Emerging evidences have demonstrated that gold nanoparticles (AuNPs) have been used for cancer treatment. The aim of this study was to investigate the effects and molecular mechanisms of AuNPs on papillary thyroid carcinoma (PTC) cells (BCPAP and TPC-1). Characterizations of AuNPs were detected by UV-Vis spectra, transmission electron microscopy (TEM), and dynamic light scattering (DLS). Cell proliferation and apoptosis, migration, and invasion of PTC cells were evaluated by MTT, flow cytometry, wound healing, and transwell assays, respectively. Furthermore, qRT-PCR and western blot assays were performed to assess the protein expressions related to apoptosis and migration including caspase-3, caspase-9, Bax, Bcl-2, MMP-2, and MMP-9. The study revealed that AuNPs significantly suppressed cell viability, migration, and invasion and remarkably induced apoptosis of BCPAP and TPC-1 cells compared with the control group. Moreover, AuNPs negatively regulated the expression of CCT3 and silencing of CCT3 obviously promoted the proliferation, migration, and invasion inhibition and apoptosis induction of PTC cells combined with AuNPs. Collectively, these results highlighted the potential application of AuNPs in PTC target therapy.

1. Introduction

Thyroid cancer is one of the most common endocrine malignancies with the incidence rate stably increasing over the past 10 years [1]. Papillary thyroid carcinoma (PTC) is the major histological type which accounts for approximately 80% of human thyroid cancers [2]. The prognosis of PTC has been proven to rely on several well-established clinicopathologic indicators such as age, tumor size, histologic subtype, extrathyroidal extension, and lymph node metastases [3]. In general, 10-15% of PTC patients are diagnosed with distant metastases or poor clinical effects [4]. Additionally, disease recurrence exists in 5-20% of all patients and even went through total thyroidectomy [1]. Despite the good prognosis for a majority of PTC patients, there are scarcely any effective therapeutic methods for cervical lymph node metastasis and early invasion [5]. Therefore, it is urgent to seek a novel and valid strategy for target therapy.
Metallic nanoparticles have been demonstrated as diagnostic agents or drug delivery system in cancer therapy owing to their availability, material properties, and its ability to enhance drug selectivity against cancer cells [6, 7]. Among diversified metallic nanoparticles, gold nanoparticles (AuNPs) have raised increasing interest for their distinctive properties including nanosize, less toxicity, relatively simple synthesis, and specific targeting [8, 9]. Recently, investigators have demonstrated that monotherapy by AuNPs may be a promising therapeutic candidate for preventing tumor growth and metastasis [10]. AuNPs can inhibit the proliferation of ovarian tumor cells through suppressing the MAPK signaling pathway and promote leukemia cell apoptosis by inducing endoplasmic reticulum stress [11, 12]. AuNPs of 13 nm have been reported to induce inflammation and apoptosis in vivo [13]. In addition, AuNPs can affect morphological changes as well as migration and adhesion of human fibroblasts [14]. Furthermore, AuNPs have been reported to damage cancer cells through different pathways such as cell necrosis, induction of proapoptotic protein (Bax) expression, inhibition of tumor cells metastasis and migration, and suppression of oxidative reactive species production after short-time exposure [15]. However, AuNPs of 1-2 nm are reported to be cytotoxic to melanoma cells [16].

The aim of this study was to investigate the effects of tannic acid synthesized AuNPs on PTC by in vitro and in vivo studies. In the present study, AuNPs were characterized for physicochemical properties including shape, size, and size distribution. And we evaluated the possible antitumor biology functions of AuNPs on PTC cells, including cell viability, apoptosis, migration, and invasion. Furthermore, we investigated the potential mechanisms by which AuNPs exerted the antitumor effects on PTC cells. Altogether, our findings may serve as a novel target for developing new strategy for papillary thyroid cancer treatment.

2. Materials and Methods

2.1. Materials. Gold (III) chloride hydrate (HAuCl₄·H₂O, ≥94% Au basis), tannic acid (C₇₆H₅₆O₄₆), and sodium citrate (C₆H₅Na₃O₇·2H₂O, ≥99%) were purchased from Sigma-Aldrich. For experiments, deionized water was used. All AuNPs were stored at darkness and refrigerated at -20°C. Metal nanoparticles, gold nanoparticles (AuNPs) have raised increasing interest for their distinctive properties including nanosize, less toxicity, relatively simple synthesis, and specific targeting [8, 9].

