Heliyon 10 (2024) e23173

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

PSMA7 promotes the malignant proliferation of esophageal cancer

Qing-hua Jiao, Yan Wang, An-na Zhang, Qian-qian Liu, Qing-bo Zhou *

Department of Geriatrics, The Second Hospital Cheeloo College of Medicine Shandong University, Jinan 250000, Shandong, China

ARTICLE INFO

Keywords:
Esophageal cancer
Proteasome
Core proteins
Proliferation
Apoptosis

ABSTRACT

Background: It is important to explore novel molecules that play a key role in esophageal cancer (ESCA) progression.
Methods: Two ESCA tissue expression profile microarrays (GSE92396 and GSE17351) data from GEO were downloaded, and differentially expressed genes (DEGs) were analyzed using GEO2R. The DEGs common to both microarrays were analyzed for protein-protein interactions, KEGG and GO. The altered expression of proteasome 20S subunit α 7 (PSMA7) in ESCA tissues was analyzed using information from publicly available databases (GEO, TCGA, TNMplot). PSMA7 was over-expressed or knocked down in Eca109 and KYSE150 cells using transfection, and the effects on cell proliferation, migration, invasion and apoptosis were examined using CCK-8, Transwell, and flow cytometry experiments.
Results: 284 common DEGs were identified, and 10 core proteins, HSP90AA1, AURKA, CDC6, PCNA, MCM5, KAT2B, GRB2, MYBL2, PSMA7, and CKAP5, involved in ESCA progression were identified. PSMA7 mRNA level was significantly increased in ESCA tissues. PSMA7 over-expression significantly promoted the proliferation, migration and invasion of Eca109 and KYSE150 cells, and significantly promoted apoptosis. In contrast, PSMA7 knockdown inhibited their proliferation and motility, and significantly suppressed apoptosis.
Conclusion: This study analyzed multiple proteins that may play a key role in ESCA progression, and identified the pro-cancer role of PSMA7.

1. Introduction

According to the GLOBOCAN Global Cancer Statistics Estimates, there are 604,100 new cases of esophageal cancer (ESCA) and 544,076 deaths worldwide in 2020 [1]. ESCA has two common histologic subtypes, esophageal squamous cell carcinoma (ESCC) and esophageal adenocarcinoma (EAC) [2]. With the use of techniques such as narrow-band imaging with magnification endoscopy and positron emission tomography, the diagnostic accuracy of ESCA has been greatly improved [3]. Endoscopic surgery and neoadjuvant chemoradiotherapy have also significantly improved the outcome of early or resectable ESCA [3]. However, due to the lack of early diagnosis, most ESCA patients are already locally advanced or metastatic by the time they become aware of any symptoms, making surgical treatment strategies targeting early or resectable stages ineffective and prognosis extremely poor [4]. The 5-year relative survival rate for patients with locally advanced disease is approximately 26 % and for patients with distant metastases is only 5 % [5]. Systemic chemotherapy is the standard of care for unresectable ESCA, but patients have limited survival benefit from it, with a median overall survival of no more than 10 months [6]. Molecularly targeted therapies and immunotherapy have not yet been able to

* Corresponding author. Department of Geriatrics, The Second Hospital Cheeeloo College of Medicine Shandong University, Jinan 250000, Shandong, China.
E-mail address: lianxiang1210@163.com (Q.-b. Zhou).

https://doi.org/10.1016/j.heliyon.2023.e23173
Received 16 April 2023; Received in revised form 20 November 2023; Accepted 28 November 2023
Available online 1 December 2023

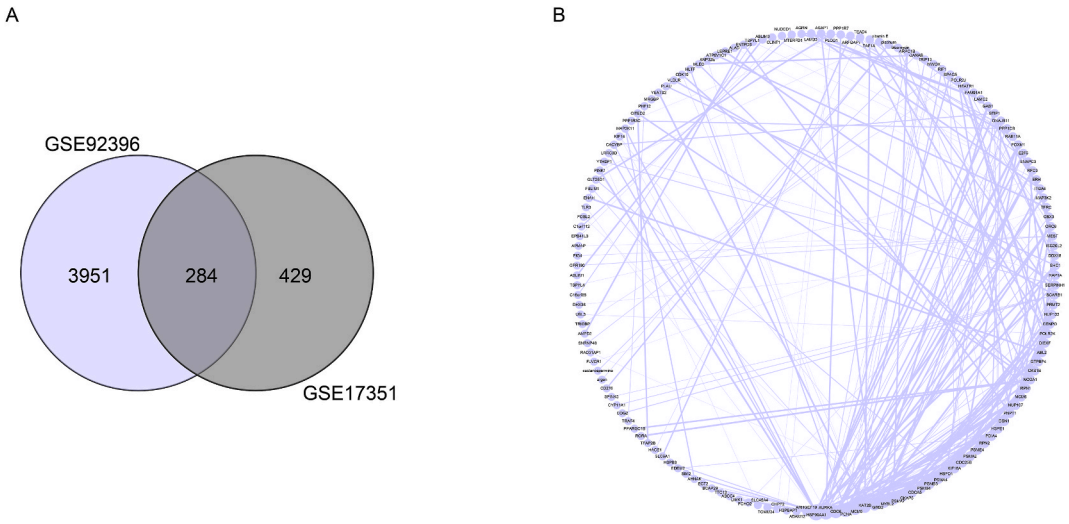

Fig. 1. Molecules that may play a key role in ESCA progression. (A) A Venn diagram of 284 common differentially expressed genes (DEGs) from GSE92396 and GSE17351. (B) The protein-protein interaction (PPI) network analysis of these 284 common DEGs using STRING.

significantly improved patient survival [7]. Therefore, it is important to explore new molecules that play a key role in ESCA progression in order to develop new therapeutic strategies.

