

Centrosomal protein 55: Research progress on biological characteristics, disease associations and clinical translational potential (Review)

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Abstract. Centrosomal protein 55 (CEP55), a core member of the CEP centrosomal protein family, is a molecule that regulates cytokinesis during the end of cell division and is also extensively involved in multiple physiological processes, including genomic stability maintenance, immune regulation and embryonic development. It has been shown that CEP55 participates in pathological processes such as tumor cell proliferation, invasion, metastasis and immune escape by modulating multiple signaling pathways including PI3K/AKT, NF- κ B and JAK/STAT. Furthermore, it exhibits a close correlation with poor prognosis among patients with cancer. In addition, dysregulated CEP55 expression is also implicated in the pathological processes of neurological disorders, reproductive-genetic diseases and chronic metabolic diseases. These findings highlight the potential clinical translational value of CEP55 for disease diagnosis, prognostic evaluation and targeted therapy. Based on recent domestic and international research, the present study systematically reviews the molecular biological properties, expression features and action mechanisms of CEP55 across multi-system diseases, and summarizes its clinical application potential, to provide a

theoretical reference for promoting relevant basic research and implementing precise clinical diagnosis and treatment.

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1. Introduction

Centrosomal Protein 55 (CEP55) was first reported by Martinez-Garay *et al* (1) in 2006. This gene is located at the q23.33 locus on human chromosome 10 and encodes a 464-amino-acid protein with a molecular mass of 55 kDa; it was previously designated c10orf3 and FLJ10540 (1,2). CEP55 was initially recognized as a core molecule governing cytokinesis at the terminal stage of cell division, mainly mediating the physical separation of daughter cells to guarantee accurate completion of cell division. Alongside advances in molecular biology techniques and deeper investigations into CEP55, its versatile functions have been progressively uncovered. CEP55 does not merely function as a pivotal hub gene for cytokinesis at the end of mitosis. Importantly, it participates broadly in a wide range of physiological and pathological processes, including cell-cycle regulation, maintenance of genomic stability, immune microenvironment remodeling, and embryonic development. Aberrant expression and dysfunction of CEP55 act as a core trigger for the onset of numerous diseases, including tumorigenesis, developmental malformations, immune dysregulation and reproductive disorders. Drawing on recent domestic and international studies, the present study systematically reviews the biological characteristics, disease expression features, and clinical-translation potential of CEP55. The present review aims to provide a reference for subsequent basic research and clinical applications.

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2. Biological characteristics of CEP55

Molecular structure and core functions. CEP55 contains highly conserved characteristic domains, which form the structural basis underlying its multifunctional properties. Its N-terminus harbors a coiled-coil region that mediates protein self-homodimerization and provides structural support for protein-protein interactions (PPIs). The central region acts as a hinge domain that regulates protein conformational changes and subcellular localization. The C-terminal ESCRT- and ALIX-binding region (EABR region) specifically recruits core components of the endosomal sorting complex required for transport (ESCRT), such as ALIX and TSG101. It serves as a key structure for proper cytokinesis execution (3,4). In addition, CEP55 possesses two NEMO-like ubiquitin-binding domains that sense and transmit ubiquitination signals. Thus, CEP55 participates in a broad range of physiological processes, including cell-cycle progression and the regulation of protein homeostasis (5,6). Existing studies have confirmed that CEP55 is a mammal-specific functional protein. In invertebrates such as *Drosophila*, loss of CEP55 can be compensated for by other homologous proteins to complete cytokinesis, highlighting the specialized role of CEP55 in regulating mammalian cell division (7).

The core physiological function of CEP55 is the precise regulation of cytokinesis at the end of mitosis. During interphase, CEP55 localizes to the centrosome; at the end of mitosis, it specifically accumulates at the midbody and directly binds ALIX and TSG101 via its EABR domain to recruit the ESCRT-I complex to the intercellular bridge. Supported by the synergistic stabilizing effect of U MAD1 protein, CEP55 further recruits the ESCRT-III complex and triggers its polymerization. This process ultimately mediates midbody abscission and daughter-cell separation to guarantee the accuracy and integrity of cell division (8,9). In addition to its classical cytokinesis function, CEP55 contributes to autophagic degradation of centrosome remnants. It mediates degradation of midbody derivatives by binding the autophagy receptor NBR1 and modulates stem-cell differentiation, cell reprogramming and tumorigenesis, thereby maintaining cellular homeostasis (10,11).

Meanwhile, CEP55 is also extensively involved in the physiological regulatory processes of multiple systems. In the reproductive system, CEP55 can regulate spermatogonia proliferation and sperm maturation, mediate oocyte meiotic spindle assembly and orderly cell cycle progression and maintain the developmental homeostasis of germ cells (12-14). During embryonic development, CEP55 participates in key processes such as embryonic brain development and ciliogenesis by regulating the cytokinesis and apoptosis of neural stem cells, rendering it an essential molecule for the normal development of mammalian embryos (15). In addition, as a crucial adaptor molecule in the ubiquitin signaling pathway, CEP55 can modulate ESCRT functions via a non-degradative ubiquitin signaling pathway, thereby mediating the regulation of various physiological processes (5). Notably, CEP55 is a typical cancer-testis antigen. It is lowly expressed only in testis and thymus tissues under normal physiological conditions, barely expressed in other normal tissues, but highly expressed in various pathological tissues, which renders it a promising potential target for tumor-targeted diagnosis and therapy (16,17). The molecular structure of CEP55 is illustrated in Fig. 1.

Molecular regulatory mechanisms and signaling pathways. At the level of cell division regulation, the subcellular localization and functional activation of CEP55 rely on precise phosphorylation modifications. Erk2/Cdk mediates the phosphorylation of CEP55 at the Ser425 and Ser428 sites, promoting its dissociation from the centriole, and subsequently interacts with Plk1 to induce phosphorylation at the Ser436 site, driving the targeted localization of CEP55 to the midbody to precisely regulate cytokinesis; abnormalities in this phosphorylation program lead to cell division failure and genomic instability (18). In addition, functional abnormalities of molecules including LNX2, NEURL and UCHL1 hinder the localization of CEP55 to the midbody, resulting in residual midbody accumulation, abnormal intercellular bridge structures, and the formation of multinucleated cells, thereby disrupting the progression of cell division (19).

The steady-state expression of CEP55 is precisely regulated at multiple levels, forming a complex and orderly molecular regulatory network. At the transcriptional level, E2F7, FOXM1 and SPI1 positively activate CEP55 expression, whereas FOXF2 and p53 exert negative inhibitory effects, jointly maintaining its moderate expression in normal cells (20-22). At the post-translational modification (PTM) level, Pin1 promotes Plk1-mediated phosphorylation of CEP55 to sustain its function. USP8 and USP9X inhibit CEP55 degradation through deubiquitination, whereas TSG101 mediates its degradation via the lysosomal pathway, collectively constructing a dynamic 'stability-degradation' balance system for the CEP55 protein (23-26). At the protein interaction level, CEP55 interacts with centrosome- and spindle-associated proteins as well as CBX2, participating in core processes such as spindle regulation and signal transduction, which further expands its biological functional network (27,28).

In tumor pathological regulation, CEP55 plays a core pro-oncogenic role via multiple pathways and mechanisms. First, CEP55 activates the PI3K/AKT/mTOR pathway, regulating downstream effector molecules (for example, pGsk3 β / β -Catenin/Myc and mTOR) to drive tumor cell proliferation, migration and invasion. This mechanism has been validated in tumors [for example, lung adenocarcinoma (LUAD), renal cell carcinoma (RCC) and gastric cancer (GC)] (29-31). Second, CEP55 disrupts the Chk1-dependent S-phase checkpoint and disorganizes microtubule structures, inducing DNA damage and genomic instability, which drives the occurrence of spontaneous tumor malignancy (29). Third, CEP55 participates in tumor progression through competing endogenous RNA (ceRNA)-mediated post-transcriptional regulation. In bladder cancer, the 3'-UTR of CEP55 competitively adsorbs microRNA (miR)-497-5p and simultaneously inhibits the transcription of miR-497-5p by activating the NF- κ B pathway. As a result, the targeted inhibition of PTHLH and HMGA2 is relieved. Accordingly, the P38MAPK/ERK1/2 pro-oncogenic pathway is activated, accelerating malignant tumor progression (32). Fourth, CEP55 is involved in remodeling the tumor immune microenvironment (TIME). By reducing T-cell infiltration within the tumor microenvironment (TME), inducing tumor immune exclusion, and reinforcing the local immunosuppressive state, CEP55 mediates resistance to immune checkpoint inhibitors (ICIs). This renders CEP55 a key regulatory molecule in tumor immune

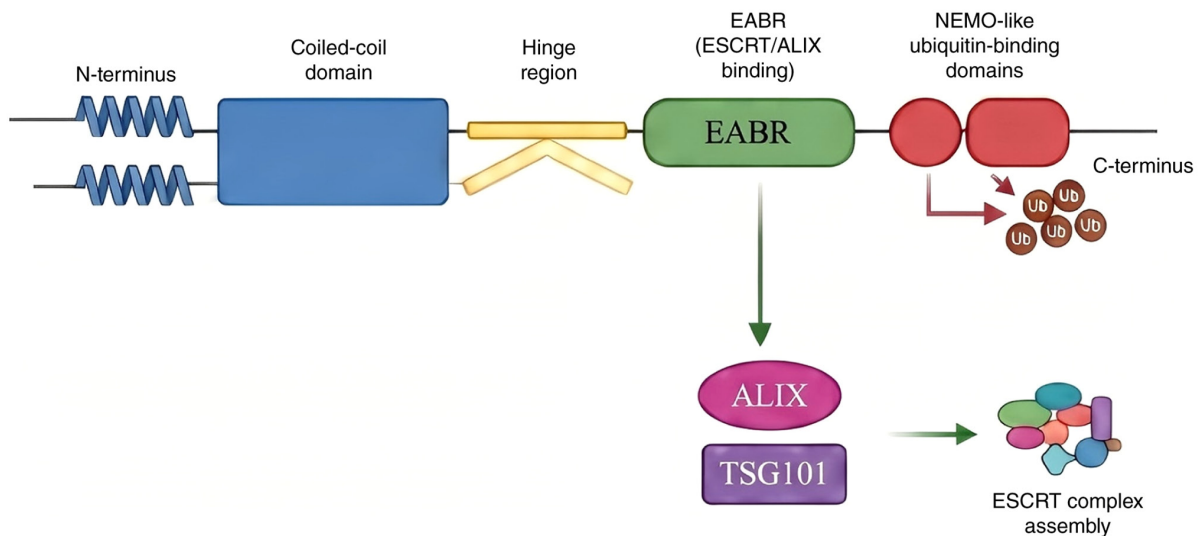


Figure 1. Molecular structure of Centrosomal protein 55. The N-terminus contains a coiled-coil domain, the central region is a hinge region, the C-terminus possesses an EABR region (which can bind TSG101 and ALIX), and the C-terminus also contains two NEMO-like ubiquitin-binding domains. ESCRT, endosomal sorting complex required for transport.

