUSIONS: A considerable proportion of women did not have adequate prior screening by age 65 years. Of these, a large proportion did not receive screening after age 65 years, except
those who had a recent abnormal screening result. Further research is needed to understand barriers for guideline adherence and rationales for clinical decision making.

PMID: 31753257 [PubMed — indexed for MEDLINE]

Mass lesions of the myometrium: interpretation and management of unexpected pathology.

Related Articles
Mass lesions of the myometrium: interpretation and management of unexpected pathology.
Authors: Porter AE, Kho KA, Gwin K
Abstract
PURPOSE OF REVIEW: Uterine leiomyomas are the most common benign uterine smooth muscle tumors. On the basis of imaging, these masses are often presumed to be benign conventional leiomyomas and surgical excision is a common treatment choice. After myomectomy or hysterectomy for presumed leiomyomas, the surgical pathology report may reveal an unexpected diagnosis of another type of mesenchymal tumor. These can range from a variant of benign smooth muscle tumors to smooth muscle tumors of uncertain malignant potential to malignant sarcomas. This review describes these variant pathologies and reviews data on recurrence risk and postoperative management.
RECENT FINDINGS: The majority of benign smooth muscle tumors will be classified as leiomyomas. Cellular, bizarre nuclei, mitotically active, epitheliod, myxoid, and dissecting are all terms that describe pathologic variants of benign leiomyomas. Smooth muscle tumors of uncertain malignant potential to malignant sarcomas. This review describes these variant pathologies and reviews data on recurrence risk and postoperative management.
SUMMARY: We advocate for the continued benefits of minimally invasive procedures in appropriately selected patients. Despite these measures, unexpected pathologic diagnoses can occur and should be managed appropriately.

PMID: 31425175 [PubMed — indexed for MEDLINE]

Invasive stratified mucin-producing carcinoma: a clinicopathological analysis of three cases.

Related Articles
Invasive stratified mucin-producing carcinoma: a clinicopathological analysis of three cases.
lesions. This cross-sectional study included all women in whom
HPV infection was found by cervical smear during routine
gynecologic health checks. Women with single or multiple HPV16
infections (n = 176) were selected for viral variant and viral load
analysis. Smear results were classified using the Bethesda system.
HPV types were classified according to the International Agency
for Research on Cancer. Odds ratios (OR) with their 95%
confidence intervals (CI) were estimated by logistic regression,
adjusted for age, immigrant status, and coinfection with other
high-risk genotypes. No statistically significant associations were
found regarding the detected viral variants. A viral load above the
median (>1,367.79 copies/cell) was associated with a significant
risk of high-grade epithelial lesion or carcinoma, after adjusting
for age, immigrant status, coinfections, and viral variant: (adjusted
OR 7.89; 95% CI: 2.75–22.68). This relationship showed a
statistically significant dose-response pattern after categorizing by
viral load tertiles: adjusted OR for a viral load greater than the
third tertile was 17.23 (95% CI: 4.20–70.65), with adjusted linear
P trend = 0.001. In patients infected with HPV16, viral load is
associated with high-grade intraepithelial lesions or cervical
carcinoma. This could be useful as prognostic biomarker of
neoplastic progression and as screening for cervical cancer.

PMID: 31208965 [PubMed — indexed for MEDLINE]

Identification of key transcription factors in endometrial cancer by
systems bioinformatics analysis.

Related Articles

Identification of key transcription factors in endometrial cancer by systems bioinformatics analysis.

J Cell Biochem. 2019 09;120(9):15443–15454

Authors: Song Y, Chen QT, He QQ

Abstract

Endometrial cancer (EC) is one of the most common malignant
diseases worldwide. Although many studies have been performed
on EC, a systems analysis between transcription factors (TFs) and
EC relationship remains poorly characterized. Here, we present a
systems bioinformatics analysis of TFs in EC patient samples to
identify key TFs in EC. First, dysregulated and survival-related TFs
were identified in EC using data from The Cancer Genome Atlas
database and Gene Expression Omnibus. Second, we investigated
the mechanisms of dysregulated TFs and tested whether their
expression is correlated with prognosis of EC. Finally, we
addressed new perspectives in EC biomarker research, including
comprehensive knowledge of previously suggested candidate
biomarkers in conjunction with novel mass spectrometry-based
proteomic technologies with enhanced sensitivity and specificity
not yet applied to EC studies, enabling a directed clinical
perspective of the study design. Our study identified three
promising TFs, E2F1, HMGAI, and PGR, which closely correlate
with EC. Although treatments targeting TFs are not always
efficient, these TFs may be useful as biomarkers for the diagnosis
and prognosis of EC. Furthermore, we found that these
dysregulated TFs and their target genes are primarily involved in
the cell cycle and may promote endometrial carcinoma occurrence
and development. Using integrated bioinformatic analysis, we
identified candidate genes and pathways in EC, which could
improve our understanding of the etiology and underlying
molecular events of EC. Furthermore, these candidate genes and
pathways could be therapeutic targets for EC.

