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KRT17 confers paclitaxel-induced resistance and migration to cervical cancer cells

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ABSTRACT

Aim: To understand potential pro-oncological effects of lower dose paclitaxel treatment in cervical cancer cells, we investigated the potential roles of KRT17 on migration and proliferation of cervical cancer cells which might respond to cytoskeletal-based drugs treatments.

Materials and methods: We extracted the clinic data of cervical cancer patients from TCGA database to investigate mRNA expression of different keratins. HPV genotypes were identified by reverse transcription PCR. krt17 mRNA and EMT markers were quantified by real-time PCR. krt17 and EMT markers protein were immunoblotted by western blot. Cell viability was detected by CCK8. Cell migration was performed by transwell migration assay.

Key findings: Our results showed that HPV16 infection correlated with the expression of KRT17 in cervical cancer cell lines. KRT17 knockdown would decrease Snail2 and elevate E-Cadherin to inhibit migration of Caski cells and SiHa cells. Lower dose of paclitaxel promoted SiHa proliferation, it also significantly promoted the migration of Caski cells. Otherwise, colchicine and higher dose of paclitaxel dose-dependently suppressed the proliferation and migration of Caski cells and SiHa cells. Moreover, KRT17 knockdown significantly facilitated cytoskeletal-based drugs to inhibit migration and induce cytotoxicity in cervical cancer cells.

Significance: KRT17 played pivotal oncogenic roles in cell survival, migration and paclitaxel-induced resistance of cervical cancer cells. Thus, KRT17 would serve as a promising target for compromising paclitaxel-induced resistance and metastasis.

1. Background

Cervical cancer remains as one of the most common gynecological cancers in the developing countries, including China, and the squamous cell carcinomas prevails in all types of cervical cancer cases. High-risk HPVs infection, including HPV16, HPV18, HPV31, HPV33 and HPV35, contributed to high morbidity of cervical cancer [1,2]. Previous studies have showed that high-risk HPVs infection were persistent and long-standing to gradually transform the cervical epithelial cells at the early premalignant stages [2,3]. On the molecular events, the viral E6/E7 protein played pivotal roles in promoting cervical epithelial hyperplasia, carcinogenesis and progression via dysfunction of p53, genomic instability, activation of oncogenic signaling [2–5].

Cytoskeleton is mainly composed of microfilaments, microtubules, and intermediate filaments. Keratins belong to intermediate filament, which distribute to various cell types, at least including keratinocytes and epithelial cells. Biologically, keratins are fibrous structural proteins which present as the key cellular structural material to form the cornified layer, which protect these cells from damage or physical stress [6,7]. Pathologically, abnormal expressions of keratins involve in non-tumor diseases and cancers [6,8]. More concretely, dysfunction of KRT8/18/19 correlated with liver diseases, and dysfunction of KRT1/

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5/10/14 correlated with epidermal skin diseases, KRT23 was elevated in microsatellite-stable colon tumors [9]. In cervical cancer, KRT7/8/13/17/18/19 might serve as the predictor which involved in carcinogenesis, migration and chemoresistance [10,11]. Among these keratins, upregulation of KRT17 was confirmed in advanced cervical cancer samples which associated with poor survival [12]. Moreover, only KRT17 was confirmed from a transgenic mouse cervical cancer model to show that it was associated with cervical carcinogenesis [13].

Chemotherapy remains as the main treatment for the higher-grade cervical cancer. In the high-grade cervical cancer, chemotherapy shrank the tumor lesions which would facilitate the success of surgery, or eliminated the residual tumor cells after surgery. However, chemoresistance and recurrence have remained as a complicated context and seemed to be inevitable in the certain cases. Recent studies showed that platinum-based chemoresistance correlated with upregulation of LGR5 in cervical cancer stem cells, increasing cervical tumor-derived G-CSF, abnormal activation of small GTPase [14–16]. The other studies showed that taxel-based chemoresistance correlated with aberrant prenylation of Ras, aberrant expression of RTN4 and MDR [17–19]. Moreover, modified dose-dense paclitaxel seemed to be a tolerable and relatively effective salvage monotherapy for recurrent cervical cancer [20], while combination of paclitaxel/ifosfamide/platinum exhibited a better response rate for recurrent cervical cancer [21].

Interestingly, accumulating studies have indicated that the EMT (epithelial-mesenchymal transition) process has a certain connection with chemoresistance during cervical cancer chemotherapy, rather than appeared as the two independent events [22]. HPV16-E7/PVT1/miR-195 axis modulated paclitaxel-related chemoresistance of cervical cancer cells via regulating EMT process [23]. Previous study had showed that HPV16/KRT17 axis played an important role in cervical carcinogenesis [13], KRT17 also promoted migration/invasion of various cancers [24–26]. However, the effect of KRT17 on migration/invasion or chemoresistance of cervical cancer remains largely unknown.

