ЭКСПРЕССИЯ ГЕНОВ МЕЖДУ НОРМАЛЬНОЙ ТКАНЬЮ И КЛЕТКАМИ ЭНДОМЕТРИОИДНОГО РАКА МАТКИ

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Аннотация

Распространенность рака эндометрия растет во всем мире, что делает его серьезной проблемой общественного здравоохранения. Понимание молекулярных процессов, лежащих в основе этого заболевания, имеет важное значение для создания успешных планов лечения. Нашей целью было описать транскрипционные изменения в тканях рака эндометрия по сравнению со здоровой тканью, которая была исправлена. С помощью секвенирования РНК было обнаружено 2483 дифференциально экспрессируемых гена (DEG), включая те, которые кодируют белки, длинные некодирующие РНК (lncRNAs) и микроРНК (miRNAs). Дифференциальная экспрессия многочисленных известных генов, связанных с раком, включая MYC, AKT3, CCND1 и CDKN2A, заслуживает внимания.

Ключевые слова: Рак эндометрия, транскриптом, дифференциально экспрессируемые гены, некодирующие РНК, анализ пути.

GENE EXPRESSION BETWEEN NORMAL TISSUE AND UTERINE ENDOMETRIOID CANCER CELLS

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Abstract

The prevalence of endometrial cancer is on the rise worldwide, making it a serious public health concern. Comprehending the molecular processes that underlie this illness is essential to creating successful treatment plans. Our goal was to describe

the transcriptional alterations in endometrial cancer tissues in comparison to healthy tissue that had been corrected. 2483 differentially expressed genes (DEGs), including those that code for proteins, long non-coding RNAs (lncRNAs), and microRNAs (miRNAs), were found by RNA sequencing. The differential expression of numerous known cancer-related genes, including MYC, AKT3, CCND1, and CDKN2A, was noteworthy.

Keywords: Endometrial cancer, transcriptome, differentially expressed genes, non-coding RNAs**,** pathway analysis.

Introduction

One of the most prevalent malignancies in women and the most prevalent gynecological cancer in developed nations is endometrial cancer. Furthermore, uterine cancer death rates [3] and incidence [1,2] are on the rise, which is alarming.

Obesity is the most significant risk factor for endometrial cancer aside from age and one of the main contributors to the elevated incidence rates [2]. Endometrial cancer has the greatest correlation with obesity among the 20 most prevalent tumor forms [4]. For every 5 kg/m2 increase in BMI, the risk of endometrial cancer increases quickly [5, 6]. The conversion of adrenal androgens into estrogen by adipose tissue raises estrogen levels. Proliferation of the endometrium is stimulated. Additionally, obesity is frequently linked to hyperinsulinemia and insulin resistance, which can increase the bioavailability of insulin-like growth factor 1 (IGF-1) and estrogen and further stimulate the endometrium. In addition to being linked to enhanced endometrial proliferation, these factors also stimulate the PI3K–AKT–mTOR signaling pathway [2]. Endometrial cancer's current molecular categorization was introduced in 2013 [8] and is still being developed []. This categorization focuses on alterations in the nuclear DNA of tumor cells, particularly copy number variations, mismatch repair (MMR) deficiencies that cause microsatellite instability, and mutations in the polymerase epsilon (POLE) and TP53 genes [7,8]. Additionally, RNA expression changes that were not caused by gene mutations were considered. The group that lacked mismatch repair was found to have lower levels of MLH1 mRNA expression. There have been reports of increased expression of RAD50 in tumors with low copy number and increased expression of mRNAs responsible for cell cycle dysregulation (CCNE1, PIK3CA, MYC, and CDKN2A) in tumors with endometrioid histology [8].

Materials and methods

5 endometrial cancer patients from Samarkand and two from Tashkent were included in the study; all had abdominal hysterectomy procedures carried out in compliance with the Declaration of Helsinki. The majority of the patients (n = 18) were Samarkandian. The patients' average age was 62.19 years, and their average

BMI was 33.06 kg/m2, albeit one patient's height was unknown. The histology of each tumor was endometrioid.

The endometrial cancer's FIGO Grades and Stages were determined by analyzing the uterine tissue. About 25 mg samples of the cancer and healthy tissues were submerged in DNA/RNA Shield (Zymo Research). After that, RNA was isolated from the sliced portions using the Quick-RNATM Miniprep Kit (Zymo Research). The creation of sequencing libraries, rRNA depletion, and reverse transcription were subsequently carried out using the RNA HyperPrep Kit with RiboErase (HMR) (KAPA). After that, the libraries were sequenced using Illumina's NextSeq 500 platform.

Results and discussion

According to KEGG pathway analysis, DEGs were implicated in a number of functions, such as circadian entrainment, cell adhesion, cGMP-PKG and oxytocin signaling, amino acid biosynthesis, glycolysis/gluconeogenesis, cell cycle control, and more (Fig. 1C). Wnt signaling, cell-extracellular matrix interactions, smooth muscle contraction, and extracellular matrix structure were all downregulated, which is consistent with the KEGG pathways, Reactome database pathways, and Gene Ontology (GO) enrichment studies. Most of the participants were 60-year-old postmenopausal women. As a known risk factor for this condition, obesity was represented by the cohort's average BMI, which was within the obese range. The relationship between BMI and differential gene expression has also been previously noted, as it has been shown that a higher BMI is linked to a non-specific molecular profile and that genes linked to obesity are markedly elevated with increasing BMI among endometrioid ECs [9,10]. The top 20 differentially expressed protein-coding genes comprised a number of known endometrial cancer prognostic markers. CTSV, CEACAM1, and PDIA3 expression is linked to positive patient outcomes, according to The Human Protein Atlas, especially when it is high, as it was in our cohort [11]. Recent studies have further clarified the roles of some of these genes in endometrial cancer: low HOXA13 expression is linked to poorer survival rates and may be a prognostic biomarker [14], DUSP1 transcription inhibits tumor growth and invasion while promoting apoptosis through regulation of the MAPK pathway [13], and KLF2 transcription suppresses cell proliferation, invasion, and migration [12].

Conclusions

By confirming and comparing its differential expression data to earlier research, this study contributes to the expanding body of knowledge on the molecular foundation of endometrial cancer and offers insights into the molecular mechanisms underlying the disease.

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