PMID: 31037767 [PubMed — indexed for MEDLINE]
Knockdown of LASP2 inhibits the proliferation, migration, and invasion of cervical cancer cells.

Related Articles

Knockdown of LASP2 inhibits the proliferation, migration, and invasion of cervical cancer cells.

J Cell Biochem. 2019 09;120(9):15389–15396
Authors: Zhang Y, Zhang L

Abstract
LIM and SH3 protein 2 (LASP2) belongs to nebulin family. It has been proven that LASP2 is involved in several cancers; however, its role in cervical cancer is unclear. Herein, we showed that LASP2 was highly expressed in cervical cancer tissues and cell lines. To knockdown LASP2 in cervical cancer cells, small interfering RNAs (siRNAs) targeting LASP2 (si-LASP2) were used. We found that cell proliferation, migration/invasion were markedly reduced after si-LASP2 transfection. A significant increase in E-cadherin expression, and decrease in N-cadherin and vimentin expressions were observed in si-LASP2 transfected cervical cancer cells. Knockdown of LASP2 caused significant inhibitory effect on the PI3K/Akt pathway. Treatment with the activator of the PI3K/Akt pathway, 740Y-P, abolished the effects of si-LASP2 transfection on cervical cancer cells. These findings suggested that LASP2 may be an oncogene through regulating the PI3K/Akt pathway in cervical cancer.

PMID: 31026088 [PubMed — indexed for MEDLINE]

Controlled Release of Therapeutic Agents with Near-Infrared Laser for Synergistic Photochemotherapy toward Cervical Cancer.

Related Articles

Controlled Release of Therapeutic Agents with Near-Infrared Laser for Synergistic Photochemotherapy toward Cervical Cancer.

Anal Chem. 2019 05 21;91(10):6555–6560
Authors: Zhu L, Wang C, Pang DW, Zhang ZL

Abstract
Different kinds of artificial drug delivery systems (DDS) have been widely exploited and utilized toward effective tumor therapy. Establishing a biocompatible DDS with a flexible release of the therapeutic agents has been a challenges and an impetus to the development of tumor diagnosis and therapy fields. Herein, the chemotherapeutic agents doxorubicin hydrochloride (DOX) and photosensitizer indocyanine green (ICG) were simultaneously packaged into the cavity of microvesicles (MVs) through the electroporation technique. With the aid of MVs-based DDS, the packaged therapeutic agents could be effectively delivered into the target tumor cells. The ambient temperature sharply increased because of controllable external near-infrared (NIR) laser irradiation, which induced the cracking of MVs-based DDS, directly accompanied by the dynamic and controllable release of DOX and ICG. Almost all the tumor cells could be killed by the synergistic effect of the released DOX and ICG. This research successfully established a smart DDS with NIR laser inducing controllable release of therapeutic agents for effective synergistic photochemotherapy toward cervical cancer.

PMID: 30994332 [PubMed — indexed for MEDLINE]

The advent of human papillomavirus detection for cervical screening.

Related Articles

The advent of human papillomavirus detection for cervical screening.

Authors: Morris BJ

Abstract
PURPOSE OF REVIEW: This review updates progress in the human papillomavirus (HPV)-based revolution in cervical screening and vaccination predicted to eventually eliminate cervical cancer.

RECENT FINDINGS: HPV PCR, patented by the author in 1987, has recently begun to replace cytology for primary cervical screening. I highlight the findings from large randomized clinical trials that have brought about this change, and progress with implementation. Australia was the first to introduce a national, publicly-funded HPV PCR-based program of primary screening, on 1 December 2017. The United Kingdom is set to follow, as are other countries. The widespread preference of self-sampling by under-screened women in particular will increase the effectiveness of population screening when using HPV tests. Coupled with improved vaccination now that more effective (nonavalent) HPV vaccines are being introduced, recent modeling predicts that cervical cancer will be markedly reduced, or even eliminated, in coming decades.

SUMMARY: The recent or pending change to more accurate cervical screening by HPV detection using PCR in various countries means less frequent screening for women. Women with an aversion to having their sample collected by a physician can collect their sample themselves, either at the doctor’s rooms or at home, the sample then being mailed to the testing laboratory.

PMID: 30946033 [PubMed — indexed for MEDLINE]
Genome-wide profiling of human papillomavirus DNA integration in liquid-based cytology specimens from a Gabonese female population using HPV capture technology.

Related Articles

Genome-wide profiling of human papillomavirus DNA integration in liquid-based cytology specimens from a Gabonese female population using HPV capture technology.