In the present study, we investigated the role of KRT17 on migration and cytoskeletal-based drugs chemotherapies of cervical cancer. In line with the others, we confirmed that Caski cells and SiHa cells were carried HPV16, but not C33A cells and Hela cells. Our results showed that HPV16 infection was correlated with the expression of KRT17 in cervical cancer cell lines. KRT17 knockdown inhibited the migration of Caski cells and SiHa cells, facilitated paclitaxel and colchicine to induce cytotoxicity in cervical cancer cell lines. Therefore, KRT17 would serve as a promising target for compromising paclitaxel-induced resistance and metastasis.

2. Methods and materials

2.1. Cell lines and culture

Hela, SiHa, C33A and Caski cells were purchased from ATCC (Manassas, VA). Caski cells was maintained in complete RPMI 1640 medium containing 10% fetal bovine serum, 100 U/ml penicillin, and 100 μg/ml streptomycin (Life Technologies, Inc., Carlsbad, CA). The other cells were maintained in complete growth Dulbecco's Modified Eagle Medium (DMEM) containing 4.5 g/L glucose (Life Technologies, Inc., Carlsbad, CA), 10% fetal bovine serum, 100 U/ml penicillin, and 100 μg/ml streptomycin. All cell lines were incubated at 37 °C with 5% CO_2.

2.2. HPV genotyping

Genomic DNA samples from cervical cancer cell lines were isolated by using EasyPure Genomic DNA Kit (Transgen Biotech, China) according to manufacturer's instruction. Sequence-specific primers for HPVs were amplified by using 2 × EasyTaq PCR SuperMix kit (Transgen Biotech, China) according to manufacturer's instruction. The primer and PCR reaction condition were described as previous study [27]. All PCR products were loaded onto a 2% agarose gel and further captured and analyzed by the Gel Logic 1500 imaging system (Eastman Kodak, USA).

2.3. Establishment of stable knockdown of KRT17 cell lines

Three pairs of specific shRNA sequences which target three sites of KRT17 encoding sequence and one pair of scramble shRNA sequence were cloned into the lentiviral shRNA-expressing vector, pHBLv-U6-Scramble-Puro (HANBIO, China). The scramble shRNA sequence was TTCTCCGAACGTGTCACGT, three KRT17 shRNA sequences were GCG TGACCAGTATGAGAAGAT, TGGTGCAGAGTGGCAAGAGTGAGAT and CTGACTCAGTACAAGAAAGAA. Scramble-shRNA-expressing and KRT17-shRNA-expressing lentiviruses were prepared according to manufacturer's instruction. sh-CTRL-SiHa cells or sh-CTRL-Caski cells were generated by the scramble shRNA lentiviral infection, sh-KRT17-SiHa cells or sh-KRT17-Caski cells were generated by the combination infection of three KRT17 shRNA lentivirus. All infected Cells were selected in the complete growth medium containing 2 μg/ml puromycin (Sigma, USA). After three weeks, the clones were expanded and subjected to determining the efficiency of knockdown of KRT17.

2.4. RNA isolation and quantitative RT-PCR

Total RNA was extracted using Trizol reagent (Invitrogen, USA) according to manufacturer's instructions. Total RNA was reversely transcribed using TransScript One-Step gDNA Removal and cDNA Synthesis SuperMix (Transgen Biotech, China). cDNA was amplified using FastSYBR Mixture with High ROX (CWBIO, China). The PCR cycling condition was set as follow: pre-denaturation at 95 °C for 10 min followed by 40 cycles of 95 °C for 15 s, 60 °C for 40 s. All real-time PCR primers were listed in Supplementary data 1. Relative mRNA expression levels of target genes were normalized by comparing to GAPDH, and calculated using the $2^{-\Delta\Delta Ct}$ method [28].

2.5. Cell counting kit-8 assay

Cells were seeded into 96-well plates at 10000 cells/well, after culture for 24 h, cells were treated with indicated concentrations of paclitaxel or colchicine (Selleck, USA) for further 24 to 48 h, and then cellular vitality was measured by cell counting kit-8 (Beyotime, China). The cytotoxicity (%) = [1 – (OD from tested cells) / OD from control cells] × 100%.

2.6. Western blot assay

Cells were collected and lysed on ice by RIPA lysis buffer (Beyotime, China) containing 1% PMSF (phenylmethanesulfonyl fluoride). Protein concentration was determined using BCA (bicinchoninic acid) protein assay kit (Beyotime, China). 50 μg of total lysate protein sample was separated by SDS-PAGE and transferred onto the PVDF membrane (BIO-RAD, USA). After blocking, membranes were incubated overnight at 4 °C with primary antibodies. Membranes were then incubated with secondary antibody for 1 h at room temperature, and results were acquired using the Gel Logic 1500 imaging system (Eastman Kodak, USA). Primary antibodies were used as following: anti-beta actin antibody (sc-47778) were purchased from Santa Cruz (Texas, USA), Epithelial-Mesenchymal Transition (EMT) Antibody Sampler Kit (#9782) and anti-TWIST1 Antibody (#46702) were purchased from Cell Signaling Technology (Beverly, MA; USA), anti-Cytokeratin 17 antibody (ab109725) was purchased from Abcam (Cambridge, UK). Anti-rabbit or anti-mouse secondary antibody was purchased from Beyotime (Shanghai, China). Beta actin was used as internal standards.