escape (33). Fifth, aberrant overexpression or functional dysregulation of CEP55 disrupts the precise spatiotemporal regulation of cytokinesis, leading to failed abscission, persistent midbody remnants and the formation of binucleated or multinucleated cells (8,9,18,19), thereby participating in tumorigenesis. These cytokinesis defects directly induce chromosomal instability and aneuploidy, both well-established drivers of tumor initiation and progression, as evidenced by the emergence of genomic instability and spontaneous tumor formation in Cep55 overexpressing mice (29) and by CEP55 mediated control of chromosomal instability through the regulation of microtubule dynamics (34). In addition, accumulated midbody remnants can further activate pro-survival signaling pathways and drive cellular reprogramming toward a stem-like, tumorigenic state (29,35). As a well-recognized driver of tumorigenesis, genomic instability in turn activates multiple oncogenic signaling pathways, including PI3K/AKT/mTOR and NF- κ B, collectively promoting malignant transformation and driving tumor proliferation, invasion and metastasis (29-31). Collectively, CEP55-mediated cytokinesis dysfunction acts as an upstream initiating event that amplifies a cellular-level defect in cytokinesis into the macroscopic pathological process of tumor initiation and progression, through both the induction of genomic instability and the activation of downstream oncogenic signaling. The expression and function of CEP55 are coordinately regulated by PTMs, protein-protein interactions and multiple signaling pathways, thereby forming a precise and multifunctional network centered on cell-cycle regulation, tumor malignant phenotypes and immune dysregulation. The biological characteristics and mechanism of action of CEP55 are depicted in Fig. 2.

3. Expression and mechanism of action of CEP55 in diseases

Expression and mechanism of action in tumors. Extensive pan-cancer studies and clinical cohort analyses have confirmed that CEP55 is significantly overexpressed in a variety of

malignant tumors. Its expression level is closely correlated with tumor pathological grade, TNM stage, invasion and metastasis, recurrence risk, and poor patient prognosis. Thus, CEP55 can act as a core oncogene with broad-spectrum and tumor-specific characteristics (36,37). A pan-cancer study based on 15,823 multicenter clinical samples demonstrated that CEP55 is significantly upregulated in 20 out of 33 tumor types. Its mRNA expression level effectively distinguishes 21 tumor types from normal tissues (AUC=0.97). Moreover, CEP55 expression is significantly correlated with tumor mutation burden, microsatellite instability, and immune microenvironment status, marking it a core target for tumor prognosis evaluation and targeted intervention (36). Meanwhile, CEP55 regulates tumor immune infiltration patterns and chemotherapy responses, thereby modulating the sensitivity of tumor cells to multiple antitumor drugs. These findings indicate that CEP55 serves as a novel biomarker for tumor prognosis prediction and a potential target for antitumor targeted therapy, with promising translational value in precision tumor diagnosis and treatment (37).

Digestive system tumors. CEP55 is abnormally overexpressed in digestive system tumors, including GC, liver cancer, colorectal cancer (CRC), pancreatic cancer and esophageal squamous cell carcinoma (ESCC). By regulating the cell cycle, pro-oncogenic signaling pathways, and the immune microenvironment, CEP55 drives the malignant progression of these tumors and provides a potential target for the precision diagnosis and treatment of digestive system malignancies.

GC: GC is a malignant digestive-tract tumor characterized by insidious early symptoms, high malignancy, strong invasive and metastatic potential, and overall poor prognosis. Previous studies have verified that dysregulated cell-cycle control, aberrant activation of signaling pathways, and imbalanced ceRNA-mediated post-transcriptional regulation represent the major pathological mechanisms underlying GC initiation and progression. In addition, multiple studies have confirmed that CEP55 is specifically overexpressed in GC tissues and exerts a critical regulatory role in GC malignant progression. The

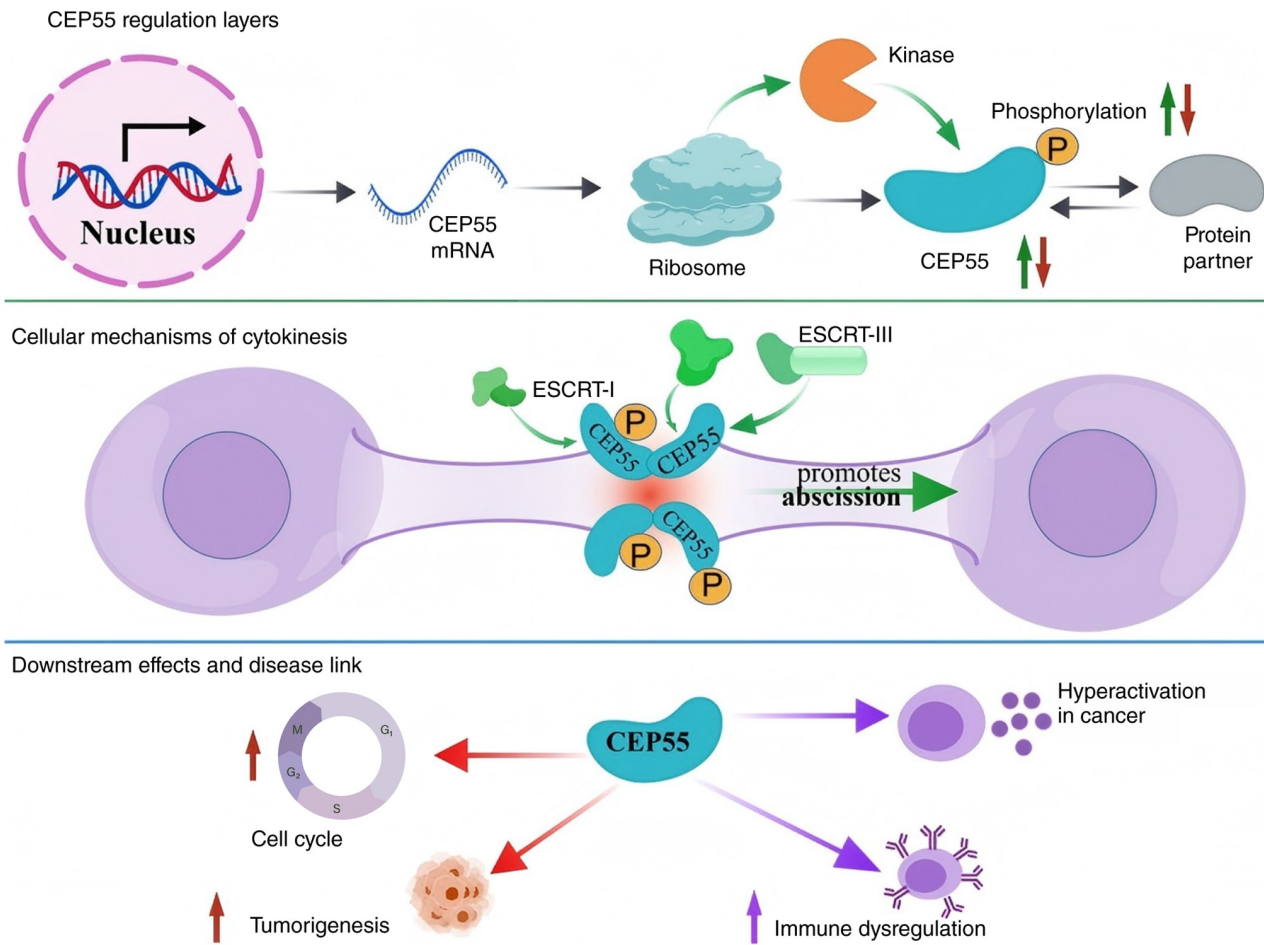


Figure 2. Biological characteristics and mechanism of action of CEP55. The core physiological function of CEP55 is to precisely regulate cell mitosis, and its aberrant expression disrupts cell cycle homeostasis, thereby mediating tumorigenesis, immune dysregulation, and other pathological processes. CEP55, Centrosomal protein 55; ESCRT, endosomal sorting complex required for transport.

underlying mechanisms are summarized as follows. CEP55 activates the AKT signaling pathway to inhibit p21 activity. Accordingly, the cell cycle can be arrested at the G2/M phase, and GC cell proliferation and *in vivo* tumorigenesis can be promoted (31). At the post-transcriptional regulatory level, LINC00662 competitively adsorbs miR-195-5p. Thus, the targeted inhibitory effect of miR-195-5p on CEP55 can be alleviated. This process forms the oncogenic LINC00662/miR-195-5p/CEP55 axis and accelerates the invasion and metastasis of GC cells (38). Clinical validation results show that the AUC value of CEP55 for GC diagnosis exceeds 0.9, demonstrating its excellent performance for early screening and differential diagnosis between benign and malignant tumors. Furthermore, high CEP55 expression indicates poor patient prognosis and acts as an independent prognostic marker for GC (39).

Liver cancer: Liver cancer is a highly malignant, rapidly progressing digestive system cancer characterized by a high recurrence rate and poor prognosis. Uncontrolled cell cycle progression, abnormal activation of pro-oncogenic signaling pathways, dysregulation of the ceRNA regulatory network, and imbalance of the TIME are the core pathological mechanisms driving the occurrence and progression of liver cancer. CEP55 is significantly upregulated in liver cancer tissues, and its expression level is closely associated with tumor grade,

clinical stage and poor patient prognosis (40,41). Mechanistic studies have shown that DNA hypomethylation serves as a critical epigenetic mechanism mediating the abnormal upregulation of CEP55 in liver cancer. Highly expressed CEP55 can activate classic pro-oncogenic pathways, including the cell cycle, mTOR and VEGF pathways, thereby continuously driving the malignant progression of liver cancer (40). At the level of phosphorylation signal regulation, CEP55 can directly bind to JAK2 and promote JAK2 phosphorylation, activate the JAK2-STAT3 pathway, and upregulate the expression of downstream MMP2 and MMP9, thereby facilitating the migration and invasion of liver cancer cells. Targeted intervention of this pathway can effectively reverse the oncogenic effect of CEP55 (42). Meanwhile, CEP55 can interact with sperm antigen 5 (SPAG5) at the protein level, induce AKT phosphorylation at the Ser473 site, and activate the PI3K/AKT pathway, which accelerates the proliferation, invasion and metastasis of liver cancer cells (43). At the post-transcriptional regulatory level, multiple ceRNA axes modulate the abnormal expression of CEP55 and participate in the malignant progression of liver cancer. Specifically, the imbalance of the CTBP1-AS2/miR-19-5p/CEP55 and miR-363-3p/SPAG5/CEP55 regulatory axes markedly promotes liver cancer progression, and lncRNA BPESC1 positively regulates CEP55 expression via miR-424, thereby participating in the occurrence and development

of early-stage liver cancer (44,45). At the immune regulatory level, CEP55 is critically involved in the remodeling of the liver cancer immune microenvironment. It can regulate the infiltration patterns of various immune cells, upregulate the expression of immune checkpoint molecules, and mediate tumor immune escape. Furthermore, CEP55 is specifically highly expressed in liver cancer subtypes with an immunosuppressive phenotype and can effectively predict immunotherapy efficacy for patients with liver cancer (46,47). In terms of clinical translation, CEP55 can be combined with multiple genes to construct a multi-gene prognostic risk score model. This model is not only applicable to the precise survival prognosis stratification of patients with different liver cancer subtypes, including hepatitis B-related liver cancer and early-stage liver cancer, but also can evaluate tumor sensitivity to radiotherapy, chemotherapy and targeted drugs, thereby guiding individualized clinical medication (48,49).