Proteasome subunit type α-7 (PSMA7) is the α subunit of the proteasome 20S core complex and is involved in ubiquitin-proteasome pathway-mediated protein degradation [8]. Its gene is located on chromosome 20q13.33 that is an amplified region of oncogenes closely associated with many tumors. PSMA7 has been reported to be significantly highly expressed in cervical cancer [9], colorectal cancer [10], gastric cancer [11,12], breast cancer [13] and hepatocellular carcinoma [14]. Knockdown of its expression inhibits proliferation and induces apoptosis of cervical cancer [9], colon cancer [15,16] and gastric cancer [11,17] cells. PSMA7 has the potential to be a molecular target for the treatment of many cancers. However, no studies of PSMA7 with ESCA have been reported.

In this study, we will use two microarray data from GEO to analyze the core protein network that plays a key role in ESCA progression and focus on revealing the effect of PSMA7 expression on ESCA cell behavior.

2. Materials and methods

2.1. Cell culture and transfection

Human ESCA cell lines (Eca109 and KYSE150) were obtained from National Biomedical Experimental Cell Repository (ID: 4201HUM-CCTCC00207 and 3101HUMTCHu236) (Beijing, China), and cultured in DMEM (KGM12800N-500, KeyGEN BioTECH) supplemented with 10 % FBS (A31608, Gibco) and 1 % penicillin/streptomycin (KGY0023, KeyGEN BioTECH) in a humidified incubator with 5 % CO_2 at 37 °C.

For PSMA7 expression plasmid (OV), the pcDNA3.1 empty vector (VT1001, YouBio) was used as a negative control (NC), and human PSMA7 (NM_002792) cDNA sequence was cloned into pcDNA3.1 vector to constitute a recombinant expression plasmid. For PSMA7 expression knockdown (KD), the pLKO.1-puro empty vector (SHC001, Sigma-Aldrich) was used as the NC, and the shRNA (targeting sequence: TCGACTTTGATGGCACTCCTA) was synthesized by Gene Pharma (China), and cloned into pLKO.1-puro vector.

All plasmids were transiently transfected into cells using Lipofectamine 2000 (11668019, Invitrogen). Briefly, plasmids (4 μg) and transfection reagents were added at a 1:2 ratio to cells at 70 % confluence. 48 h after transfection, cellular RNA and protein were extracted to detect the expression level of PSMA7 and transfection efficiency.

2.2. Western blot

Cells were lysed on ice with ice-cold strong RIPA buffer (CW2333S, CWBIO) for 10 min. The lysate was centrifuged at 12,000g for 10 min at 4 °C to remove precipitates, such as cell debris, and the protein was obtained in the supernatant. Protein concentration was determined by BCA assay kit (CW0014S, CWBIO). Protein samples were boiled for denaturation, and 1 × loading buffer was added. Subsequently, 20 μg of protein in each sample was subjected to SDS-PAGE loading and electrophoresis for separation (spacer gel, constant voltage 80V; 12 % separating gel, constant current 30 mA) based on molecular weight size. Then, the proteins were electrotransferred onto (constant voltage 110V, 90 min) a PVDF membrane (0.45 μm, IPVH00010; Millipore). The membrane was incubated with 5 % skim milk for 1 h at room temperature for non-specific antigen blocking, and incubated with primary antibody solution (anti-PSMA7, 1:1000, 67817-1-Ig, Proteintech; anti-GAPDH, 1:5000, ab8245, Abcam) overnight at 4 °C and with the corresponding secondary antibody for 2 h at room temperature. The bands were subjected to chemiluminescence using Enhanced