2.7. Cell adhesion and viability assay

Cells were seeded into 96-well plates at 5000 cells/well, the growth medium was pre-added CCK8 solution, after incubating 30 min, cellular viability of each well was measured, and set as the 0.5 h timepoint. After acquiring the OD value, each well was washed with PBS triple times, and then added equal volume of fresh cells growth medium plus CCK8 solution to incubate it for next 30 min, OD value was acquired and set as the 1 h timepoint. Each well was again washed with PBS triple times, and added equal volume of fresh cells growth medium to incubate it for 30 min, CCK8 was re-added to each well and incubated it for next 30 min, OD value was acquired and set as the 2 h timepoint. Each well was again washed with PBS triple times, and then added equal volume of fresh cells growth medium to incubate it for 1 h and 30 min, CCK8 was re-added to each well and incubated it for next 30 min, OD value was acquired and set as the 4 h timepoint. Each well was again washed with PBS triple times, and then added equal volume of fresh cells growth medium to incubate it for 1 h and 30 min, CCK8 was re-added to each well and incubated it for next 30 min, OD value was acquired and set as the 6 h timepoint. Each well was again washed with PBS triple times, and then added equal volume of fresh cells growth medium to incubate it for 5 h and 30 min, CCK8 was re-added to each well and incubated it for next 30 min, OD value was acquired and set as the 12 h timepoint.

2.8. Transwell migration assay

24-well transwell polystyrene plates with inserts containing 8.0 μM pore size in a polycarbonate membrane (REF. 3422) was purchased from COSTAR (Kennebunk ME, USA). 5000 single cells were re-suspended in 100 μl FBS-free medium and added to each insert, lower chamber contained 10% FBS medium with or without drugs which depended on the design of experiment. After incubation for the indicated time, cells those remained in the inserts were gently wiped by cotton sticks, those migrated cells were fixed and stained by 1% crystal violet, and then captured by microscope. All pictures were analyzed by Image J software from National Institutes of Health (http://rsb.info.nih.gov/ij/download.html).

2.9. Statistical analysis

Numerical data were expressed as mean ± S.D., and statistical analyses were performed using unpaired *t*-test and one-way ANOVA (GraphPad Software Inc., La Jolla, CA). $p < 0.05$ was considered to be statistically significant. Experiments were independently performed at triplicated or more, and results were qualitatively identical. Representative experiments were shown.

3. Results

3.1. The expression of HPV and keratins in cervical cancer cell lines

HPV infections are very common and potential risk in the initiation of cervical cancer. Herein, we first used the cBioPortal online analyzing tool (the cBioPortal for Cancer Genomics) (Ceramiet al, 2012; Gao et al., 2013) to extract cervical cancer patients' data from The Cancer Genomic Atlas (TCGA) database to investigate the expression of high-carcinogenic keratins. Our results showed that expression of KRT17 was the highest among these keratins (Fig. 1A). We then screened the expression of high-risk HPVs in a panel of cervical cancer cell lines. Our results showed that the expression of HPV-16/18/31/33/35 were negative in C33A cells, while the expression of HPV-16 was positive in Caski cells and SiHa cells, the expression of HPV-18 was positive in Hela cells (Fig. 1B). Moreover, the mRNA and protein expression of KRT17 were extremely higher in HPV-16 positive cervical cancer cells lines (Caski cells or SiHa cells) while compared to HPV-16 negative cervical cancer cells lines (C33A cells or Hela cells) (Fig. 1C and D).

3.2. KRT17 knockdown decreased migration and viability in cervical cancer cell lines

To investigate the bio-function of KRT17 in cervical cancer, we first downregulated the expression of KRT17 in Caski cells and SiHa cells, our results showed that KRT17 was successfully downregulated by lentiviral-induced RNAi (RNA interference) (Fig. 2A). KRT17 knockdown slightly decreased the adhesion at 0.5 h timepoint in SiHa cells, yet there was no statistic difference. On the other hand, KRT17 knockdown significantly decreased cell viability under stress condition (Fig. 2B). KRT17 knockdown decreased almost 1.9 fold and 1.8 fold migration at 4 h and 8 h timepoint in SiHa cells (Fig. 2C and D). KRT17 knockdown dramatically decreased migration at 24 h timepoint in Caski cells, while there was almost decreasing 1.7 fold migration at 48 h timepoint (Fig. 2E and F).

3.3. KRT17 regulated expressions of EMT markers in cervical cancer cell lines

We next investigated the effect of KRT17 on expressions of EMT markers in cervical cancer cell lines. We first screened expression of EMT markers in cervical cancer cell lines. We found that CDH1/2, Twist2 and Vimentin were highly expressed in the $HPV16^{-}KRT17^{low}$ cell lines (C33A cells or Hela cells), while Twist1, Snail2 or EpCAM was highly expressed in the $HPV16^{+}KRT17^{high}$ cell lines (Caski cells or SiHa cells). The expression of Snail 1 remained as a complex context in cervical cancer cell lines (Supplementary data 2). Our results further showed that expression of EpCAM, Snail2, Twist1 and CDH1 were higher than expression of the other EMT markers in Caski cells (Fig. 3A). KRT17 knockdown significantly elevated the mRNA and protein level of CDH1 (E-Cadherin), while significantly decreased the mRNA and protein level of Snail2 in Caski cells, yet there was no significant difference of the other EMT marker (Fig. 3B and E). Expression of EpCAM, Snail2, Twist1 and CDH1 were also higher than expression of the other EMT markers in SiHa cells (Fig. 3C). KRT17 knockdown also significantly elevated the mRNA and protein level of CDH1 (E-Cadherin) in SiHa cells, while significantly decreased the mRNA and protein level of Snail2 and Twist1 (Fig. 3D and E).