Abstract
Human papillomavirus (HPV) is recognized as the cause of precancerous and cancerous cervical lesions. Furthermore, in high-grade lesions, HPV is frequently integrated in the host cell genome and associated with the partial or complete loss of the E1 and E2 genes, which regulate the activity of viral oncoproteins E6 and E7. In this study, using a double-capture system followed by high-throughput sequencing, we determined the HPV integration status present in liquid-based cervical smears in an urban Gabonese population. The main inclusion criteria were based on cytological grade and the detection of the HPV16 genotype using molecular assays. The rate of HPV integration in the host genome varied with cytological grade: 85.7% (6÷7), 71.4% (5÷7), 66.7% (2÷3), 60% (3÷5) and 30.8% (4÷13) for carcinomas, HSIL, ASC-H, LSIL and ASCUS, respectively. For high cytological grades (carcinomas and HSIL), genotypes HPV16 and 18 represented 92.9% of the samples (13÷14). The integrated form of HPV16 genotype was mainly found in high-grade lesions in 71.4% of samples regardless of cytological grade. Minority genotypes (HPV33, 51, 58 and 59) were found in LSIL samples, except HPV59, which was identified in one HSIL sample. Among all the HPV genotypes identified after double capture, 10 genotypes (HPV30, 35, 39, 44, 45, 53, 56, 59, 74 and 82) were detected only in episomal form. Our study revealed that the degree of HPV integration varies with cervical cytological grade. The integration event might be a potential clinical prognostic biomarker for the prediction of the progression of neoplastic lesions.

PMID: 30728408 [PubMed — indexed for MEDLINE]

Near-Infrared Afterglow Semiconducting Nano-Polycomplexes for the Multiplex Differentiation of Cancer Exosomes.

Related Articles

Near-Infrared Afterglow Semiconducting Nano-Polycomplexes for the Multiplex Differentiation of Cancer Exosomes.
Angew Chem Int Ed Engl. 2019 04 01;58(15):4983–4987
Authors: Lyu Y, Cui D, Huang J, Fan W, Miao Y, Pu K

Abstract
The detection of exosomes is promising for the early diagnosis of cancer. However, the development of suitable optical sensors remains challenging. We have developed the first luminescent nanosensor for the multiplex differentiation of cancer exosomes that bypasses real-time light excitation. The sensor is composed of a near-infrared semiconducting polyelectrolyte (ASPn) that forms a complex with a quencher-tagged aptamer. The afterglow signal of the nanocomplex (ASPNC), being initially quenched, is turned on in the presence of aptamer-targeted exosomes. Because detection of the afterglow takes place after the excitation, background signals are minimized, leading to an improved limit of detection that is nearly two orders of magnitude lower than that of fluorescence detection in cell culture media. Also, ASPNC can be easily tailored to detect different exosomal proteins by changing the aptamer sequence. This enables an orthogonal analysis of multiple exosome samples, potentially permitting an accurate identification of the cellular origin of exosomes for cancer diagnosis.

PMID: 30702188 [PubMed — indexed for MEDLINE]

A DHX9-lncRNA-MDM2 interaction regulates cell invasion and angiogenesis of cervical cancer.

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A DHX9-lncRNA-MDM2 interaction regulates cell invasion and angiogenesis of cervical cancer.
Cell Death Differ. 2019 09;26(9):1750–1765
Authors: Ding X, Jia X, Wang C, Xu J, Gao SJ, Lu C

Abstract
Cervical cancer (CC) is the third most common carcinoma and the fourth leading cause of cancer-associated mortality in women. Here, we report that MDM2-DHX9 interaction mediates CC motility and angiogenesis in a long noncoding RNA-dependent fashion. A long noncoding RNA, named Inc-CCDST, is significantly downregulated in CC tissues, and binds to pro-oncogenic DHX9.
DHX9 is upregulated in CC tissue, and promotes CC cell motility and angiogenesis. The lnc-CCDST and DHX9 interaction promotes DHX9 degradation through the ubiquitin proteasome pathway. Furthermore, DHX9 bound to E3 ubiquitin ligase MDM2, and this interaction is enhanced by lnc-CCDST. Thus, lnc-CCDST promotes DHX9 degradation by serving as a scaffold to facilitate the formation of MDM2 and DHX9 complexes. Moreover, HPV oncogenes E6 and E7 abolish the expression of lnc-CCDST resulting in the increase of DHX9. Our results have revealed a novel mechanism by which high-risk HPVs promote motility and angiogenesis of CC by inhibiting expression of lnc-CCDST to disrupt MDM2 and DHX9 interaction, and DHX9 degradation, and identified a potential therapeutic target for CC.

PMID: 30518908 [PubMed — indexed for MEDLINE]