CRC: CRC is a highly prevalent, aggressive malignant tumor of the digestive system with poor late-stage prognosis and high susceptibility to immunotherapy resistance. Existing studies show that core pathological mechanisms mediating the occurrence, invasion and recurrence of CRC encompass cell-cycle dysregulation, aberrant activation of signaling pathways, imbalanced ceRNA regulation, and suppression of the immune microenvironment. In addition, CEP55 is commonly abnormally overexpressed in CRC tissues and has been repeatedly identified as a hub gene in bioinformatics screening (50). Promoter DNA hypomethylation of CEP55 represents a characteristic molecular event in early-stage CRC, and this alteration can be utilized for early non-invasive screening (51). High CEP55 expression is closely associated with high histological grade, advanced TNM stage and KRAS mutation in CRC. It significantly lowers survival rates among patients with advanced lymph-node metastasis and serves as an independent poor-prognosis marker for CRC (52,53). At the molecular-mechanism level, CEP55 regulates the cell cycle by activating the PI3K/AKT and p53/p21 pathways. Thus, tumor proliferation and invasion can be promoted (53,54). At the post-transcriptional level, lncRNA NEAT1 relieves the targeted inhibition of CEP55 by sequestering miR-195-5p. This process forms the NEAT1/miR-195-5p/CEP55 pro-oncogenic regulatory axis, inhibits tumor-cell apoptosis, and accelerates malignant progression (55). At the immune-regulation level, CEP55 reduces intratumoral CD8⁺ T-cell infiltration and mediates resistance to ICIs. Targeted silencing of CEP55 can reshape the anti-TIME and reverse immune resistance (33). Meanwhile, acting as a tumor-specific antigen, CEP55-derived antigen peptides can activate specific cytotoxic T lymphocytes to precisely eliminate CRC stem cells and induce a potent antitumor response via the development of mixed peptide vaccines. They provide a novel direction for the research and development of CRC vaccines (56,57).

Pancreatic cancer: Pancreatic cancer is a highly malignant tumor of the digestive system characterized by rapid disease progression, difficulty in early diagnosis, high mortality and extremely poor prognosis. Previous studies have found that the abnormal activation of signaling pathways, the imbalance of centrosome homeostasis, and the disruption of the TIME are the core pathogenic mechanisms of pancreatic cancer. In addition, existing studies have reported that CEP55 is significantly

overexpressed in pancreatic adenocarcinoma, and its expression level is correlated with the clinical characteristics and prognosis of patients (58,59). The underlying mechanism is that CEP55 activates the PI3K/AKT/mTOR pathway by binding to PI3K-p110 and simultaneously activates the NFκB/IκBα pathway to upregulate the expression of cyclin D1, MMP2 and MMP9, thereby driving tumor proliferation, invasion and tumorigenesis; moreover, mTOR inhibitors can effectively reverse the pro-oncogenic effects of CEP55 (60,61). Furthermore, CEP55 induces the imbalance of centrosome homeostasis and genomic instability, thus participating in the early malignant transformation of pancreatic cancer (62). In terms of clinical translation, CEP55 has been incorporated into a multi-gene prognostic model for pancreatic cancer, and the risk score constructed based on CEP55 combined with multiple indicators can accurately achieve prognostic stratification and guide individualized postoperative treatment for patients (63,64).

ESCC is a common malignant tumor of the digestive system characterized by a high recurrence rate and poor prognosis. Previous studies have suggested that persistent activation of pro-oncogenic signaling pathways, dysregulation of the ceRNA regulatory network, and imbalance of the TIME constitute important pathological bases for its malignant progression. In addition, multiple studies have confirmed that CEP55 is significantly overexpressed in ESCC tissues; this overexpression is closely associated with poor tumor differentiation, depth of invasion, lymph node metastasis, and postoperative recurrence, and acts as an independent poor-prognosis risk factor, including in the N0 stage (65,66). The underlying mechanism may involve CEP55 regulating programs governing the malignant phenotype of tumors by activating multiple pathways such as Src/FAK/ERK and PI3K/AKT, thereby promoting tumor cell proliferation, migration, invasion and epithelial-mesenchymal transition (EMT) (66,67). At the transcriptional regulatory level, miR-148a-3p can specifically target and repress CEP55 expression. The imbalanced expression pattern of low miR-148a-3p and high CEP55 is commonly observed in esophageal cancer tissues. miR-148a-3p upregulation can effectively inhibit malignant tumor progression (68). In terms of immune regulation, CEP55 participates in immune microenvironment remodeling in ESCC. As a core molecule within the miR-378-5p-APOC1/CEP55 immune regulatory pathway, its aberrant expression correlates strongly with activation of tumor immune regulatory pathways and dysregulated immune-cell infiltration, and it can modulate tumor progression and influence immunotherapy responses (69). In summary, CEP55 has multifaceted value for prognostic stratification, malignant-progression regulation and immune-intervention guidance in ESCC, making it a credible potential target for prognostic assessment and combined targeted and immune therapy for this disease.

Respiratory system tumors. Lung cancer is a malignant tumor of the respiratory system with extremely high clinical incidence and mortality rates, as well as substantial heterogeneity, with non-small cell lung cancer (NSCLC) being its predominant pathological type. Cell cycle dysregulation, abnormal epigenetic modifications, imbalance of the ceRNA regulatory network, and tumor immune dysregulation are the core pathological mechanisms driving the occurrence,

proliferation, invasion, metastasis and drug resistance of lung cancer. In addition, CEP55 is significantly overexpressed in NSCLC, and its prognostic value is subtype-specific, serving as an independent poor prognostic factor only for the overall survival (OS) and recurrence-free survival of patients with LUAD, with no significant prognostic implication for squamous cell carcinoma (70). High expression of CEP55 is closely associated with advanced tumor stage, pleural invasion, poor differentiation and postoperative recurrence in LUAD, and it exhibits prognostic stratification value in early-stage and smoking-type LUAD populations (71,72). At the epigenetic level, DNA hypomethylation contributes to the abnormal upregulation of CEP55, which, as a downstream gene can mediate the pro-oncogenic processes of tumors (73). Mechanistically, CEP55 inhibits tumor cell apoptosis by regulating the p53, Myc and G2M checkpoint pathways, thereby promoting lung cancer invasion and metastasis (74,75). At the post-transcriptional regulatory level, multiple ceRNA regulatory axes can modulate CEP55 expression and mediate the malignant progression of lung cancer. Among these axes, microRNAs including miR-195-5p, miR-144-3p, miR-514a-3p and miR-148b-3p can directly target and inhibit CEP55, whereas non-coding RNAs such as LINC01087, TYMSOS, TMPO-AS1 and circ_0120376 can alleviate this inhibitory effect through endogenous competition, thereby forming multiple pro-oncogenic pathways. Meanwhile, CEP55 overexpression can mediate gemcitabine chemotherapy resistance in LUAD, and downregulating CEP55 can effectively reverse the drug-resistant phenotype (20,76-78). In terms of immune regulation, CEP55 can regulate interferon-related signaling and the PD-1/PD-L1 immune checkpoint pathway, participating in the remodeling of the TIME, and the multi-gene immune prognostic model incorporating CEP55 can accurately predict patient prognosis and immunotherapy response (79). In clinical translation, CEP55 can be combined with genes including APOBEC3B, CDC6 and TYMS to construct a multi-dimensional prognostic and metastasis assessment model, which can predict immunotherapy efficacy. Additionally, CEP55 can serve as an ALK fusion partner gene affecting targeted therapy response, providing an important basis for the precision diagnosis and treatment of lung cancer (79,80).

Reproductive system tumors. CEP55 is abnormally overexpressed in reproductive system tumors including breast cancer (BC), ovarian cancer (OC), cervical cancer (CC) and prostate cancer (PCa). It participates in the regulation of tumor malignant progression. It is closely correlated with patient prognosis. Furthermore, it provides a novel direction for the precision diagnosis and treatment of reproductive system tumors.

BC: BC is a neoplastic disease characterized by complex subtyping, strong invasiveness and significant prognostic differences in various subtypes. Previous studies have demonstrated disordered cell mitosis, abnormal activation of signaling pathways, and TME remodeling as the major pathological mechanisms of BC. CEP55 is a microtubule-bundling protein. It participates in the regulation of cell mitosis and genomic stability. Moreover, it is markedly overexpressed in BC tissues. Its expression is modulated by multiple mechanisms, including DNA hypomethylation, SPI1 transcriptional activation, USP8-mediated deubiquitination and stabilization,

and negative regulation by miR-144 (81,82). At the molecular-mechanism level, CEP55 may promote tumor proliferation and glucose metabolic reprogramming, suppress cell apoptosis and ferroptosis, and concurrently induce type 2 macrophage polarization to remodel the immunosuppressive microenvironment by activating the PI3K/AKT and MEK1/2-MYC pathways (22,24). Furthermore, as a cancer-testis antigen, CEP55 can be processed into specific antigenic peptides to trigger antitumor immune responses, making it suitable for immune intervention in drug-resistant BC. CEP55 deficiency can increase the sensitivity of triple-negative BC (TNBC) to mitotic drugs (17,83). In clinical translation, CEP55 can accurately assess the prognosis of different BC subtypes and predict bone-metastasis risk. Its specific inhibitor CD-437 and corresponding peptide vaccines provide novel strategies for targeted therapy and immunotherapy of BC (84-86).