2.2. Preparation of Gold Nanoparticles. AuNPs were prepared by a chemical reduction method as described [17]. Briefly, an aqueous solution of gold chloride hydrate was heated to boil point and stirred under reflux. Then, a reducing mixture of aqueous solutions of sodium citrate and tannic acid was added. AuNPs were formed when the color of the reducing mixture changed to red, and the mixture was stirred for another 15 min under reflux and cooled down to room temperature.

2.3. Characterizations of AuNPs. The size and shape of AuNPs were determined by transmission electron microscopy (TEM). The colloidal stability test was recorded at room temperature for 4 weeks, and absorption spectra of AuNPs were analyzed in the range of 400-700 nm by a UV-visible spectrophotometer (Shimadzu, Kyoto, Japan). The hydrodynamic diameter distribution was measured by dynamic light scattering (DLS) (Brookhaven Instruments Co., Holtsville, NY, USA). All tested nanoparticles were measured in triplicate.

2.4. Cell Culture. Two types of PTC cell lines (BCPAP and TPC-1 cells, Braunschweig, Germany) were used for biological effect research. Cells were cultured in RPMI 1640 supplemented with 10% fetal bovine serum (FBS) and 100 U/mL penicillin and 100 μg/mL streptomycin. All cell lines were maintained under a humidified condition with 5% CO₂ at 37°C.

2.5. Cell Viability Assay. The cell viability of AuNPs was assessed by MTT assay. In brief, the two cell lines were grown in a 96-well plate and treated with 50 μg/mL AuNPs at 37°C for 24 h, 48 h, and 72 h. The cells were further incubated with MTT solution (2 mg/mL) for another 4 h. The supernatants were then flicked off and dissolved in 100 μL of DMSO. The absorbance was determined at 490 nm using a microplate reader (Epoch, Biotek).

2.6. EdU Proliferation Assay. EdU assay was conducted to detect cell proliferation using a Cell Light EdU kit (Ribobio). Cells were seeded in a 96-well plate and transfected for 48 h, and 50 μM of EdU was added for an additional 2 h. Then, cells were fixed with 4% formaldehyde for 30 min and incubated by 2 mg/mL glycine for 10 min. At last, cells were permeabilized by 0.5% Triton X-100 for 20 min and coincubated with DAPI. The percentage of EdU-positive cells was assessed by a fluorescence microscope.

2.7. Apoptosis Assay. To evaluate cell apoptosis, annexin V apoptosis detection kit I (BD Biosciences, USA) was employed. Simply, 50 μg/mL of AuNP-treated cells was trypsinized and suspended in 300 μL of 1x binding buffer. Then, 5 μL of annexin V-PE was added for 15 min and mixed with 5 μL 7-AAD solution for another 5 min. At last, 200 μL of 1x binding buffer was added and analyzed by a flow cytometer (BD Biosciences, USA). Here, the control cells were incubated without nanoparticle treatment.

2.8. Wound Healing Assay. Cells in the presence and absence of AuNPs were cultivated in a six-well plate until reaching single-layer confluence. Linear wounds were created using pipette tips. Then cells were washed with PBS and maintained with fresh media at 37°C for 48 h. The wound was monitored by a microscope (Nikon, Tokyo, Japan), and the gap widths were measured using ImageJ software.

2.9. Transwell Migration and Invasion Assays. The migration and invasion of BCPAP and TPC-1 cells were performed by...
transwell chambers (8 μm, Corning, USA) as described. For the migration assay, BCPAP and TPC-1 cells at a density of 5 × 10^4 cells per well were seeded into an upper chamber with serum-free medium, while the lower chamber was filled with 500 μL of medium supplemented with 20% FBS. After incubation with AuNPs for 48 h, cells on the lower surface of the membrane were fixed and stained with crystal violet. Cell migration ability was examined by counting cells under a microscope (Olympus, Tokyo, Japan) in 3 randomly selected fields.

For the invasion assay, after precoating with Matrigel (BD Biosciences, CA), BCPAP and TPC-1 cells at a density of 5 × 10^4 cells per well were seeded into an upper chamber with serum-free medium, while the lower chamber was filled with 500 μL of medium supplemented with 20% FBS. After incubation with AuNPs for 48 h, the cells that remained on the upper side of the membrane were removed with cotton swabs. Cells on the lower surface of the membrane were fixed and stained with crystal violet. Cell migration and invasion ability were examined by counting cells under a microscope (Olympus, Tokyo, Japan) in 3 randomly selected fields.