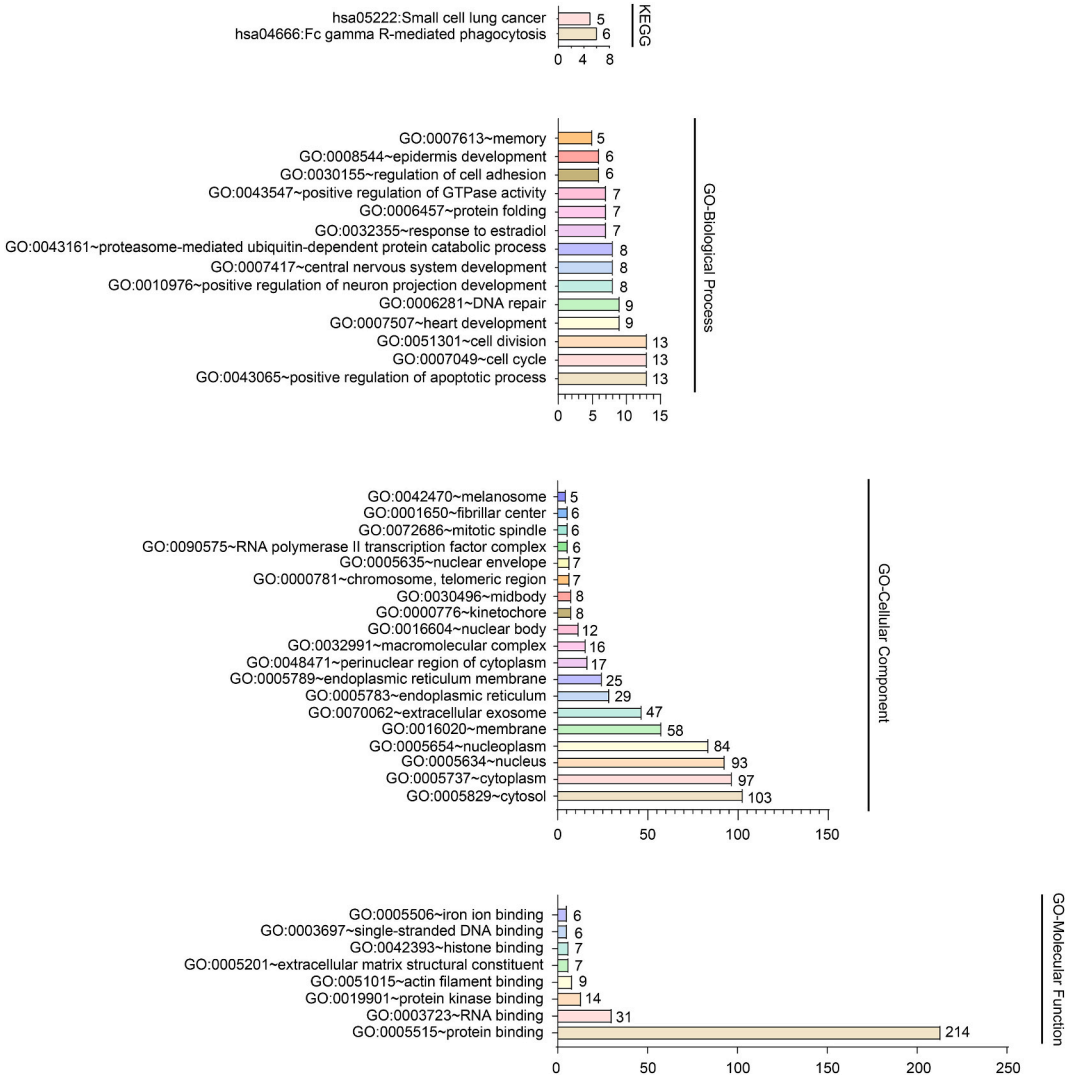

Fig. 2. KEGG and GO analyses of 284 common differentially expressed genes.

Chemiluminescence reagent (RPN2105, Amersham).

2.3. CCK-8 assay

5×10^3 transfected cells were inoculated into the well in a 96-well plate, and incubated for 6 h to adhere (this is the starting point of the experimental setup, 0 h). The old culture medium was removed, 10 μL CCK-8 reagent (PF00004, PTG) and 90 μL DMEM were added and incubated for 2 h at 37 °C. Subsequently, the absorbance (OD) value of each well at 450 nm was measured using a microplate reader (Thermo, USA). The measurements were taken after each 24 h incubation. After a total of four measurements, growth curves were plotted based on OD values.

2.4. Flow cytometry for apoptosis

Apoptosis was detected using the Annexin V-FITC/PI Kit (FXP018-100, 4A BIOTECH) according to the manufacturer's instructions. Briefly, after transfection, the cells were cultured for 48 h, digested with EDTA-free trypsin (KGM25200, KeyGEN BioTECH) and harvested. Cells were suspended with 1 × binding buffer, and the cell density was adjusted to 1×10^6/ml. 5 μl Annexin V/FITC was added to 100 μl of cell suspension and incubated in the dark at room temperature for 5 min. Then, 10 μl of PI staining solution and 400 μl of PBS were added to the mixture, gently shaken and immediately measured on the machine.