OC: OC is a neoplastic disease characterized by strong occultness, high metastatic and recurrent potential, diverse pathological subtypes and poor prognosis. Previous studies have identified that microtubule dynamic imbalance, activation of pro-oncogenic signaling pathways, and abnormal epigenetic regulation constitute the major pathological mechanisms of OC. In addition, CEP55 is significantly overexpressed in epithelial OC and high-grade serous OC. Its overexpression is closely correlated with tumor stage, metastasis and recurrence, and adverse prognosis, and acts as an independent prognostic risk factor (87). Mechanistically, ALKBH5 degrades FOXP2 mRNA through m6A demethylation, thereby relieving transcriptional inhibition of CEP55. Upregulated CEP55 promotes EMT in OC cells, inhibits cell-cycle arrest, and facilitates malignant tumor progression (88). Meanwhile, CEP55 maintains microtubule stability, modulates the dynamic balance of spindle microtubules, promotes microtubule polymerization while inhibiting microtubule depolymerization, induces chromosomal instability, and exacerbates malignant tumor progression (34). In clinical translation, CEP55 can function as a high-quality biomarker for OC, especially for high-grade primary OC and high-grade serous OC, and serves as a reliable indicator for early diagnosis, disease assessment and prognostic evaluation (89).

CC: CC is a neoplastic disease characterized by strong occultism, a high tendency for metastasis, insidious progression, and distinct prognostic heterogeneity. Previous studies have demonstrated that imbalanced regulation of non-coding RNAs, HPV-mediated transcriptional abnormalities, and dysregulated inflammatory signaling pathways constitute the primary pathological mechanisms of CC. Furthermore, CEP55 is persistently overexpressed in CC tissues, and its expression level increases gradually during the malignant transformation from cervical intraepithelial neoplasia to invasive carcinoma. This aberrant expression is closely correlated with advanced tumor stage, lymph node metastasis, and reduced patient survival rates (90,91). CEP55 is negatively regulated by miR-144-3p and the miR-497/195 gene cluster. Moreover, miR-144-3p delivered by exosomes derived from bone marrow mesenchymal stem cells can effectively down-regulate CEP55 expression and thereby inhibit cervical tumor progression (92,93). Mechanistically, CEP55 drives malignant tumor phenotypes by promoting the proliferation, invasion and EMT of CC cells and suppressing cellular apoptosis.

Meanwhile, CEP55 participates in the modulation of inflammatory pathways and HPV-mediated tumor transcriptional regulation (90,94). Clinically, CEP55 can act as a specific diagnostic and prognostic assessment marker for CC. High CEP55 expression indicates a poor prognosis in patients and aids in predicting the risk of metastasis (90). Additionally, CEP55 has been integrated into the precision prognostic assessment model for CC, providing a molecular basis for the formulation of clinical diagnosis and therapeutic strategies for advanced CC (95).

Urinary system tumors. Among urological tumors, CEP55 is significantly overexpressed in renal cancer, bladder cancer and other urological malignancies. It participates in regulating malignant tumor progression and possesses potential clinical application value.

Renal cancer: RCC [including clear-cell RCC (ccRCC)] and adrenocortical carcinoma are common, highly aggressive, metastatic neoplastic diseases of the urinary and endocrine systems with markedly heterogeneous prognoses. Previous studies have found that activation of pro-oncogenic signaling pathways such as PI3K/AKT/mTOR, dysregulation of the ceRNA network, and disruption of the TIME constitute the major pathological mechanisms underlying the development of these tumors. In addition, CEP55 is significantly overexpressed in ccRCC and adrenocortical carcinoma; this overexpression correlates with tumor stage, invasion, metastasis and poor prognosis, indicating its favorable diagnostic and prognostic evaluation value (96,97). Mechanistically, CEP55 induces EMT by activating the PI3K/AKT/mTOR pathway, thereby promoting cancer-cell proliferation and invasion (30). Its expression is regulated by multiple ceRNA axes: circ_001287 targets and sponges miR-144 to relieve inhibitory effects on CEP55, whereas lncRNA-SNHG12 binds E2F1 to upregulate CEP55 at the transcriptional level, jointly facilitating the malignant progression of renal cancer (98,99). Furthermore, CEP55 can also modulate the TIME, alter immune-checkpoint expression, and mediate resistance to targeted immunotherapy (97,100,101). In terms of clinical translation, CEP55 can be used for the diagnosis and prognostic assessment of renal cancer and adrenocortical carcinoma. The multi-gene model constructed based on CEP55 can accurately stratify patient prognosis, and CEP55 is also a key gene and potential small-molecule drug target for renal cancer identified through bioinformatics screening (102).

Bladder cancer: Bladder cancer is a neoplastic disease of the urinary system characterized by a high incidence rate, diverse pathological subtypes, a tendency to recur, and substantial difficulty in early diagnosis. Previous studies have found that the imbalance of ceRNA network regulation, activation of pro-oncogenic signaling pathways, and cellular dysregulation are the primary pathological mechanisms underlying bladder cancer. Furthermore, as a typical cancer-testis antigen, CEP55 is specifically highly expressed in bladder cancer tissues, barely expressed in adjacent normal tissues, and presents even higher expression levels in muscle-invasive bladder cancer (16). Specific upregulation of CEP55 mRNA can be detected in the urine of patients with non-muscle-invasive bladder cancer, serving as a novel biomarker for non-invasive screening, differentiation of benign and malignant hematuria, and postoperative recurrence monitoring (16,103).

Mechanistically, CEP55 acts as a ceRNA via its 3'-UTR to silence miR-497-5p, thereby relieving the inhibitory effects on PTHLH and HMGA2. Meanwhile, it downregulates the transcription of miR-497-5p through the NF- κ B pathway and activates the P38MAPK and ERK1/2 pathways to promote tumor EMT and cisplatin resistance (32). Additionally, CEP55 participates in the regulation of the cell cycle and cytokinesis in bladder cancer cells; mulberry fruit water extract combined with ionizing radiation inhibits Aurora B activity and induces mitotic catastrophe, accompanied by altered CEP55 expression, thereby enhancing radiosensitivity and providing an experimental basis for radiosensitization and chemo-sensitization therapy for bladder cancer (104). In clinical translation, CEP55 can serve as a specific diagnostic biomarker for bladder cancer, applicable to early non-invasive screening and differentiation of benign and malignant hematuria, and its combination with other genetic tests can improve diagnostic efficacy; meanwhile, as a core immune-related biomarker, it provides a basis for immune-targeted therapy and tumor vaccine development (16,105).

PCa. PCa is one of the most common malignancies of the male reproductive system, whose malignant progression typically proceeds from a hormone-sensitive state to castration-resistant PCa (CRPC) and further to the more aggressive neuroendocrine (NE) subtype. Previous studies have established that genetic and molecular mechanisms, including cell-cycle dysregulation and aberrant chromosome segregation and mitosis, act as important drivers of PCa initiation and progression, and the role of tumor mutational burden (TMB)-related genes in evaluating tumor malignancy and prognosis has attracted increasing attention. Transcriptome profiling has demonstrated that CEP55 is highly expressed in PCa and progressively upregulated alongside malignant progression, with the highest expression levels observed in NE PCa (106). Mechanistically, CEP55 is a direct target gene of the tumor-suppressor miR-144-3p; downregulation of miR-144-3p in PCa and CRPC alleviates its targeted repression of CEP55, thereby facilitating tumor-cell proliferation, migration and invasion, abrogating G1/S cell-cycle arrest, and inhibiting apoptosis (107,108). Furthermore, CEP55 modulates tumor-cell plasticity, upregulates NE tumor markers, and mediates cisplatin chemoresistance via CDK1 phosphorylation at Tyr15, thus driving the phenotypic transition of tumors from the hormone-sensitive state to castration-resistant and NE subtypes (106). In addition, as a core TMB-related hub gene, CEP55 participates in cell-cycle progression, chromosome segregation and mitosis, correlates with patient disease-free survival (DFS) and OS, and can be combined with TMB to assess PCa malignancy, prognosis and immunotherapy efficacy (109).

Thyroid cancer (TC). TC is a common endocrine malignancy encompassing papillary (PTC), follicular (FTC), medullary (MTC) and anaplastic (ATC) subtypes that exhibit marked differences in biological behavior and prognosis. Among these subtypes, ATC features extremely high malignancy together with potent invasive and metastatic potential, resulting in generally poor prognosis for affected patients. Previous studies have shown that aberrant regulation of cell-cycle pathways constitutes a key mechanism underlying TC initiation and malignant progression, and relevant

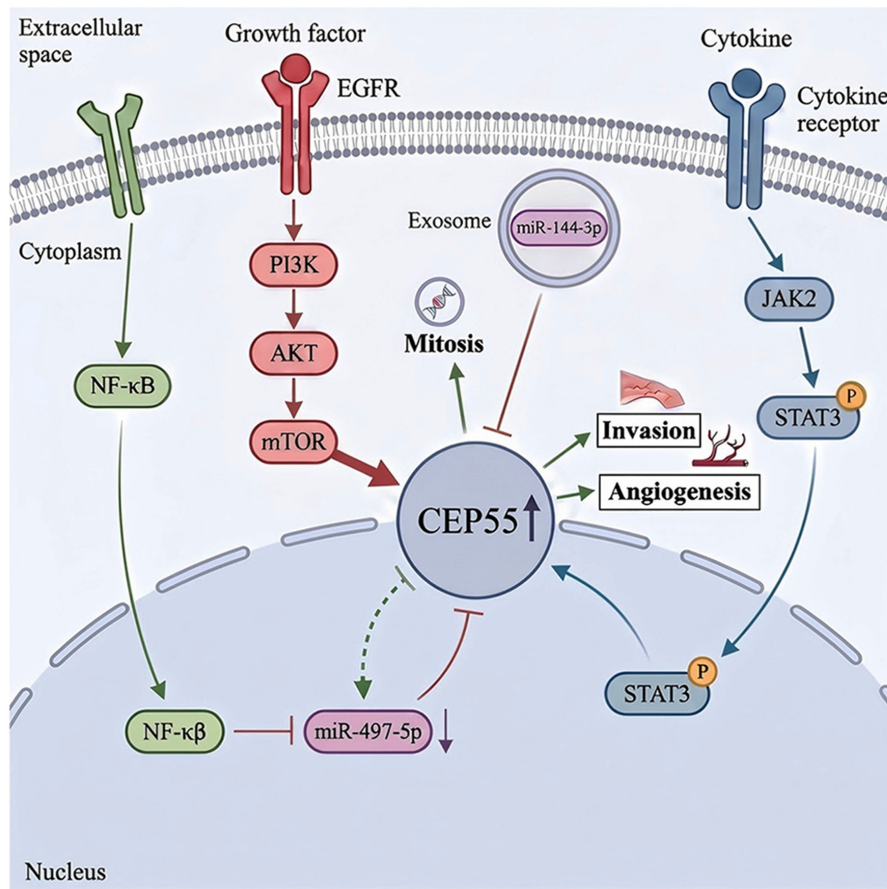


Figure 3. Dysregulated CEP55 expression mediates tumorigenesis. Growth factors and cytokines within the tumor microenvironment activate the PI3K/AKT/mTOR pathway and JAK2/STAT3 pathway, respectively, alongside intracellular NF-κB pathway activation, which collaboratively upregulate CEP55 expression. Exosome-carried miR-144-3p directly suppresses CEP55 expression, whereas the NF-κB pathway downregulates the tumor-suppressive miR-497-5p, relieving the post-transcriptional inhibitory effect of miR-497-5p on CEP55 and further sustaining high CEP55 levels. Collectively, multiple signalling pathways synergistically elevate CEP55. Upregulated CEP55 facilitates mitotic progression to accelerate tumor cell proliferation, and simultaneously drives tumor invasion and angiogenesis to amplify malignant phenotypes, ultimately mediating tumor initiation and progression. CEP55, Centrosomal protein 55; miR, microRNA.