3.4. KRT17 knockdown reversed paclitaxel-induced migration and proliferation in cervical cancer cell lines

As KRT17 belongs to the skeletal protein, we then investigated the potential effect of KRT17 on regulating EMT process with/without treatments of cytoskeletal-based drugs. Our results showed that paclitaxel induced cytotoxicity in a dose and time dependent manner in Caski cells (Fig. 4A). Interestingly, lower dose of paclitaxel was more prone to elevate viability of SiHa cells, prolonging the time of paclitaxel treatment significantly induced resistance in SiHa cells (Fig. 4B). Colchicine also induced cytotoxicity in a dose and time dependent manner in Caski and SiHa cells, but it didn't induced resistance in Caski cells or SiHa cells at any indicated dose (Fig. 4C and D).

We then used lower dose (below its IC50 value) of cytoskeletal-based drugs for further experiments. Our results showed that 1 ng/ml paclitaxel significantly promoted migration in Caski cells, yet KRT17 knockdown abolished this effect. Moreover, KRT17 knockdown facilitated paclitaxel and colchicine to inhibit migration in Caski cells, but there was no significant difference at 30 ng/ml colchicine treatment (Fig. 4E and G). KRT17 knockdown also facilitated paclitaxel and colchicine to inhibit migration in SiHa cells, except 30 ng/ml colchicine treatment (Fig. 4F and H). KRT17 knockdown also significantly facilitated paclitaxel and colchicine to decrease cellular viability in SiHa cells (Fig. 4I and J).