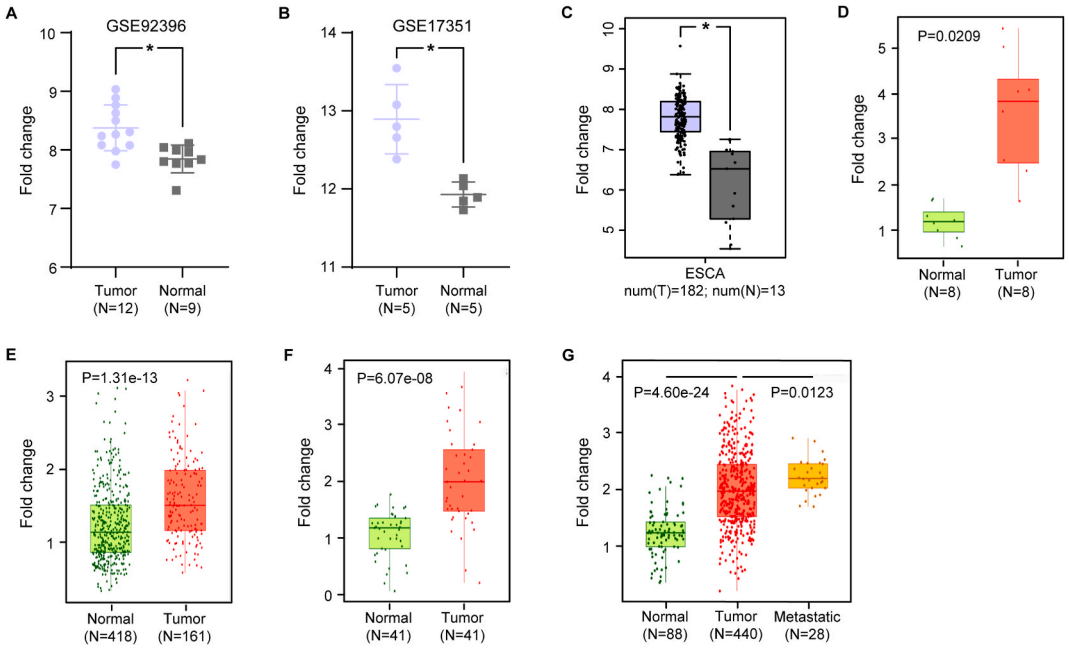

Fig. 3. PSMA7 mRNA level is significantly increased in ESCA tissues. PSMA7 mRNA levels in ESCA (tumor) tissues and normal esophageal tissues from GSE92396 (A), GSE17351 (B), TCGA (C), and TNMplot (D–G). *P < 0.05.

2.5. Transwell assay

For migration assays, 150 μl of cell suspension (DMEM suspension without serum) containing 1×10^4 cells was added to the upper of a Transwell chamber placed in a 24-well plate. In the lower layer, 400 μl of DMEM containing 10 % FBS was added. After 20 h of incubation, the number of cells crossing the membrane was measured. Measurements are performed as follows: The cells on the upper chamber were removed using PBS and a cotton swab. Cells attached to the membrane in the lower chamber were fixed with 4 % paraformaldehyde for 30 min and stained with 0.1 % crystal violet staining solution for 10 min. Finally, the cells on the membrane were imaged and counted. For invasion assays, the membranes of the Transwell chambers were coated with Matrigel (1:6 dilution, BD, Franklin Lakes), and other experimental steps were consistent with the migration assay.

2.6. Statistical analysis

All cell experiments were repeated independently at least 3 times. Data were analyzed using GraphPad Prism 8.0 software, and values are expressed as mean ± standard deviation (SD). Two groups were compared using the Student's t-test. Differences of $P < 0.05$ were considered statistically significant.

3. Results

3.1. Molecules that may play a key role in ESCA progression

We downloaded the data of GSE92396 and GSE17351 from the publicly available database GEO. GSE92396 includes the expression profile data of 9 normal esophageal tissue samples and 12 EAC tissue samples. GSE17351 includes the expression profile data of 5 pairs of ESCC tissue samples and the corresponding adjacent normal esophageal mucosal tissue samples. Subsequently, we analyzed the genes differentially expressed in the esophageal cancer tissues using GEO2R, which were 4235 and 713, respectively, with 284 differentially expressed genes (DEGs) in common (Fig. 1A). Next, we performed protein-protein interaction (PPI) network analysis of these 284 common DEGs using STRING, and obtained the most core 10 proteins, HSP90AA1, AURKA, CDC6, PCNA, MCM5, KAT2B, GRB2, MYBL2, PSMA7, and CKAP5 (Fig. 1B). In addition, KEGG and GO analyses were performed for these 284 DEGs, as shown in Fig. 2.

3.2. PSMA7 mRNA level is significantly increased in ESCA tissues

Based on the progress of the study at that time, we selected PSMA7 among the core 10 proteins for the follow-up study. According to the data from GSE92396 (Fig. 3A) and GSE17351 (Fig. 3B), PSMA7 mRNA levels were significantly increased in ESCA tissues. In addition, analysis of data from TCGA, including transcriptomic data from 182 ESCA tissues and 13 normal esophageal tissues, similarly