core differentially expressed genes may provide a potential molecular basis for disease screening and pathological classification (110). Furthermore, integrated bioinformatics analyses have revealed that CEP55 is highly expressed in TC, with particularly prominent expression in ATC; its high expression is closely linked to tumor metastasis and represents an independent adverse prognostic factor that shortens OS in these patients. Mechanistically, CEP55 activates the PI3K/AKT signaling pathway and, by enhancing phosphorylation of pathway-associated proteins, promotes TC cell proliferation and metastasis and fuels malignant progression; by contrast, CEP55 downregulation reduces such phosphorylation and consequently halts the malignant progression of TC. Accordingly, CEP55 may function as a prognostic biomarker and a candidate therapeutic target for ATC (111).

Besides the aforementioned tumors, CEP55 is also aberrantly overexpressed in endometrial cancer (112) and osteosarcoma (113), wherein it drives malignant progression via regulating cell proliferation and invasion. However, available studies of these tumors are restricted to small-sample basic validations and bioinformatics predictions, with a lack of evidence from multicenter clinical cohorts. Their precise regulatory mechanisms and clinical translational value still warrant further in-depth investigation.

Among the above malignant tumors, the tumorigenic mechanism driven by dysregulated CEP55 expression are illustrated in Fig. 3. The tumor-specific expression profile, regulatory pathways and mechanisms of CEP55 are summarized in Table I.

Expression and mechanism of action in non-neoplastic diseases. Beyond neoplastic diseases, accumulating evidence suggests that CEP55 is also involved in the development and progression of certain genetic disorders, inflammatory and immune-mediated diseases, and chronic non-communicable diseases, predominantly through modulation of the cell cycle, inflammatory activation, and embryonic development. Since the present review focuses on the oncogenic functions of CEP55, this section briefly outlines key findings regarding non-neoplastic diseases.

Immune and inflammatory diseases. CEP55 contributes to autoimmune and inflammatory diseases through its functions in cell-cycle regulation, inflammatory activation and immune-cell differentiation and migration (114-116); its dysregulated expression mediates functional imbalances in keratinocytes, lymphocytes and macrophages, rendering CEP55 a candidate biomarker for multiple autoimmune diseases. Among autoimmune skin disorders, CEP55 has

Table I. Summary of CEP55 expression in neoplastic diseases.

Disease	Pathway	Mechanism	Clinical sample validation or not	Cytology or animal experiments	(Refs.)
Gastric cancer	PI3K/AKT	Activated PI3K/AKT signaling suppresses p21 expression, thereby inducing G2/M phase arrest	No	Cell line	(31,38,39)
Hepatocellular carcinoma	JAK2-STAT3, PI3K/AKT	It interacts with JAK2/SPAG5 to activate JAK2-STAT3 and PI3K/AKT signaling, thereby upregulating CEP55 expression	Yes, n=846	Cell line	(40-45)
Colorectal cancer	PI3K/AKT, p53/p21	CEP55 regulates the cell cycle by activating the PI3K/AKT and p53/p21 pathways, thereby promoting tumor proliferation and invasion	Yes, n=169	Cell line	(50-55)
Pancreatic cancer	PI3K/AKT/ mTOR, NF- κ B/ I κ B α	Combined PI3K signaling activates PI3K/AKT/mTOR; NF- κ B/I κ B α activation upregulates MMP2/MMP9	Yes, n=1163	Cell line, both	(58-64)
Esophageal cancer	Src/FAK/ERK, PI3K/Akt	Activation of Src/FAK/ERK and PI3K/Akt pathways promotes proliferation, invasion and EMT	Yes, n=322	Cell line, both	(65-69)
Lung cancer	PI3K/AKT, RhoA/ROCK1	Activates the PI3K/AKT and RhoA/ROCK1 pathways; Exosomal transport of CEP55 activates mTOR to promote angiogenesis	Yes, n=157	Cell line	(70-79)
Breast cancer	MEK1/2-MYC, PI3K/AKT	Downstream effector of MEK1/2-MYC; promotes CHMP6 expression to inhibit ferroptosis and induce M2 macrophage polarization; transcriptionally activated by SPI1/FOXM1 and stabilized via USP8-mediated deubiquitination	Yes, n=596	Cell line, both	(17,20,22,24,81-86)
Ovarian cancer	EMT	ALKBH5 downregulates FOXP2 to upregulate CEP55, thereby modulating cell cycle and EMT	Yes, n=333	Cell line	(34,87-89)
Cervical cancer	miR-144-3p/ CEP55	Exosomes derived from hBMSCs deliver miR-144-3p to downregulate CEP55	Yes, n=480	Cell line	(90-95)
Renal cell carcinoma	PI3K/AKT/ mTOR	Activation of the PI3K/AKT/ mTOR pathway induces EMT	Yes, n=1009	Cell line, both	(30,96-102)
Bladder cancer	NF- κ B/ P38MAPK/ ERK1/2	Sponges miR-497-5p via the 3'untranslated region and activates NF- κ B, which downregulates miR-497-5p, upregulates PTHLH/HMGA2, triggers p38 MAPK/ERK1/2 signaling and induces EMT	Yes, n=433	Cell line	(16,32)

EMT, epithelial-mesenchymal transition; miR, microRNA.

been reported as a dysregulated core gene in psoriasis and atopic dermatitis. In psoriasis, CEP55 participates in cell-cycle progression, mitosis and cytoskeletal remodeling and may act as a potential biomarker (115). It also functions as a shared mediator in psoriasis comorbid with Crohn's disease, and its targeted inhibition represses the release of inflammatory cytokines (117). In atopic dermatitis, CEP55 is overexpressed in lesional keratinocytes and can be integrated into machine-learning-based diagnostic models (114,116). For systemic autoimmune diseases, CEP55 exhibits high expression in peripheral blood and lesional tissues from patients with systemic lupus erythematosus (SLE), where it is enriched within plasmacytoid cells and CD4⁺ T lymphocytes; by disrupting oxidative phosphorylation and cell-cycle programs, it participates in SLE pathogenesis and may represent an auxiliary diagnostic target (118). In ulcerative colitis (UC), CEP55 expression fluctuates in activated macrophages and colonic lesional tissues, promotes chronic intestinal inflammation, and offers a candidate non-invasive biomarker (119). In primary Sjögren's syndrome, chronic pulmonary inflammation upregulates CEP55 through the JAK2/STAT3 axis, which may mediate malignant transformation into LUAD (120).

From an evidence-grading perspective, the aforementioned findings are heterogeneous in their level of support. The psoriasis, atopic dermatitis, SLE and UC studies are predominantly computational: CEP55 was identified by differential-expression analysis, immune-infiltration analysis, weighted gene co-expression network analysis or machine-learning modeling of public transcriptomic datasets, without independent patient-cohort validation (114-116,118,119). By contrast, the shared psoriasis-Crohn's disease biomarker study and the primary Sjögren's syndrome study combined bioinformatics with experimental verification, thereby providing wet-lab support for the predicted pathogenic mechanisms (117,120). Overall, however, independent multicenter clinical cohort validation of CEP55 in immune and inflammatory diseases is still lacking, and its diagnostic and therapeutic value in this setting remains to be established.

Reproductive and hereditary diseases. CEP55 regulates fertilized egg cleavage, neural stem cell proliferation, and multi-organ differentiation via its ubiquitin-binding domain, centrosome-localization domain, and multiple signaling pathways including PI3K/AKT, p53 and Hippo. Pathogenic mutations in CEP55 cause a spectrum of congenital genetic diseases, and its dysregulation also contributes to reproductive disorders and pregnancy-related complications.

In reproductive system diseases, CEP55 participates in meiosis, cytokinesis and gamete maturation. Its expression imbalance contributes to azoospermia, oocyte developmental arrest and impaired endometrial receptivity. In male reproduction, CEP55 functions together with TEX14 and MKLP1 to maintain intercellular bridges in germ cells. In transgenic mouse models, its overexpression persistently activates the PI3K/Akt/FoxO1 pathway, blocks spermatogonial differentiation and causes male infertility (121). By contrast, clinical sample analysis shows that CEP55 is significantly downregulated in the testicular tissues of patients with non-obstructive azoospermia (NOA), and it may serve as a non-invasive diagnostic marker (122). In female reproduction, CEP55 localizes to the oocyte spindle and midbody; its deficiency disrupts

spindle assembly and arrests meiosis, leading to chromosomal abnormalities and aneuploid gametes (14,123). In addition, CEP55 is involved in regulating the proliferation of endometrial epithelial cells and may also participate in the modulation of endometrial receptivity, which warrants further investigation (124).

During embryonic development, CEP55 is essential for sustaining fertilized egg meiosis, early embryonic cleavage, blastocyst formation and tissue differentiation. It modulates cytoskeletal and mitochondrial homeostasis and may cooperate with the p53 and Hippo pathways to govern symmetric/asymmetric cell division (125). CEP55 deficiency accelerates proteasomal degradation of Akt protein, which induces cell-cycle disorders, apoptosis and embryonic developmental arrest (126). In neural development, CEP55 interacts with the ESCRT complex to guarantee proper neural stem cell abscission. CEP55 knockout activates the p53 pathway, resulting in widespread brain apoptosis, microcephaly, and neonatal death in mice (15).