2.10. Packaging of Lentivirus. The lentivirus vector system is constituted of the vector pGCSIL-GFP which expressed short hairpin RNA (shRNA) and green fluorescent protein (GFP), pHelper1.0 (gag/pol element), and pHelper2.0 (VSVG element). The vectors were purchased from GeneChem (Shanghai, China). The transfection assay was performed using Lipofectamine 2000 (Invitrogen). Target sequences are shown in Table 1.

2.11. Reverse Transcription Quantitative Polymerase Chain Reaction (qRT-PCR). Total RNA was isolated and purified using TRIzol reagent (Thermo Fisher), according to the manufacturer’s instructions. Reverse transcription was performed using M-MLV reverse transcriptase (Promega Corporation, WI, USA). The mRNA level of CCT3 was performed by qRT-PCR using SYBR Green PCR master mix (Applied Biosystems) and normalized to GAPDH. qPCR primers are shown in Table 2. qPCR data was analyzed by the ΔΔCt method.

2.12. Western Blot Analysis. For protein expression analysis, total protein was extracted according to the manufacturer’s protocol and detected using a BCA kit (Thermo Fisher Scientific). Approximately 50 μg of proteins was resolved on 10% SDS polyacrylamide gels and then transferred to PVDF membrane. After being blocked with 5% nonfat milk, the membranes were probed with primary antibodies overnight at 4°C following incubation with the secondary antibodies for 2 h at room temperature. Protein expression was examined using an enhanced chemiluminescence detection system. Antibodies used in western blot were as follows: anti-CCT3 (1:500; ab174255; rabbit polyclonal, Abcam), anti-rabbit IgG (catalog no. 14708; Cell Signaling Technology), MMP-2 (1:1,000; catalog no. 4022; Cell Signaling Technology), MMP-9 (1:1,000; catalog no. 3852; Cell Signaling Technology), caspase-3 (1:1,000; catalog no. 9662; Cell Signaling Technology), caspase-9 (1:1,000; catalog no. 2772; Cell Signaling Technology), and GAPDH (1:1,000; catalog no. 2774; Cell Signaling Technology), Bcl-2 (1:1,000; catalog no. 2774; Cell Signaling Technology), Bax (1:1,000; catalog no. 2774; Cell Signaling Technology), and GAPDH (1:1,000; catalog no. 2774; Cell Signaling Technology). Antibodies used in western blot were as follows: anti-CCT3 (1:500; ab174255; rabbit polyclonal, Abcam), anti-rabbit IgG (catalog no. 14708; Cell Signaling Technology), MMP-2 (1:1,000; catalog no. 4022; Cell Signaling Technology), MMP-9 (1:1,000; catalog no. 3852; Cell Signaling Technology), caspase-3 (1:1,000; catalog no. 9662; Cell Signaling Technology), caspase-9 (1:1,000; catalog no. 2772; Cell Signaling Technology), and GAPDH (1:1,000; catalog no. 2774; Cell Signaling Technology).

2.13. Immunoﬂuorescence. BCPAP and TPC-1 cells adhered to coverslips were treated with or without AuNPs for 24 h. Next, cells were ﬁxed with 4% paraformaldehyde for 15 min at room temperature, stained with an anti-CCT3 primary antibody (1:500; Abcam), and detected with the secondary antibody (catalog no. 14708; Cell Signaling Technology). The coverslips were counter stained with 10 μL/mL DAPI and imaged with a ﬂuorescence microscope (X51, Olympus).

2.14. Statistical Analysis. All data were performed by three-time independent experiments and expressed as the mean ± standard errors. Statistical analysis was calculated using GraphPad Prism 6.0 (GraphPad Software Inc., USA). Student’s t-test was carried out to compare the difference between the control group and AuNP group, AuNP group, and sh-CCT3+AuNP group. A p value < 0.05 was considered a signiﬁcant difference.