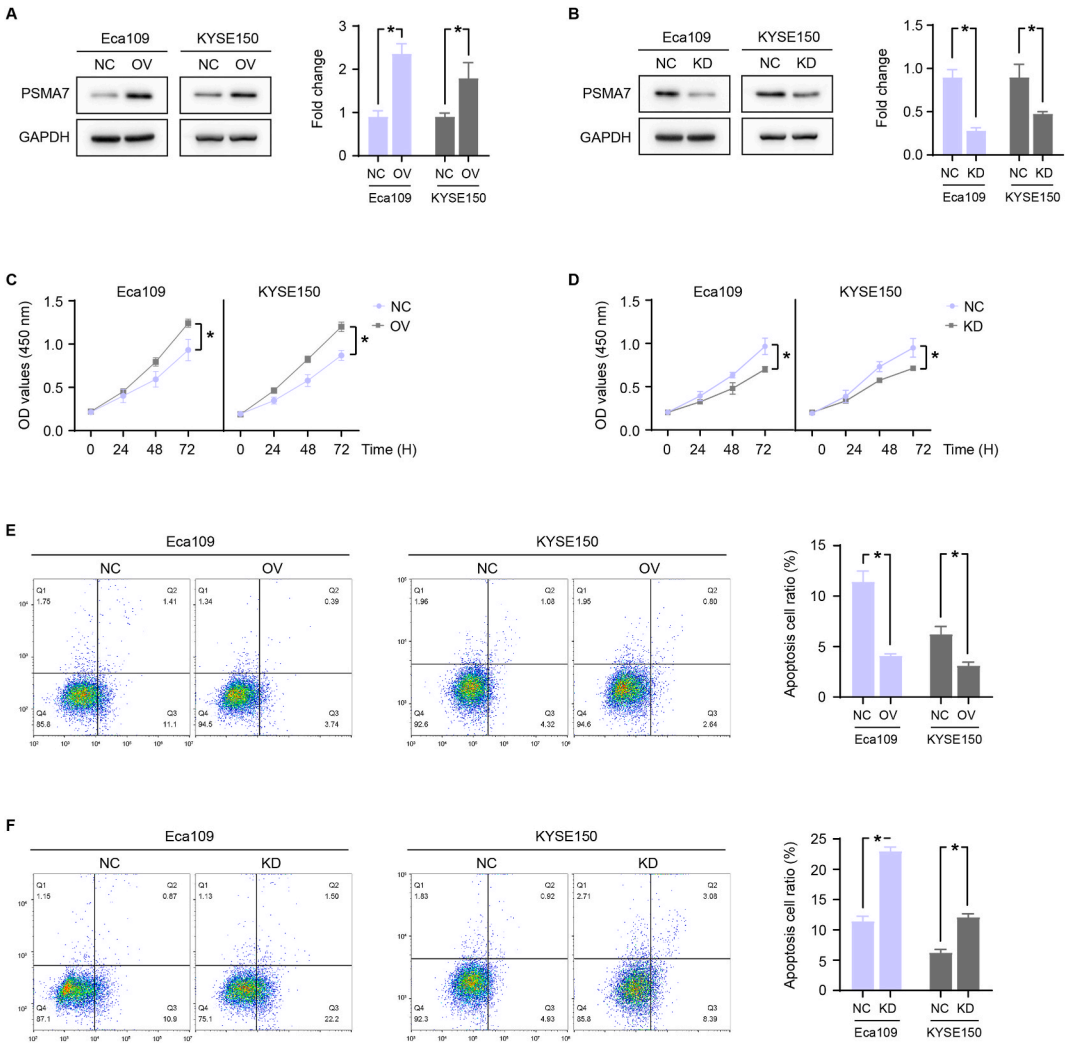

Fig. 4. PSMA7 promotes the proliferation of ESCA cells *in vitro*. The protein levels of PSMA7 with Western blot in Eca109 and KYSE150 cells that transfected with PSMA7 expression plasmid (OV) (A) or targeting shRNAs (KD) (B). (C and D) The absorbance values of cells at 450 nm with CCK-8 assay. (E and F) The Annexin V/FITC and/or PI satin of cells with flow cytometry. *P < 0.05.

revealed that PSMA7 mRNA levels were significantly upregulated in ESCA tissues compared to normal esophageal tissues (Fig. 3C). Furthermore, the RNA seq data of 8 paired ESCA and adjacent normal tissues (Fig. 3D), and non-paired ESCA (n = 418) and normal (n = 161) tissues (Fig. 3E), and the Gene chip data of 41 paired ESCA and adjacent normal tissues (Fig. 3F), and non-paired ESCA (n = 88), normal (n = 440) and metastatic (n = 28) tissues (Fig. 3G), from TNMplot (tnmplot.com) were analyzed and showed that PSMA7 mRNA levels were significantly up-regulated in ESCA tissues, compared with the normal esophageal tissues. Moreover, PSMA7 was expressed at higher levels in metastatic samples compared to primary ESCA samples (Fig. 3G), suggesting a potential correlation between high PSMA7 expression and ESCA metastasis.

3.3. *PSMA7 promotes the proliferation of ESCA cells in vitro*

To determine its specific role plays in ESCA progression, PSMA7 was overexpressed (OV) (Fig. 4A) or knocked down (KD) (Fig. 4B) in the Eca109 and KYSE150 cells, respectively (the uncropped images of the blots shown in Supplementary Fig. 1). The results of the CCK-8 assay showed that PSMA7 overexpression significantly promoted the proliferation of Eca109 and KYSE150 cells (Fig. 4C), whereas PSMA7 knockdown inhibited their proliferation (Fig. 4D). In addition, using flow cytometry, we also found that the percentage of apoptotic cells was significantly lower in the PSMA7 overexpression group (Fig. 4E), while the percentage of apoptotic cells was significantly higher in the PSMA7 knockdown group (Fig. 4F). Taken together, PSMA7 promoted the proliferation and inhibited the apoptosis of ESCA cells *in vitro*.