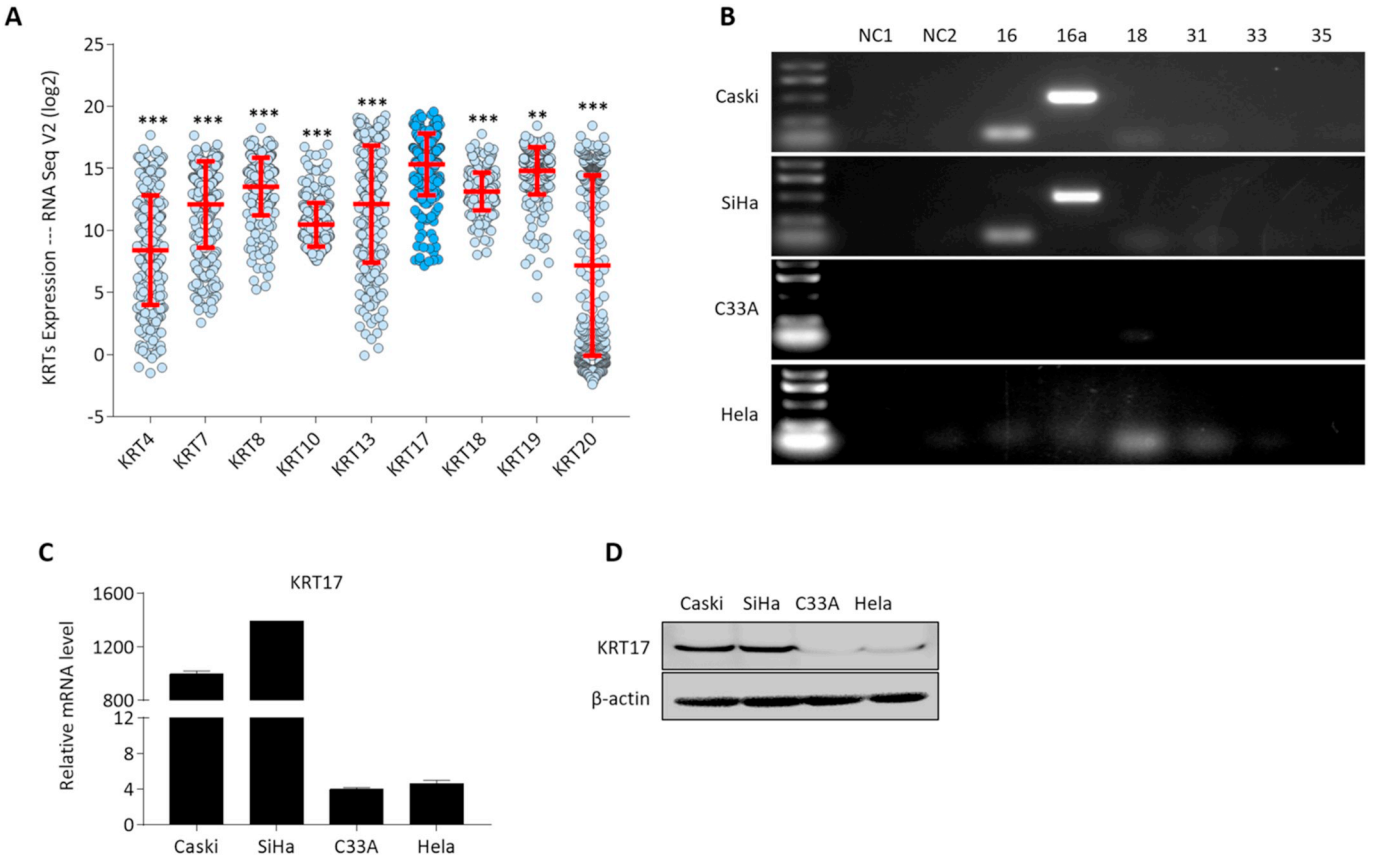

Fig. 1. HPV16 infection correlated with the expression of KRT17 in cervical cancer cell lines. (A) Keratins expression of 307 cervical cancer patients were extracted from TCGA database, and then processed by cBioPortal online analyzing tools (KRT17 vs the other keratin). (B) The expression of high-risk HPVs in cervical cancer cell lines, sample of NC1 was amplified by SiHa genome DNA without any primers, sample of NC2 was amplified by HPV16 primers without any DNA template. Besides, both of HPV16 and HPV16a were used to amplify the HPV16 cDNA, but the sequence of primers was different from each other. (C) The mRNA expression of KRT17 in cervical cancer cell lines. (D) The protein expression of KRT17 in cervical cancer cell lines. $^{*}p < 0.05$. $p^{**} < 0.01$, $p^{***} < 0.001$.

4. Discussion

Taxane-based drugs remain as the first line chemotherapy medications in a variety of cancers, though chemoresistance and serious side effects are inevitable [29]. There is a dilemma in design of taxane-based drugs. Previous taxane-based drugs presented lower biological availability and higher elimination, and required higher dose delivery to cover these defects, but which caused serious side effects. Otherwise, simplified structures of paclitaxel would compromise its certain bioactivities [30]. The concentration of paclitaxel within tumor was usually too low to reach the effective concentration, which was due to its fast clearance rate in systemic circulation. Moreover, lower concentration of paclitaxel within tumor might also issue other problems. In the present study, we uncovered a potential mechanism of paclitaxel chemoresistance. Lower dose paclitaxel promoted migration and survival of cervical cancer cells, KRT17 knockdown impaired migration and decreased viabilities of cervical cancer cells, and then facilitated cytoskeletal-based drugs to induce cytotoxicity.

Previous studies had shown that keratins served as diagnostic markers in cervical cancer [9–11]. In the present study, we thus screened the expression of keratins in cervical cancer patient's data from TCGA database. The result showed that KRT17 was higher expressed than the other keratin in cervical cancer patients. In line with this finding, previous study showed that KRT4 was downregulated in cervical cancer patients, while KRT17 was elevated in advanced cervical cancer patients and correlated with poor diagnosis [12]. KRT17 knockout would attenuate the tumorigenesis and progression of HPV16 knockin mice [13]. We then screened the expression of high-risk HPVs and KRT17 in a panel of cervical cancer cell lines, our results showed that HPV16 infection was positively correlated with the expression of KRT17 in cervical cancer cell lines, the other study also found that transgenically expressing high-risk HPV16 E7 oncoprotein in mice skin would present with epithelial hyperplasia via increasing expression of stress keratins KRT6, KRT16, and KRT17 [31]. Thus, we used Caski cells and SiHa cells for subsequent experiments.

Previous studies had shown that KRT17 played important roles in maintaining multiple functions of keratocyte, which contributed to formation, maintenance and repair of various skin and its appendages [32,33]. We then downregulated expression of KRT17 to explore the bio-function of KRT17 in cervical cancer cells. Our results showed that KRT17 knockdown significantly decreased cellular viability under stress condition. In line with the other study, they also found that intermediate filaments were involved in stress response and other basic cell functions [34]. Our results further showed that KRT17 knockdown also significantly decreased migration of Caski cells and SiHa cells. To investigate the candidate EMT markers which were regulated by KRT17, we screened mRNA expression of EMT markers in a panel of parent cervical cancer cell lines. Our results suggested that expression of Twist1, Snail2 and EpCAM positively correlated with expression of KRT17, which might promote migration of Caski cells and SiHa cells. Otherwise, expression of CDH1 negatively correlated with expression of KRT17, which would inhibit migration of Caski cells and SiHa cells. We further downregulated KRT17 expression to investigate potential relationship between KRT17 and these EMT markers. Our results showed that KRT17 knockdown significantly elevated mRNA and protein level of E-Cadherin in Caski cells and SiHa cells, while significantly decreased mRNA and protein level of Snail2. KRT17 knockdown didn't change the expression of Twist1 in Caski cells, but it did significantly