At the hereditary disease level, CEP55 mutation subtypes directly determine the severity of congenital malformations and survival prognosis. Homozygous nonsense and frame-shift mutations usually lead to perinatal-lethal syndromes, including MARCH syndrome and Meckel-Gruber syndrome, which are characterized by multisystem malformations such as hydrocephalus, polycystic kidney disease and cerebellar malformation (127-131). Compound heterozygous missense mutations located at critical C-terminal sites also give rise to severe MARCH syndrome (132). By contrast, common missense variants, compound heterozygous variants within non-critical regions, and terminal splice-site variants produce milder, viable phenotypes such as developmental delay, syndactyly and limb malformations (133). The genotype-phenotype correlations of CEP55 mutations are summarized in Table II.

With respect to evidence grading, this section is comparatively well supported by wet-lab data: The reproductive and developmental functions of CEP55 were established in Cep55-overexpressing and Cep55-knockout mouse models, in zebrafish and porcine embryo models, and in oocyte, spermatogonial and endometrial epithelial cell systems (121-126), whereas the congenital malformation spectrum rests on case-based genetic analyses of affected families (127-133). Independent clinical cohort validation nevertheless remains scarce. To date, only the NOA study incorporated an independent patient cohort, in which CEP55 downregulation was verified by reverse transcription-quantitative PCR (RT-qPCR) and western blotting in a small series of testicular specimens (n=6) and its diagnostic value was assessed by ROC analysis (121); most other reproductive findings still await confirmation in larger, multicenter patient cohorts.

Other diseases. CEP55 also exhibits aberrant expression in several non-cancerous diseases, including diabetic cardiomyopathy, chronic kidney disease (CKD), pulmonary arterial hypertension, acute spinal cord injury (SCI), interstitial cystitis and post-COVID-19 syndrome (134-139).

Diabetic cardiomyopathy: In a rat model of diabetic cardiomyopathy combined with high-glucose-treated H9C2 cardiomyoblasts, CEP55 was shown to bind β -hydroxy-butyrylated ANXA11 and to co-regulate centrosome amplification (γ -tubulin and PLK4) and mitochondrial dysfunction (134).

Table II. Genotype-phenotype correlations of CEP55 pathogenic mutations.

Authors, year	Mutation type	Specific variant	Protein consequence	Clinical phenotype	Survival	(Refs.)
Bondenson <i>et al</i> , 2017	Homozygous non-sense	c.256C>T (p.Arg86*)	Truncated protein, complete loss of function	Meckel-Gruber syndrome, Potter sequence, cystic renal dysplasia, hydranencephaly	Perinatal lethal	(130)
Frosk <i>et al</i> , 2017; Rawlins <i>et al</i> , 2019	Homozygous frameshift	Various truncating variants	Loss of CEP55 protein function	MARCH syndrome: hydrocephalus, polycystic kidney disease, renal dysplasia, cerebellar malformation, oligohydramnios	Perinatal lethal	(129,131)
Fu <i>et al</i> , 2025	Compound heterozygous missense (C-terminal critical sites)	Biallelic missense in EABR/ubiquitin-binding domains	Impaired midbody localization and ESCRT recruitment	Severe prenatal MARCH syndrome with multi-system malformations	Perinatal lethal	(132)
Barrie <i>et al</i> , 2020	Missense/compound heterozygous (non-critical regions)	Various missense variants outside critical domains	Partial protein function retained	Developmental delay, anencephaly, syndactyly, limb malformations	Viable	(133)
Barrie <i>et al</i> , 2020	Terminal splice site variants	Splice-site variants at gene termini	Altered splicing with residual function	Mild to moderate congenital malformations	Viable	(133)

CKD: Bioinformatic re-analysis of public datasets (GSE66494 and GSE80247) identified CEP55 as one of seven hub mRNAs within the LINC01094/miR-513b-5p/MELK ceRNA module; its underlying mechanism, however, remains unclear and warrants further investigation (135).

Pulmonary hypertension: Bioinformatics analysis of the GSE144274 dataset (idiopathic pulmonary arterial hypertension vs. healthy controls), combined with functional enrichment and PPI analyses, identified CEP55 as one of six core hub genes; its mechanistic role, however, remains unclear and warrants further investigation (136).

Acute SCI: Reanalysis of the public blood transcriptome dataset GSE151371 and the spinal cord dataset GSE45376 identified CEP55 as one of the top 15 hub genes, suggesting its involvement in the pathogenesis of acute SCI; the underlying mechanism remains unclear and warrants further investigation (137).

Interstitial cystitis: Integrated GEO-based differential-expression and immune-infiltration analyses identified CEP55 as one of 10 immune-related hub genes, and its diagnostic performance was evaluated using ROC curves; its mechanistic role, however, remains unclear (138).

Long COVID: Machine-learning-based screening of GEO transcriptomic datasets identified a four-gene signature comprising CEP55, CDCA2, MELK and DEPDC1B, which yielded a combined ROC value of 0.876 for the diagnosis of COVID-19 infection; the mechanistic basis of CEP55 in

this setting remains unclear and warrants further investigation (139).

In summary, the aforementioned findings are largely derived from bioinformatic screening of public transcriptomic datasets or from small-sample assays, and only a few have been further confirmed by cellular experiments; independent, large-scale clinical cohort validation is still lacking for most of these conditions. Nevertheless, CEP55 not only plays a pivotal role in tumor-related and immune-related diseases, but also exhibits significant importance in other conditions, including CKD, pulmonary arterial hypertension, acute SCI and interstitial cystitis. Further exploration of its potential regulatory molecular mechanisms may enhance the translational potential and clinical application of CEP55. The expression profiles and action mechanisms of CEP55 in non-tumor diseases are summarized in Fig. 4 and Table III.

4. Clinical translational application of CEP55

Diagnostic and prognostic evaluation value. CEP55, as a typical cancer-testis antigen, is characterized by highly restricted expression in normal tissues and specific abnormal expression in diseased tissues. It is lowly expressed only in normal human testis and thymus tissues and almost undetectable in other normal tissues, while its expression is significantly elevated under various pathological conditions, including tumors, autoimmune diseases and genetic diseases (16,17). Its

Table III. Summary of CEP55 expression in non-tumor diseases.

Authors, year	Disease	Pathway	Mechanism	Whether clinical sample validation (and sample size)	Cytology or animal experiments	(Refs.)
Yue <i>et al</i> , 2022; Li <i>et al</i> , 2025	Psoriasis	/	Hub genes derived from psoriasis-related differentially expressed genes	NO	Cell line	(115,117)
Li <i>et al</i> , 2025; Wu <i>et al</i> , 2023	Atopic dermatitis	/	Significantly expressed in key keratinocytes	NO	Cell line	(114,116)
Wang <i>et al</i> , 2025	Systemic lupus erythematosus	/	Imbalance of oxidative phosphorylation; oxidative phosphorylation imbalance	NO	Both	(118)
Li <i>et al</i> , 2024	Primary Sjögren's syndrome	JAK2/STAT3	Chronic pulmonary inflammation upregulates CEP55 through the JAK2/STAT3 axis, which may mediate malignant transformation into lung adenocarcinoma	NO	Both	(120)
Sinha <i>et al</i> , 2018; Shen <i>et al</i> , 2022	Male infertility (azoospermia)	PI3K/AKT	CEP55 overexpression activates PI3K/Akt to elevate FOXO1 phosphorylation and inhibit its nuclear retention	Yes, number of samples (n=6)	Both	(121,122)
Liu <i>et al</i> , 2018; Amanda <i>et al</i> , 2024	Endometriosis	p53	Regulates the proliferation of endometrial epithelial cells; its possible role in modulating endometrial receptivity remains to be clarified	NO	Cell line	(124,143)
Barrie <i>et al</i> , 2020	Viable congenital malformation	/	Missense/compound heterozygous/specific splice site variants can lead to non-lethal phenotypes	NO	Both	(133)
Wang <i>et al</i> , 2023; Yanagi <i>et al</i> , 2019; Frosk <i>et al</i> , 2017; Bondeson <i>et al</i> , 2017; Rawlins <i>et al</i> , 2019	MARCH syndrome	/	Homozygous nonsense/frameshift loss-of-function mutations lead to loss of CEP55 protein function	NO	Both	(127-131)

Table III. Continued.

Authors, year	Disease	Pathway	Mechanism	Whether clinical sample validation (and sample size)	Cytology or animal experiments	(Refs.)
Liu <i>et al</i> , 2025	Diabetic cardiomyopathy	/	It binds to ANXA11 to upregulate γ -tubulin and PLK4, driving abnormal centrosome expansion and participating in the pathological progression of DCM	NO	Cell line	(134)
Zhang <i>et al</i> , 2025	Chronic kidney disease	/	It is a core gene of the lncRNA-miRNA-mRNA ceRNA network	NO	Cell line	(135)
Li <i>et al</i> , 2023	Pulmonary hypertension	/	Participate in cell division, inflammatory response, and the regulation of pathways such as IL-17, mediating the pathological process of PAH	NO	Cell line	(136)
Lv <i>et al</i> , 2026	Interstitial cystitis	/	Participate in immune regulation and inflammatory response, and mediate chronic bladder inflammation	NO	Cell line	(138)
Chen <i>et al</i> , 2023	Acute spinal cord injury	/	Identified as one of the top 15 hub genes by reanalysis of the public blood transcriptome dataset GSE151371 and the spinal cord dataset GSE45376	NO	Cell line	(137)
Hou <i>et al</i> , 2025	Long COVID	/	Machine-learning-based screening of GEO transcriptomic datasets identified a four-gene signature comprising CEP55, CDCA2, MELK and DEPDC1B (combined ROC=0.876)	NO	Cell line	(139)

unique expression characteristics effectively compensate for the limitations of traditional tumor markers, such as insufficient tissue specificity, high false-positive rates, and limited diagnostic efficacy. CEP55 is expected to become a novel

non-invasive molecular marker for diagnosis and prognosis with high translational value across multiple disease areas. It can be widely applied in various clinical scenarios, including early disease screening, differentiation between benign and