3. Results

3.1. AuNP Characterization. Before biological assessments, AuNPs were characterized. The morphology and size of AuNPs were detected by TEM, the hydrodynamic parameters were measured with DLS technique, and the stability of AuNPs was identiﬁed by DLS and UV-Vis spectra. The TEM images, DLS data, and UV-Vis spectra of AuNPs are shown in Figures 1(a)–1(c). The average size of AuNPs was 7.73 nm, and the hydrodynamic size was 9.2 ± 0.6 nm, which were in accordance with previous reports [18]. The difference between the sizes measured by TEM and hydrodynamic size may be related to the shell of stabilizers adsorbed on the surface of NPs. The shells on NP surface consisted of mixtures of tannic acid and sodium citrate, which served as reducing and stabilizing agents during the biosynthesis [19]. The absorption band maxima for AuNPs was observed at 517.5 nm by UV-Vis spectra, which was attributed to surface plasmon excitation [20]. DLS results as well as UV-Vis spectra and TEM measurements conﬁrmed high stability of AuNPs.

3.2. AuNPs Inhibited Cell Proliferation in Papillary Thyroid Carcinoma Cells. To explore the potential function of AuNPs, we ﬁrstly examined the cell proliferation by MTT and EdU assays in BCPAP and TPC-1 cells. As illustrated in Figure 2(a), when cells were treated with AuNPs at a dose of 50 μg/mL for 24 h, 48 h, and 72 h, the viability showed a time-dependent manner. The results showed that there was
no significance between the control group and AuNP groups at 24 h ($p > 0.05$). After 48 h of culture, the AuNP groups had a lower proliferation rate than the control group ($p < 0.05$) (Figure 2(a)). In addition, EdU assay revealed the similar results. The percentage of EdU positive cells in AuNP-treated cells was reduced (Figure 2(b)) compared to the control one. Based on these, we chose AuNPs at a dose of 50 μg/mL for 48 h for a further study [21].

3.3. AuNPs Induced Apoptosis in Papillary Thyroid Carcinoma Cells. In an attempt to investigate whether AuNPs have influence on apoptosis in BCPAP and TPC-1 cells, flow cytometry was employed. After cells were treated with 50 μg/mL AuNPs for 48 h, cells were stained with annexin V/PI. Early and late apoptosis and necrotic cells were distinguished. The quantities of total cell apoptosis in BCPAP and TPC-1 cells were 11.4% and 17.2%, whereas only 4.06% and 6.25% apoptotic cells were observed in the control groups (Figure 3(a)). We further evaluated the expression variations of apoptosis-related proteins including caspase-3, caspase-9, Bcl-2, and Bax by western blot. Our results showed that the expression of proapoptotic proteins (caspase-3, caspase-9, and Bax) was increased, while the expression of antiapoptotic protein (Bcl-2) was decreased in both BCPAP and TPC-1 cells after 48 h treatment of AuNPs (Figure 3(b)).

3.4. AuNPs Suppressed Migration and Invasion of Papillary Thyroid Carcinoma Cells. As cancer cell migration and invasion play a key role in disease progression [22], we accessed the effects of AuNPs on migration and invasion ability of BCPAP and TPC-1 cells. Wound healing and transwell assays were conducted to detect the migratory capability; as shown in Figures 4(a) and 4(b), AuNPs inhibited the migration dramatically. Compared with the control group, AuNPs decreased the wound closure rate from 85% to 70% and migratory ability from 195% to 150%. We also found that AuNPs reduced BCPAP and TPC-1 cell invasion capacities (Figure 4(b)), which was similar to the results of migration. Matrix metalloproteinases (MMPs) are recognized enzymes that digest the main proteins involved in cell motility [23]. The suppression efficacy of AuNPs on cell migration and invasion prompted us to monitor the change of MMP expressions. As illustrated in Figure 4(c), the protein levels of MMP-2 and MMP-9 were also decreased after AuNP treatment. Collectively, these results suggested that AuNPs inhibited migration and invasion of PTC cells by decreasing the expressions of MMP-2 and MMP-9.

3.5. AuNPs Downregulated CCT3 in Human Papillary Thyroid Carcinoma Cells. CCT3 plays a central role in
Figure 2: Effects of AuNPs on cell proliferation of BCPAP and TPC-1 cells. (a) Cells were incubated with AuNPs at a dose of 50 μg/mL for 24 h, 48 h, and 72 h, and the cell viability was measured by MTT assay and expressed as % control for undosed cells. (b) Cells were incubated with AuNPs at a dose of 50 μg/mL for 48 h, and cell proliferation was measured by EdU assay. *p < 0.05 and **p < 0.01 compared with the control group.