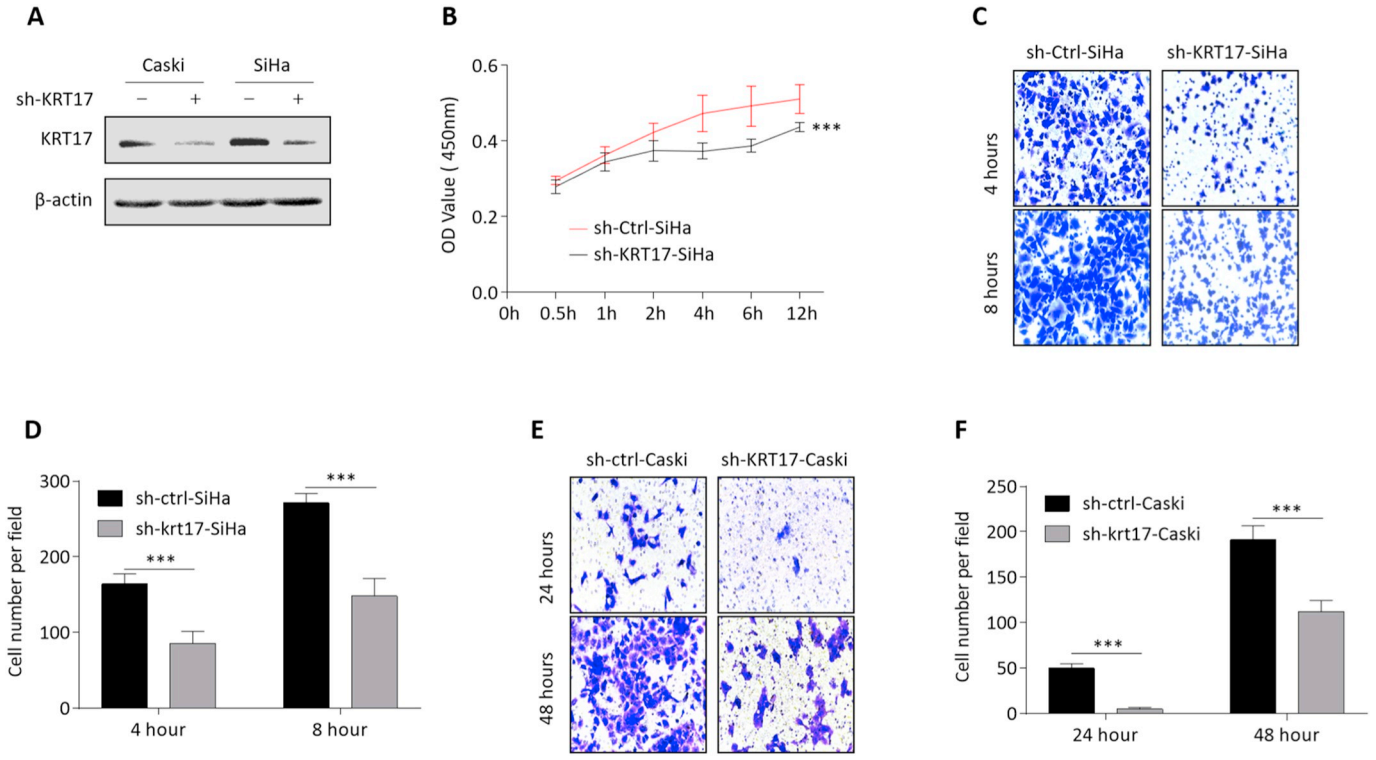

Fig. 2. KRT17 knockdown decreased viability and migration in cervical cancer cell lines. (A) Immunoblot analysis confirmed the KRT17 knockdown efficiency in Caski cells and SiHa cells with or without lentiviral-induced RNAi. (B) After seeding the indicated cells, each well was washed with PBS tripe times at the end of the indicated timepoint, and then cellular viability was quantified by CCK8 assay at each timepoint. (C) Migration of sh-Ctrl-SiHa cells and sh-KRT17-SiHa cells were measured by the transwell migration assay (200X). (D) Migrated cell number per field from (C) was quantified by Image J software. (E) Migration of sh-Ctrl-Caski cells and sh-KRT17-Caski cells were measured by the transwell migration assay (200X). (F) Migrated cell number per field from (E) was quantified by Image J software. $p^* < 0.05$, $p^{**} < 0.01$, $p^{***} < 0.001$.