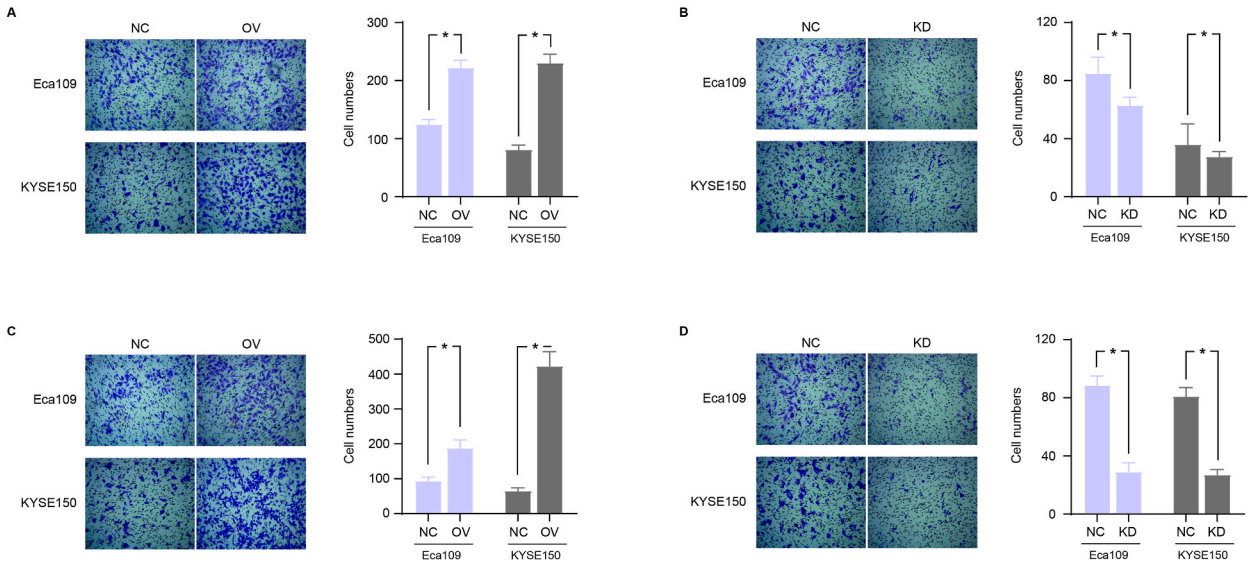

Fig. 5. PSMA7 promotes migration and invasion of ESCA cells. Eca109 and KYSE150 cells were transfected with PSMA7 expression plasmid (OV) or targeting shRNAs (KD), and the invasion (A and B) and migration (C and D). *P < 0.05.

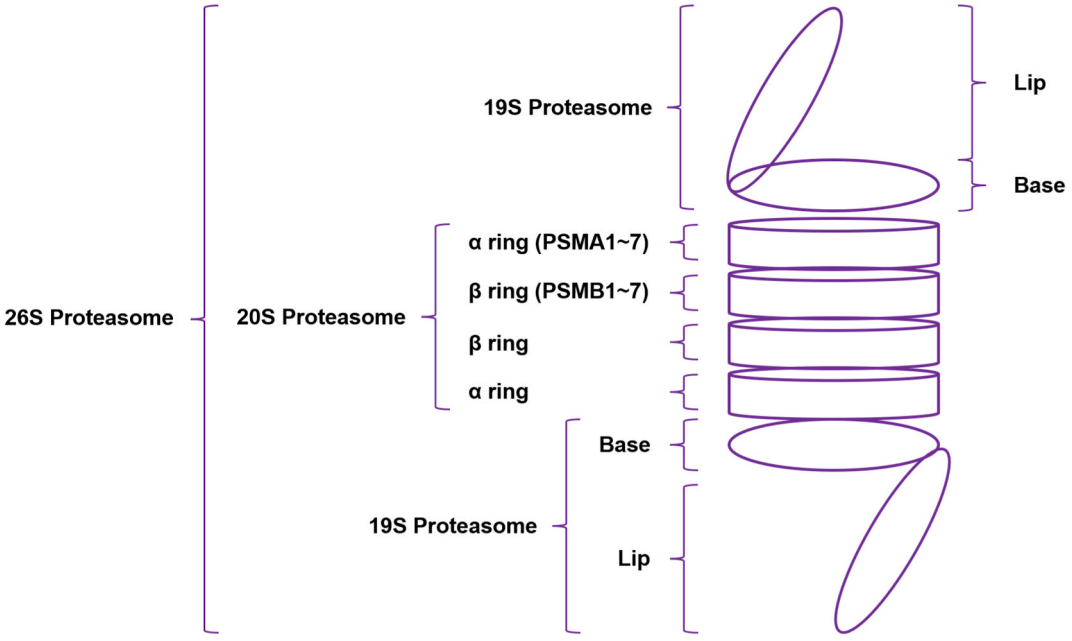

Fig. 6. A brief structural schematic of 26S proteasome.

3.4. PSMA7 promotes migration and invasion of ESCA cells

Finally, we also analyzed the effect of PSMA7 expression on cell motility using Transwell assay. As shown in Fig. 5, PSMA7 overexpression significantly increased the number of cells that completed invasion (Fig. 5A and B) and migration (Fig. 5C and D) *in vitro*, while PSMA7 knockdown significantly inhibited migration and invasion of Eca109 and KYSE150 cells.