Figure 3: Effects of AuNPs on cell apoptosis of BCPAP and TPC-1 cells. (a) Cells were incubated with AuNPs at a dose of 50 μg/mL for 48 h, and cell apoptosis was evaluated by flow cytometry. (b) Western blot was employed to analyze the apoptosis-related proteins including Bax, Bcl-2, caspase-3, and caspase-9. **p < 0.01 compared with the control group.
maintaining cellular proteostasis as one of the subunits of molecular chaperone CCT/TRiC complex [24]. Accumulated studies demonstrated that inhibition of CCT3 could suppress malignant proliferation of human PTC, making CCT3 a promising molecular marker of PTC [25]. Since we observed the significant inhibition effect of AuNPs on the metastasis of PTC cells, we examined the molecular mechanisms with respect to CCT3. Stimulated by AuNPs, the mRNA level of CCT3 in BCPAP and TPC-1 cells reduced (Figure 5(a)), and the protein level of CCT3 was also decreased (Figure 5(b)) which was further confirmed by immunofluorescence (Figure 5(c)). These results demonstrated that CCT3 may have a major role in the mechanism of inhibition effects of AuNPs in PTC cells.

3.6. AuNPs Inhibited Proliferation, Migration, and Invasion, and Induced Apoptosis via Downregulating CCT3 in Papillary Thyroid Carcinoma Cells. To deeply investigate the mechanism of inhibition effects of AuNPs on PTC cells, we knocked down CCT3 by shRNA in BCPAP and TPC-1 cells which have the highest expression of CCT3 among PTC cell lines. Hence, we detected the mRNA and protein levels of CCT3 in BCPAP and TPC-1 cells after transfection by qRT-PCR and western blot. As shown in Figures 6(a)
Figure 5: AuNPs reduced the expression of CCT3 in BCPAP and TPC-1 cells. (a) qRT-PCR was used to detect the mRNA level of CCT3. (b) Western blot was used to detect the protein expression level of CCT3. (c) Immunofluorescence was used to analyze the protein expression of CCT3 qualitatively. **p < 0.01 compared with the control group.
Figure 6: AuNPs exerted antiproliferation by downregulating CCT3 in BCPAP and TPC-1 cells. AuNPs and CCT3 knockdown inhibited the mRNA and protein expression of CCT3 by qRT-PCR (a) and western blot (b). (c) Cell proliferation was accessed by EdU. (d) Cell apoptosis was analyzed by flow cytometry. **p < 0.01 compared with the control group.
and 6(b), the mRNA and protein levels of CCT3 were decreased to a certain content which exhibited the successfully knocked down of CCT3. In addition, the mRNA and protein levels of CCT3 were much lower after treated with AuNPs as determined. Firstly, we found that both AuNPs and sh-CCT3 inhibited cell proliferation, and combined treatment of AuNPs and sh-CCT3 influenced the cell viability markedly than either one of AuNPs and sh-CCT3 did in both BCPAP and TPC-1 cells (Figure 6(c)). Subsequently, cotreatment of AuNPs and sh-CCT3 was more efficient on inhibiting cell apoptosis than treated individually (Figure 6(d)). Furthermore, we investigated whether CCT3 knockdown could inhibit the migratory abilities of BCPAP and TPC-1 cells by performing the wound healing, transwell migration, and invasion assays. The results depicted that sh-CCT3 suppressed the migration and invasion efficiently in the presence than the absence of AuNPs (Figures 7(a) and 7(b)). Altogether, these findings indicated that AuNP-mediated suppression of PTC was at least partially through downregulating the mRNA level of CCT3.

4. Discussion

AuNPs have been applied in the biomedical field as intrinsic anticancer agents [26]. Unmodified AuNPs have been shown to affect the growth and metastasis of cancer cells. For instance, AuNPs were able to inhibit the cell viability and induce apoptosis in various cancer cell lines including HepG2 hepatocellular cancer cells [27], MCF-7 breast cancer cells [28], and B16F10 melanoma cells [29]. Furthermore, previous studies have indicated that AuNPs inhibited cell proliferation by downregulating cell cycle genes [30, 31]. Our results showed that unmodified AuNPs of 8 nm could reduce the survival of papillary thyroid carcinoma cells (BCPAP and TPC-1) in a dose-dependent manner. The size of AuNPs is known to influence the effects on the proliferation of various types of cells [10]. AuNPs with sizes between 1 and 2 nm have been shown to be highly toxic for different cells, while those of 14-100 nm have been reported to be comparatively nontoxic [16]. The cytotoxicity of AuNPs to cells varies upon cell types except size and concentration. To ensure safety, AuNPs with medium size between 5 and 10 nm were selected for further evaluations.