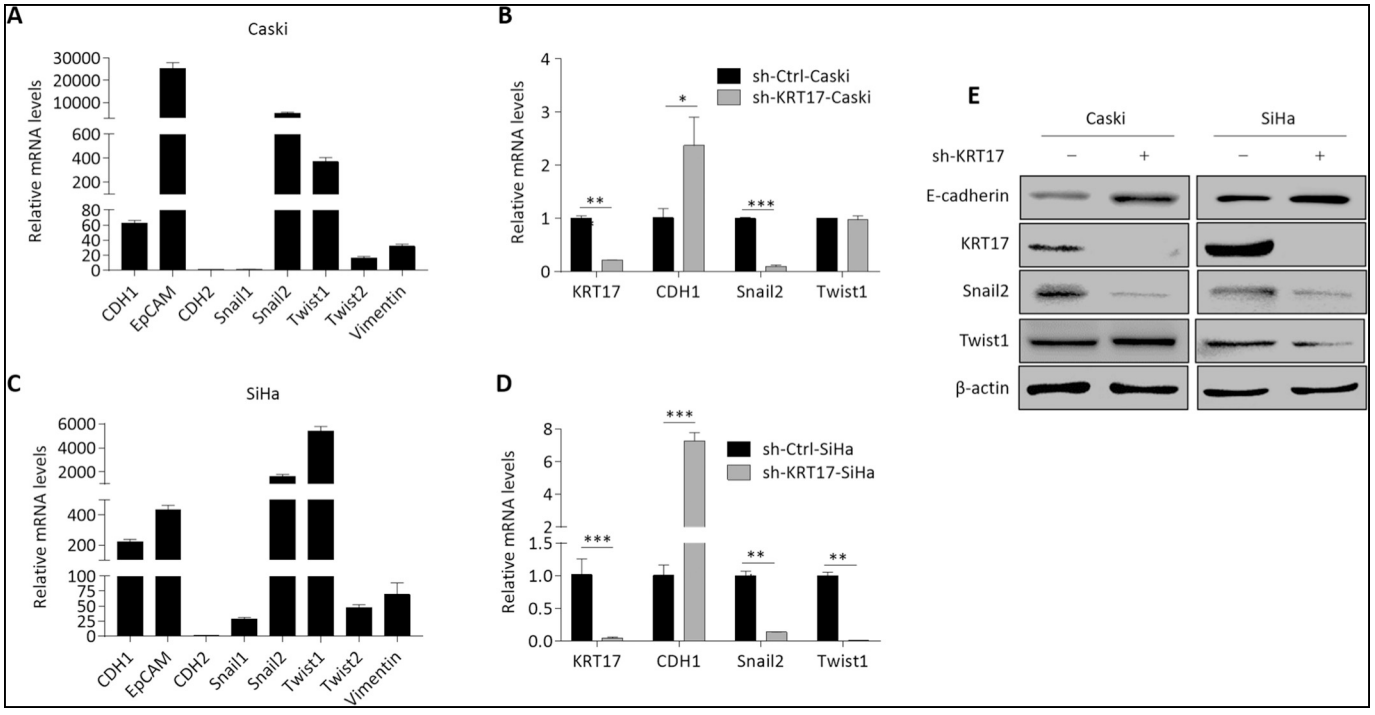

Fig. 3. KRT17 regulated expressions of EMT markers in cervical cancer cell lines. (A) The mRNA expression of indicated genes in Caski cells. (B) The mRNA expression of indicated genes in SiHa cells. (C) The mRNA expression of indicated genes in sh-Ctrl-Caski cells and sh-KRT17-Caski cells. (D) The mRNA expression of indicated genes in sh-Ctrl-SiHa cells and sh-KRT17-SiHa cells. (E) Immunoblot analysis for the indicated proteins in sh-Ctrl-Caski cells, sh-KRT17-Caski cells, sh-Ctrl-SiHa cells and sh-KRT17-SiHa cells. $p^* < 0.05$, $p^{**} < 0.01$, $p^{***} < 0.001$.