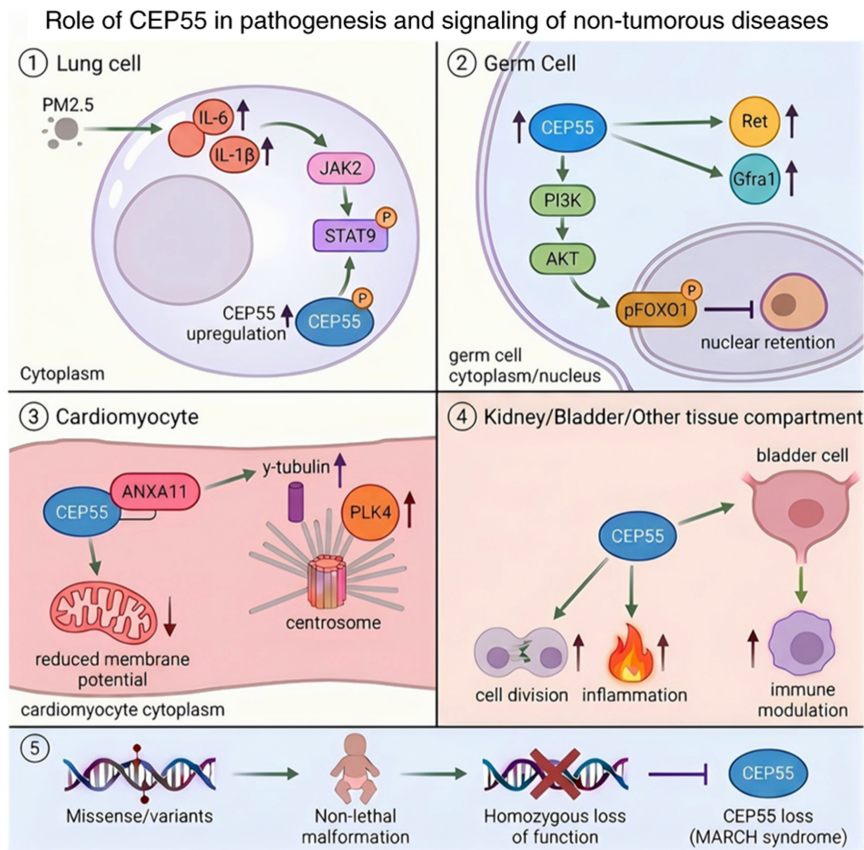


Figure 4. Pathogenic mechanism of CEP55 in non-tumorous diseases. Panel 1: Chronic pulmonary inflammation induces the secretion of pro-inflammatory cytokines IL-6 and IL-1 β in lung cells to activate JAK2/STAT3 signaling, ultimately triggering cytoplasmic upregulation of CEP55; Panel 2: Elevated CEP55 increases Ret and Gfra1 expression via activating the PI3K/Akt cascade, which phosphorylates FOXO1 and blocks FOXO1 nuclear retention in germ cells; Panel 3: CEP55 binds ANXA11 in cardiomyocytes to upregulate γ -tubulin and PLK4 for centrosome overexpansion while simultaneously reducing cellular membrane potential, driving dilated cardiomyopathy progression; Panel 4: Overexpressed CEP55 facilitates aberrant cell division, aggravates inflammatory response, and mediates immune modulation in bladder and renal tissue compartments; Panel 5: CEP55 missense variants lead to non-lethal developmental malformations, whereas homozygous loss-of-function mutations result in complete CEP55 depletion and the onset of MARCH syndrome. Collectively, aberrant CEP55 expression driven by environmental stimuli, signalling cascades, protein interactions and genetic variants mediates inflammatory, developmental, cardiac, reproductive and renal pathological processes to initiate a spectrum of non-tumor diseases. CEP55, Centrosomal protein 55.

malignant lesions, dynamic monitoring of disease progression, prognostic risk stratification, and prediction of therapeutic efficacy, thereby demonstrating excellent translational application potential.

In terms of tumor diagnosis, multiple pan-cancer large-sample bioinformatics analyses combined with clinical cohort validation have confirmed that CEP55 can serve as a broad-spectrum specific diagnostic marker for malignancies across multiple systems with favorable diagnostic accuracy. A pan-cancer study based on 15,823 multicenter samples covering 33 types of human malignant tumors showed that the abnormal expression characteristics of CEP55 mRNA could effectively distinguish 21 types of tumor tissues from their matched normal tissues, with an overall area under the receiver operating characteristic (AUC) value of up to 0.97 (sensitivity 0.91, specificity 0.93) (36). For specific cancer subtypes, the diagnostic AUC of CEP55 expression detection in GC tissues is higher than 0.9, which can effectively distinguish benign gastric hyperplasia, gastric inflammation and gastric malignant lesions, providing a reliable basis for early non-invasive auxiliary diagnosis of GC (39). Regarding the malignant progression of liver cancer and CRC, hypomethylation of the CEP55 promoter DNA is a characteristic

molecular event occurring in the early stage of tumorigenesis. This molecular alteration can capture malignant transformation signals and be applied to the screening of occult early tumors (40,51). In gastrointestinal cancers, the multi-gene diagnostic model constructed based on CEP55, AURKA, DTL and TTK achieves an AUC of 0.80. This model can accurately identify early micro-lesions and precancerous lesions that are difficult to detect via imaging examination, thereby effectively reducing the risk of missed diagnosis (140).

The non-invasive detection using body fluid specimens represents the core translational value of CEP55 that distinguishes it from traditional tumor markers, overcoming the clinical limitations of invasive tissue biopsy, complex procedures, and difficulties in dynamic follow-up. In urological tumors, CEP55 mRNA is significantly upregulated in bladder cancer tissues, with higher levels in muscle-invasive than in non-muscle-invasive lesions, and its expression abundance is positively correlated with invasion depth (16); meanwhile, specific upregulation of CEP55 mRNA can also be detected in the urine of patients with non-muscle-invasive bladder cancer, which can serve as a non-invasive urinary diagnostic marker for early screening, differentiation of benign and malignant hematuria, and postoperative recurrence monitoring, and is

applicable to large-scale population screening (103). Compared with invasive examinations such as cystoscopy, urinary CEP55 detection has the advantages of non-invasiveness, convenience, and repeatability, which can effectively improve the current status of bladder cancer diagnosis. Other studies have also identified abnormal CEP55 expression in the peripheral blood of patients with lung cancer and BC, providing a new direction for the establishment of a non-invasive peripheral blood diagnostic platform for multiple tumors (37).

Although CEP55 shows favorable diagnostic performance across diverse sample types, uniform cut-off values have not yet been established, largely owing to several confounding factors that can be documented directly in the published CEP55 literature. The key factors, together with the supporting evidence, are as follows:

(i) Sample-source heterogeneity. CEP55 abundance differs systematically among specimen types, therefore a single reference interval cannot be applied across matrices. In bladder cancer, tissue-based and urine-based assays interrogate different analyte pools: CEP55 mRNA and protein were quantified in surgically resected tumor tissues, whereas urinary CEP55 mRNA reflects shed tumor cells and is additionally influenced by urinary dilution, hematuria and urinary tract infection (16,103). At the pan-cancer level, the diagnostic AUC of 0.97 was estimated from tissue transcriptomes, whereas blood transcriptomic profiling identified CEP55 only as one hub gene within a multi-gene panel, yielding different absolute levels and different optimal cut-points (36,137). Tissue-, urine- and blood-derived values are therefore not interchangeable.

(i) Detection-platform variability. Differences in analyte (mRNA vs. protein), methodology and normalization generate non-comparable results. A representative example comes from bladder cancer, where RT-qPCR quantification of CEP55 mRNA discriminated muscle-invasive from non-muscle-invasive disease (relative fold expression 7.88 ± 3.88 vs. 4.75 ± 2.30 , $P=0.01$), whereas immunohistochemical evaluation of CEP55 protein in the same cohort showed no significant difference (72.2% vs. 69.0%, $P=0.774$) (16). Likewise, RT-qPCR with different reference genes, semiquantitative immunohistochemical scoring, ELISA and RNA-seq/microarray-based quantification each produce distinct dynamic ranges, thus a cut-off derived on one platform cannot be transferred to another (16,30,35,36,103).

(iii) Patient-background heterogeneity. Effect sizes, and even the direction of the association, vary with patient background. In NSCLC, CEP55 is an independent adverse prognostic factor for LUAD but not for squamous cell carcinoma (70); in CRC, the five-year survival rate was similarly significantly reduced among patients with lymph-node involvement and high CEP55 expression (52), which is consistent with its adverse prognostic role reported in unselected cohorts and in data-mining studies with experimental validation (53). Prognostic performance is further modified by disease stage, smoking status, viral etiology and molecular subtype, as shown for stage I LUAD, smokers with LUAD, hepatitis B-related hepatocellular carcinoma (HCC) and TNBC (22,48,71,72), and prior treatment reshapes CEP55 expression through gemcitabine- and cisplatin-resistant phenotypes (20,32). In non-neoplastic settings, blood transcriptomic comparisons show a similarly strong context dependence, with CEP55

differing between acute SCI and trauma controls and between patients with and without progression to long COVID (137,139). Age, sex and comorbidities add further variability.

(iv) Pre-analytical variables. No study has yet systematically evaluated pre-analytical variables for CEP55 itself, but the specimen types on which CEP55 assays depend are highly susceptible to such effects. For urinary RNA biomarkers, storage temperature and isolation workflow significantly alter transcript recovery: kidney-derived mRNAs decreased after urine storage at -20°C compared with 80°C , and different isolation workflows captured transcripts with different efficiencies (141). For blood RNA assays, delayed processing and collection into EDTA tubes cause substantial *ex vivo* transcript degradation and gene induction, whereas RNA-stabilizing collection tubes markedly reduce these changes (142). Because collection timing, storage conditions, freeze-thaw cycles and nucleic-acid/protein extraction methods are not harmonized across published CEP55 studies, this variability is superimposed on the biological variation.

Collectively, these sample, platform, patient and pre-analytics related factors prevent the formulation of standardized diagnostic thresholds for CEP55. Largescale, multicenter prospective studies using harmonized preanalytical and analytical protocols, with specimen-specific and platform-specific cut-off determination, are required before CEP55 can be adopted as a quantitative clinical biomarker.

In terms of tumor prognosis assessment and treatment efficacy prediction, CEP55 has been proven to be an independent adverse prognostic marker for a variety of malignant tumors. Its expression level is closely associated with tumor pathological grade, TNM stage, lymph node metastasis, distant metastasis, recurrence risk, and long-term survival status of patients (36,37). Studies have shown that in malignant tumors including LUAD, HCC, CRC, BC and OC, patients with high CEP55 expression exhibit significantly reduced OS and DFS, and this prognostic efficacy remains stable in early lesions and various tumor molecular subtypes (40,52,70,84,87). Further subtype analysis revealed that CEP55 can effectively identify the prognostic risk of high-risk subtypes, including hepatitis B-related HCC, TNBC and smoking-related LUAD (22,48,72). A multi-gene prognostic risk model constructed with CEP55 as the core can achieve precise stratification of tumor patients, providing key molecular support for the formulation of post-operative adjuvant therapy regimens and the optimization of follow-up cycles (49,64,72). In addition, CEP55 can predict tumor treatment response and drug-resistant phenotypes: Aberrantly high expression of this gene induces gemcitabine chemotherapy resistance in LUAD, cisplatin chemotherapy resistance in bladder cancer, and resistance to HER2-targeted therapy and endocrine therapy in BC, respectively. It can be used as a clinical indicator for drug resistance monitoring, facilitating the formulation of individualized treatment plans and reducing the incidence of ineffective treatment (20,32,83).