In our study, AuNPs were synthesized using tannic acid and sodium citrate and characterized by UV-Vis spectra, TEM, and DLS; the results were agreed with previous reports [28]. To evaluate the biological effects of AuNPs in BCPAP and TPC-1 cells, we employed MTT and EdU assays. AuNPs were found to be capable of suppressing cell proliferation in a dose-dependent manner, which was in accordance with previous reports [17]. We also discovered the roles of AuNPs in cell apoptosis by a flow cytometer and found that AuNPs could enhance apoptosis in BCPAP and TPC-1 cells. Existing reports have shown that AuNPs could induce apoptosis in human leukemia cells [12]. In addition, AuNPs caused an increase in the level of proapoptosis proteins and decreased expression of antiapoptosis protein (Bcl-2), all of which also exhibited the induction of apoptosis in BCPAP and TPC-1 cells. Previous reports have shown that similar AuNPs of 5-6 nm could induce the expression of Bax, a proapoptotic protein in the intrinsic apoptotic pathway mediated by the process of mitochondrial outer membrane permeabilization [32].

Most researches on AuNPs emphasize on cytotoxicity. However, the effects of AuNPs on cellular behaviors are very important. Many malignant tumors exert capability of metastasis which is the main reason of cancer-related mortality [33]. The migration of tumor cell is well-known to be a key step in tumor progression and metastasis [34]. In our study, the strong inhibition efficacy of AuNPs on migration and invasion was observed in papillary thyroid carcinoma cells (Figure 4), which were in line with other groups [35, 36] indicating that AuNPs may have potential function in the metastasis of papillary thyroid carcinoma. Previous reports have depicted that AuNPs could inhibit the migration and invasion of ovarian cancer cells through increasing nuclear stiffness [37]. AuNPs have also been demonstrated to influence the bidirectional crosstalk between pancreatic stellate cells and pancreatic cancer cells to suppress the migration [38].

We also explored the molecular mechanism of inhibition effects of AuNPs on thyroid cancer cells. The chaperonin containing TCP-1 (CCT) is necessary for the production of actin, tubulin, and other proteins, some of which are involved in cell progression [39, 40]. As one of the chaperonin compounds, the CCT is undertaking the folding of about 10% of the proteome in cell. Consequently, CCT compound was demonstrated to affect cancer cell proliferation [41]. CCT3 was previously identified as highly expressed protein among CCT complex in some human cancers including PTC cells [25] and hepatoma carcinoma cells [42]. A previous study also demonstrated that CCT3 depletion could cause cell apoptosis and decreased capability of migration [24]. In our study, we used qRT-PCR, western blot, and immunofluorescence assays to analyze the mRNA and protein levels of CCT3 in BCPAP and TPC-1 cells after incubated with AuNPs and found that both the mRNA and protein levels of CCT3 were reduced compared with the control group. To further investigate whether AuNPs exerted its antitumor effects by downregulating CCT3, we knocked down CCT3 in PTC cell lines and measured cell proliferation using EdU assay. qPCR and western blot confirmed that CCT3 mRNA and protein levels were reduced to a certain content, and the much lower level of CCT3 after treated with AuNPs. EdU assay showed that silencing CCT3 greatly suppressed the proliferation of BCPAP and TPC-1 cells combined with AuNPs. We further observed that cell apoptosis was increased in the presence than the absence of AuNPs in BCPAP and TPC-1 cells after transfection. Moreover, similar results were suggested by wound healing and transwell migration assays.

5. Conclusions

In summary, our study provided evidence for the first time that AuNPs inhibited the growth of papillary thyroid cancer cells (BCPAP and TPC-1) including cell proliferation, migration, and invasion. In addition, we demonstrated that AuNPs
exerted the antitumor effects through downregulating the mRNA expression of CCT3 of papillary thyroid cancer cells. These findings may serve as a novel target for developing new strategy to treat papillary thyroid cancers.

**Data Availability**

The [figures] data used to support the findings of this study are included within the article.

**Conflicts of Interest**

The authors declare that there is no conflict of interest regarding the publication of this paper.

**Authors’ Contributions**

Fangzhou Liu and Dawei Ma contributed equally to this study.

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