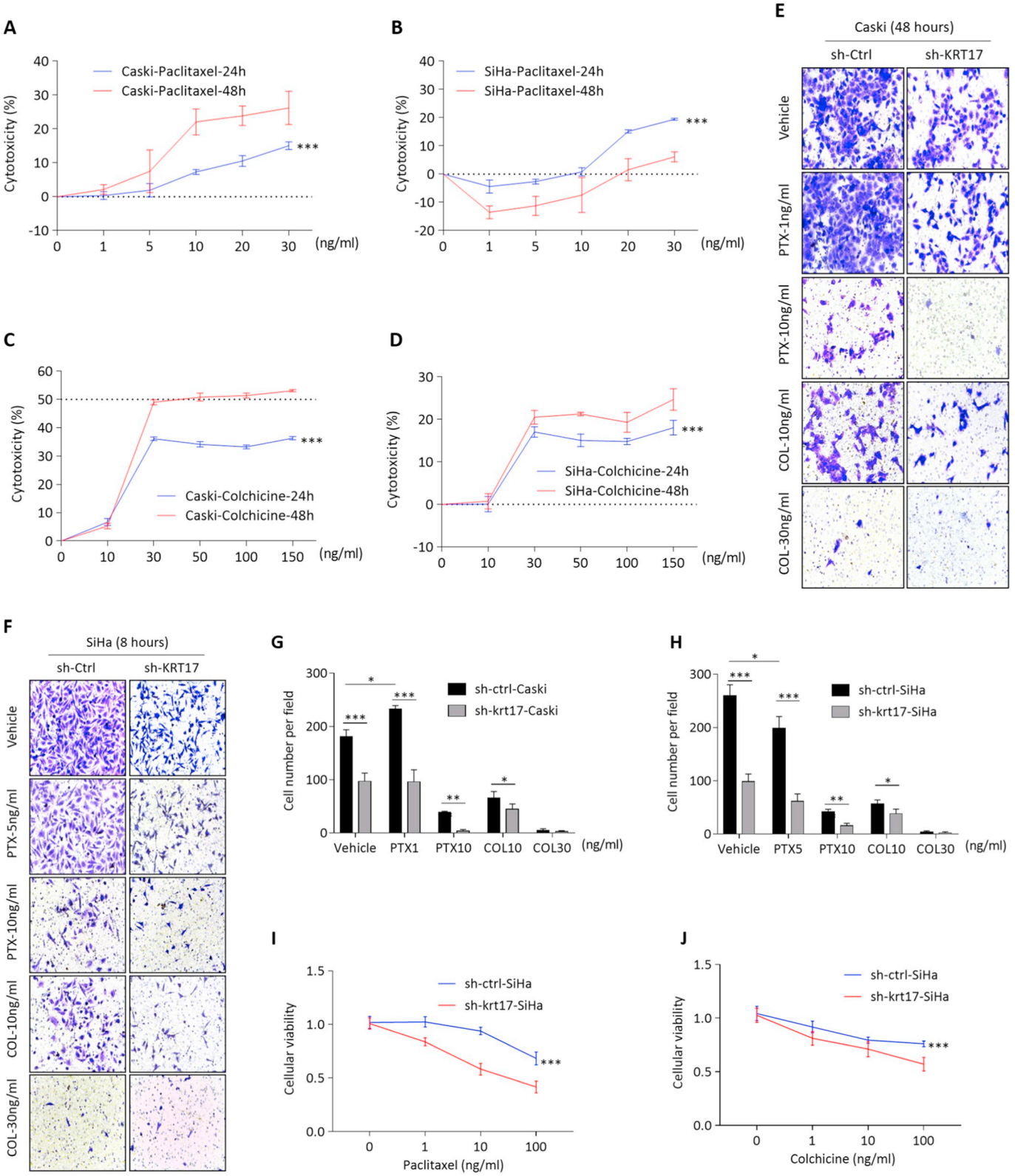

Fig. 4. KRT17 knockdown reversed paclitaxel-induced migration and proliferation in cervical cancer cell lines. (A–D) Measure paclitaxel and colchicine induced cytotoxicity in Caski cells and SiHa cells by the time- and dose- dependent experiments. (E) After treated with a series of paclitaxel (PTX) or colchicine (COL) for 48 h, migration of sh-Ctrl-Caski cells or sh-KRT17-Caski cells was measured by the transwell migration assay (200X). (F) After treated with a series of paclitaxel (PTX) or colchicine (COL) for 8 h, migration of sh-Ctrl-SiHa cells or sh-KRT17-SiHa cells was measured by the transwell migration assay (200X). (G) Migrated cell number per field from (E) was quantified by Image J software. (H) Migrated cell number per field from (F) was quantified by Image J software. (I–J) After treated with a series of paclitaxel (PTX) or colchicine (COL) for 24 h, cellular viability of sh-Ctrl-SiHa cells and sh-KRT17-SiHa cells were measured by CCK8 assay. $p^{*} < 0.05$, $p^{**} < 0.01$, $p^{***} < 0.001$.

decrease the mRNA and protein level of Twist1 in SiHa cells. Thus, our results showed that KRT17 would upregulate Snail2 and attenuate E-Cadherin to promote migration of Caski cells and SiHa cells.

Previous studies had indicated that coordination of intermediate filament and microtubule networks played important roles in cell polarization and migration [35–37]. Paclitaxel stabilizes the microtubule polymer to inhibit mitotic spindle assembly, while colchicine inhibits microtubule polymerization to suppress mitosis, thus cytoskeletal-based drugs have been widely used in cancer chemotherapy [38]. Clinically, the concentration of anticancer drug within the tumor tissue was usually very low, which might initiate another issue rather than cytotoxicity. In the present study, we treated the cervical cancer cells with low dose of cytoskeletal-based drugs to test this hypothesis. Interestingly, our results showed that lower dose of paclitaxel induced resistance in SiHa cells, in line with this finding, previous study showed that low dose paclitaxel was insufficient to inhibit wild-type cancer cell division, and even was required for growth of paclitaxel-dependent cancer cells which were isolated from parent cancer cells [39]. We next chose the dose that under its IC50 value for subsequent experiments. Our results showed that lower dose of paclitaxel significantly promoted migration of Caski cells, yet KRT17 knockdown abolished this effect. Besides, KRT knockdown facilitated paclitaxel and colchicine to significantly inhibit migration of Caski cells and SiHa cells. Otherwise, KRT knockdown significantly promoted paclitaxel and colchicine to decrease cellular viability in SiHa cells.

5. Conclusion

In the present study, we found that lower-dose of paclitaxel induced proliferation and paclitaxel-resistance in certain cervical cancer cells, while also promoted migration in the other cervical cancer cells. Interestingly, KRT17 knockdown abolished above effects of paclitaxel, which facilitated cytoskeletal-based drugs to inhibit migration and induce cytotoxicity in these cervical cancer cells.

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Conflict of interest

None declared.

Authors contribution

NHL and SQL conceived and designed the study. JYL, QFC, ZDD, XTC and HL performed the experiments, JYL and QFC analyzed and validated the data under supervision of YT, XYW and SQL. NHL prepared and submitted the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

None.

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