4. Discussion

Using tissue expression profiling and PPI analysis, we obtained some key proteins that may play an important role in ESCA progression, including members of the proteasome subunit (Fig. 1B). The 26S proteasome is a 2.5 MDa hollow cylindrical multiprotein

structure that contains the regulatory particle (RP) (19S proteasome) and the central particle (CP) (20S proteasome) (Fig. 6). The RP contains a lip and a base subcomplex, and plays a role in the recognition of ubiquitinated protein substrates, deubiquitination and ubiquitin molecule recycling from recognized proteins, unfolding and delivery to the CP of protein substrates. The CP consists of a stack of four loops, each of which includes seven member proteins. The two identical peripheral rings are called the α-loop (subunits PSMA1-7) and the two identical central rings are called the β-loop (subunits PSMB1-7) [18]. The α-loop forms a gated channel that controls substrate entry into the central protein hydrolysis compartment. The protease activity of the proteasome is present on PSMB5, PSMB6, and PSMB7 of the β-loop. The proteasome is at the center of cellular protein homeostasis, and involved in almost all cellular processes. Therefore, it is also an important regulator of carcinogenesis [19].

Three proteasome inhibitors, bortezomib, carfilzomib, and ixazomib, have been approved by the FDA for the treatment of multiple myeloma [20–22]. Another inhibitor, marizoib, is in clinical trials for the treatment of multiple myeloma and glioblastoma [23]. Due to the enormous load placed on protein quality control mechanisms by the synthesis and secretion of large amounts of immunoglobulins, multiple myeloma cells are particularly sensitive to proteasome inhibitors [24]. These inhibitors inhibit the active sites of the PSMB5, PSMB6 and PSMB7 responsible for protein hydrolysis [25].

In the present study, we identified a role of the α-loop member, PSMA7, in ESCA progression. The massive synthesis of proteins required for malignant proliferation of cancer cells places demands on the protein control system as well. Disruption of the protein control system may be able to cause cancer cell death. As found in the present study, PSMA7 overexpression significantly promoted ESCA cell proliferation, migration and invasion and inhibited apoptosis, whereas PSMA7 knockdown inhibited ESCA cell proliferation, migration and invasion and significantly induced apoptosis. Thus, it is not only inhibitors targeting the active site of the proteasome subunit responsible for protein hydrolysis that have cancer therapeutic effects, but other inhibitors or antibodies that broadly or universally target other protein control systems should also have cancer therapeutic effects.

In conclusion, this study analyzed a number of protein molecules that may play a key role in ESCA progression, and identified the pro-cancer role of PSMA7.

Data availability

Data included in article/supp. material/referenced in article.

CRediT authorship contribution statement

Qing-hua Jiao: Writing – review & editing, Writing – original draft, Visualization, Validation, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Yan Wang:** Writing – review & editing, Writing – original draft, Visualization, Validation, Methodology, Investigation. **An-na Zhang:** Writing – review & editing, Writing – original draft, Visualization, Validation, Methodology, Investigation. **Qian-qian Liu:** Writing – review & editing, Writing – original draft, Visualization, Validation, Methodology, Investigation. **Qing-bo Zhou:** Writing – review & editing, Writing – original draft, Supervision, Resources, Project administration, Methodology, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

Not applicable.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2023.e23173.

References

[1] H. Sung, J. Ferlay, R.L. Siegel, M. Laversanne, I. Soerjomataram, A. Jemal, et al., Global cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality worldwide for 36 cancers in 185 countries, CA Cancer J Clin 71 (3) (2021) 209–249, https://doi.org/10.3322/caac.21660.
[2] A.P. Thrift, The epidemic of oesophageal carcinoma: where are we now? Cancer Epidemiol 41 (2016) 88–95, https://doi.org/10.1016/j.canep.2016.01.013.
[3] C. Yang, K. Chen, Long non-coding RNA in esophageal cancer: a review of research progress, Pathol. Oncol. Res. 28 (2022), 1610140, https://doi.org/10.3389/pore.2022.1610140.
[4] A.K. Rustgi, H.B. El-Serag, Esophageal carcinoma, N. Engl. J. Med. 371 (26) (2014) 2499–2509, https://doi.org/10.1056/NEJMra1314530.
[5] Y. Nagata, S. Yamamoto, K. Kato, Immune checkpoint inhibitors in esophageal cancer: clinical development and perspectives, Hum Vaccin Immunother 18 (6) (2022), 2143177, https://doi.org/10.1080/21645515.2022.2143177.

[6] M. Moehler, A. Maderer, P.C. Thuss-Patience, B. Brenner, J. Meiler, T.J. Ettrich, et al., Cisplatin and 5-fluorouracil with or without epidermal growth factor receptor inhibition panitumumab for patients with non-resectable, advanced or metastatic oesophageal squamous cell cancer: a prospective, open-label, randomised phase III AIO/EORTC trial (POWER), Ann. Oncol. 31 (2) (2020) 228–235, https://doi.org/10.1016/j.annonc.2019.10.018.
[7] Y. Yan, X. Feng, C. Li, T. Lerut, H. Li, Treatments for resectable esophageal cancer: from traditional systemic therapy to immunotherapy, Chin Med J (Engl). 135 (18) (2022) 2143–2156, https://doi.org/10.1097/CM9.0000000000002371.
[8] H. Du, X. Huang, S. Wang, Y. Wu, W. Xu, M. Li, PSMA7, a potential biomarker of diseases, Protein Pept. Lett. 16 (5) (2009) 486–489, https://doi.org/10.2174/092986609788167824.
[9] C.C. Ren, L. Yang, L. Liu, Y.N. Chen, G.M. Cheng, X.A. Zhang, et al., Effects of shRNA-mediated silencing of PSMA7 on cell proliferation and vascular endothelial growth factor expression via the ubiquitin-proteasome pathway in cervical cancer, J. Cell. Physiol. 234 (5) (2019) 5851–5862, https://doi.org/10.1002/jcp.26408.
[10] X.T. Hu, W. Chen, D. Wang, Q.L. Shi, F.B. Zhang, Y.Q. Liao, et al., The proteasome subunit PSMA7 located on the 20q13 amplicon is overexpressed and associated with liver metastasis in colorectal cancer, Oncol. Rep. 19 (2) (2008) 441–446.
[11] S. Xia, L. Ji, L. Tang, L. Zhang, X. Zhang, Q. Tang, et al., Proteasome subunit alpha type 7 promotes proliferation and metastasis of gastric cancer through MAPK signaling pathway, Dig. Dis. Sci. 67 (3) (2022) 880–891, https://doi.org/10.1007/s10620-021-06903-9.
[12] S. Xia, Q. Tang, X. Wang, L. Zhang, L. Jia, D. Wu, et al., Overexpression of PSMA7 predicts poor prognosis in patients with gastric cancer, Oncol. Lett. 18 (5) (2019) 5341–5349, https://doi.org/10.3892/ol.2019.10879.
[13] C.C. Chiao, Y.H. Liu, N.N. Phan, N.T. An Ton, H.D.K. Ta, G. Anuraga, et al., Prognostic and genomic analysis of proteasome 20S subunit alpha (PSMA) family members in breast cancer, Diagnostics 11 (12) (2021), https://doi.org/10.3390/diagnostics11122220.
[14] J. Tu, J. Chen, M. He, H. Tong, H. Liu, B. Zhou, et al., Bioinformatics analysis of molecular genetic targets and key pathways for hepatocellular carcinoma, OncoTargets Ther. 12 (2019) 5153–5162, https://doi.org/10.2147/OTT.S198802.
[15] X.T. Hu, W. Chen, F.B. Zhang, Q.L. Shi, J.B. Hu, S.M. Geng, et al., Depletion of the proteasome subunit PSMA7 inhibits colorectal cancer cell tumorigenicity and migration, Oncol. Rep. 22 (5) (2009) 1247–1252, https://doi.org/10.3892/or_00000561.
[16] K. Honma, I. Takemasa, R. Matoba, Y. Yamamoto, F. Takeshita, M. Mori, et al., Screening of potential molecular targets for colorectal cancer therapy, Int. J. Gen. Med. 2 (2009) 243–257, https://doi.org/10.2147/ijgm.s5158.
[17] S. Xia, L. Zhang, F. Cheng, Z. Feng, L. Lu, [Expression of PSMA 7 and its effect on proliferation, invasion, migration and tumorigenesis of gastric cancer], Nan Fang Yi Ke Da Xue Xue Bao 39 (4) (2019) 387–393, https://doi.org/10.12122/j.issn.1673-4254.2019.04.02.
[18] D.H. Wolf, W. Hilt, The proteasome: a proteolytic nanomachine of cell regulation and waste disposal, Biochim. Biophys. Acta 1695 (1–3) (2004) 19–31, https://doi.org/10.1016/j.bbamcr.2004.10.007.
[19] I.A. Voutsadakis, Proteasome expression and activity in cancer and cancer stem cells, Tumour Biol 39 (3) (2017), 1010428317692248, https://doi.org/10.1177/1010428317692248.
[20] A.L. Goldberg, Development of proteasome inhibitors as research tools and cancer drugs, J. Cell Biol. 199 (4) (2012) 583–588, https://doi.org/10.1083/jcb.201210077.
[21] P. Lawasut, D. Chauhan, J. Laubach, C. Hayes, C. Fabre, M. Maglio, et al., New proteasome inhibitors in myeloma, Curr Hematol Malig Rep 7 (4) (2012) 258–266, https://doi.org/10.1007/s11899-012-0141-2.
[22] L.D. Fricker, Proteasome inhibitor drugs, Annu. Rev. Pharmacol. Toxicol. 60 (2020) 457–476, https://doi.org/10.1146/annurev-pharmtox-010919-023603.
[23] B.C. Potts, M.X. Albitar, K.C. Anderson, S. Baritaki, C. Berkers, B. Bonavida, et al., Marizomib, a proteasome inhibitor for all seasons: preclinical profile and a framework for clinical trials, Curr. Cancer Drug Targets 11 (3) (2011) 254–284, https://doi.org/10.2174/156800911794519716.
[24] S. Cenci, L. Oliva, F. Cerruti, E. Milan, G. Bianchi, M. Raule, et al., Pivotal Advance: protein synthesis modulates responsiveness of differentiating and malignant plasma cells to proteasome inhibitors, J. Leukoc. Biol. 92 (5) (2012) 921–931, https://doi.org/10.1189/jlb.1011497.
[25] A.F. Kisselev, Site-specific proteasome inhibitors, Biomolecules 12 (1) (2021), https://doi.org/10.3390/biom12010054.