Beyond the field of oncology, CEP55 is also of great significance in various non-oncological diseases and possesses application value for dynamic disease diagnosis and monitoring. In autoimmune diseases, CEP55 has been reported as a core differentially expressed gene in diseases (for example, psoriasis, SLE and UC). Its abundance shows a significant positive correlation with systemic inflammatory burden, disease

activity index, and the extent of immune cell infiltration within lesions. It can dynamically monitor disease progression and evaluate clinical drug response, serving as a potential novel biomarker for monitoring the activity status of autoimmune diseases (115,118,119). In reproductive and genetic disorders, imbalances in the CEP55 gene and its expression contribute to the onset and progression of male azoospermia, endometriosis and fetal congenital malformations (122,133,143). Its expression profiles can be leveraged to support etiological classification of reproductive system diseases, whereas detection of gene-locus mutations can be implemented for prenatal risk screening of congenital malformations including MARCH syndrome, fetal hydrocephalus and renal dysplasia (127,129,131). Other studies demonstrate that CEP55 displays distinct aberrant expression in chronic illnesses such as diabetic cardiomyopathy, CKD and pulmonary hypertension, participates in core pathological cascades of these ailments, and offers novel molecular targets and research directions for mechanistic investigation, early warning, and disease monitoring of the aforementioned conditions (134-136).

Potential for targeted therapy. As a key hub molecule, CEP55 is extensively involved in maintaining cell cycle homeostasis, activating signaling pathways, remodeling the TIME, and regulating inflammatory responses. Its aberrant activation is a key driver of the proliferation, invasion and metastasis of malignant tumors, immune escape, treatment resistance, as well as inflammatory disorders in non-tumor diseases and abnormal embryonic and tissue development (29,33). Compared with traditional therapeutic targets, CEP55 presents tissue specificity characterized by high expression in lesion tissues and low expression in normal tissues, which can effectively reduce the toxic and side effects caused by clinical intervention. This target is applicable to multiple therapeutic modalities including small molecule drug therapy, gene silencing, immune targeting and multi-pathway combination therapy, holding broad clinical translation prospects in the precision treatment of multi-system diseases.

In the field of small-molecule targeted drug research and development for tumors, abundant basic research findings focusing on specific drugs and CEP55-targeted pathways have been accumulated, laying a theoretical and experimental foundation for the precise intervention of drug-resistant tumors. The small-molecule inhibitor CD-437 specifically binds to CEP55 protein, blocks downstream cell cycle proliferation signaling, and effectively inhibits the proliferation and migration of BC cells. It is also expected to reverse cellular resistance to targeted drugs and endocrine therapy, rendering it a promising candidate drug for the treatment of refractory BC (86). The PI3K/AKT/mTOR axis serves as the core CEP55-mediated pathway in tumorigenesis, and the application of mTOR inhibitors can effectively suppress the proliferation, EMT, as well as invasive and metastatic capacities of pancreatic NE tumors and RCC. This combined targeted intervention model has shown favorable effects in preclinical models (30,60). In terms of combined intervention with natural drugs, mulberry fruit aqueous extract combined with ionizing radiation can induce mitotic catastrophe by inhibiting Aurora B activity, accompanied by downregulated CEP55 expression, thereby enhancing the radiosensitivity of bladder cancer cells and providing an

experimental basis for the development of low-toxicity and high-efficiency comprehensive treatment regimens for bladder cancer (104).

Gene-targeted silencing technology provides a precise and efficient intervention approach for the clinical translation of CEP55 research. Small interfering RNA (siRNA)- and short hairpin RNA-mediated CEP55 knockdown can inhibit CEP55 expression at the transcriptional level, exerting prominent tumor-suppressive and drug-resistance-reversing effects in a variety of tumors. In LUAD, CEP55-siRNA can effectively downregulate target-gene expression, arrest the tumor-cell cycle at the G2/M phase, suppress cell proliferation and invasive capacity, and reverse gemcitabine chemotherapy resistance, thereby restoring tumor-cell responsiveness to chemotherapeutic agents (78). In CRC, targeted silencing of CEP55 can remodel the tumor immunosuppressive micro-environment, markedly increase intratumoral infiltration of CD8⁺ cytotoxic T cells, impair tumor immune-escape capacity, and consequently improve the therapeutic efficacy of anti-PD1 ICIs, offering a feasible strategy to overcome immunotherapy resistance in CRC (33). In gallbladder cancer, esophageal cancer and other tumor types, siRNA-mediated downregulation of CEP55 expression can inhibit activation of pro-oncogenic pathways including AKT/ERK and Src/FAK/ERK, block EMT, and restrain malignant tumor progression (66,144). Furthermore, combined application of Aurora-A inhibitors and CEP55-targeted drugs can target the Aurora-A-CEP55-PI3K signaling axis, block oncogenic signal transduction at multiple nodes, and synergistically inhibit proliferation of head-and-neck squamous-cell carcinoma cells, opening a new direction for tumor targeted-combination therapy (145).

Tumor immune-targeted therapy represents a highly innovative clinical-translation direction for CEP55. As a classic cancer-testis antigen, CEP55 exhibits favorable tumor-targeting specificity and can precisely mediate anti-tumor immune responses. This protein can be enzymatically cleaved into specific restricted antigen peptides inside tumor cells. These peptides activate adaptive immunity via the host antigen-presentation system, induce the generation and activation of tumor-specific cytotoxic T lymphocytes, and thereby precisely target and eliminate tumor stem cells and malignantly proliferating tumor cells. Currently, the CEP55 peptide tumor vaccine remains at the basic-research-and-development stage, and its potent antitumor immune-activating effect has been fully validated in CRC and BC research models (17,57). Within combination-therapy regimens, synergistic use of the CEP55 peptide vaccine with PD-1/PD-L1 immune inhibitors can effectively relieve the immunosuppressive state of the TME, reverse tumor immune resistance, and substantially amplify the host's systemic antitumor immune response, providing novel target support and a theoretical basis for optimizing and constructing a pan-cancer immune-combination-therapy system (33). Other studies have demonstrated that down-regulating CEP55 can inhibit activation of the MEK1/2-MYC pro-oncogenic pathway and enhance the response of TNBC to mitosis-targeting drugs, offering a feasible strategy for combination chemotherapy for this high-risk BC subtype (22,83).

In the field of precision treatment for non-tumor diseases, CEP55-targeted intervention can effectively regulate

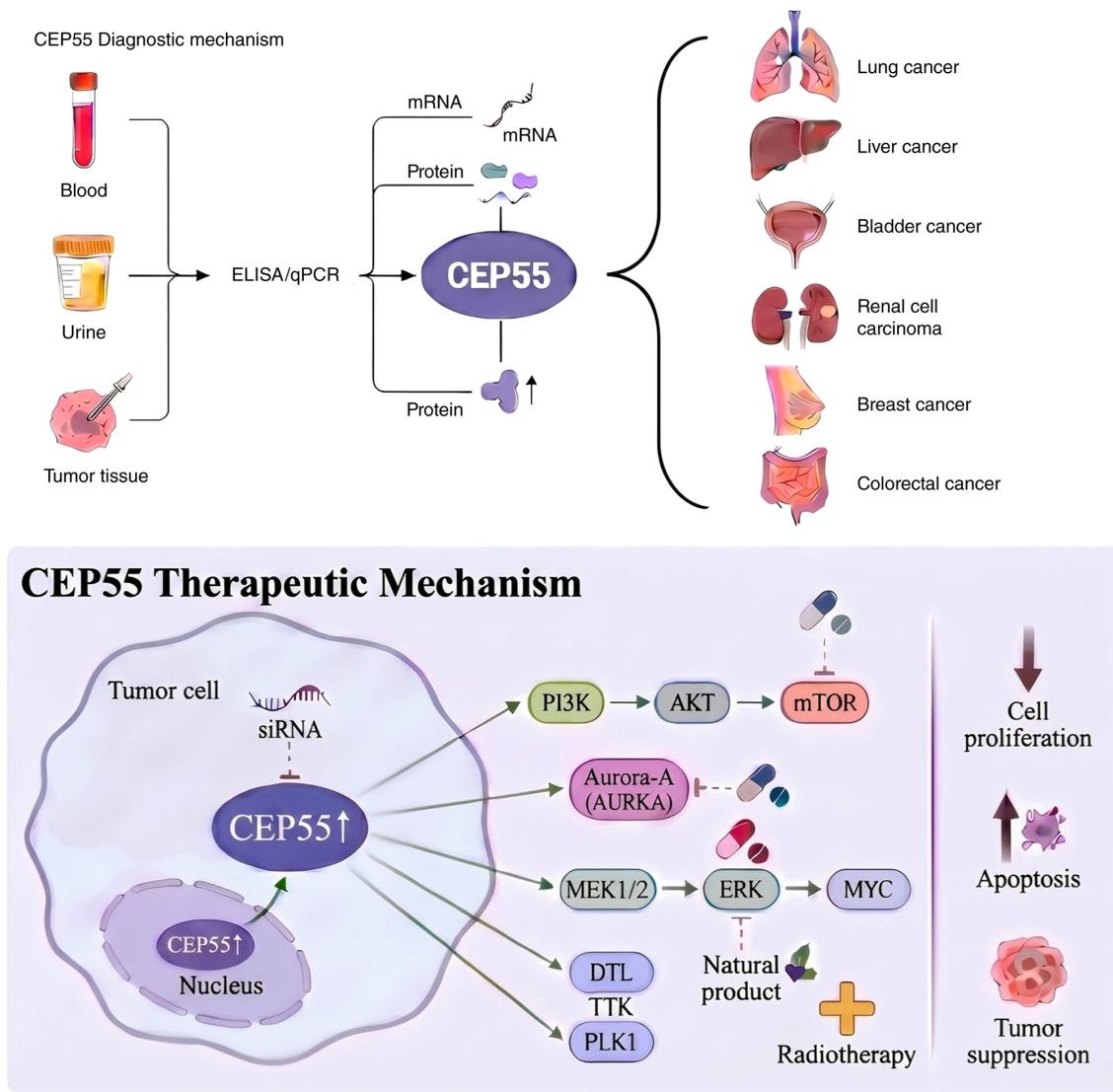


Figure 5. Clinical translational application of CEP55. Detecting the expression abundance of CEP55 in patients' blood, urine, and pathological tissues via ELISA qPCR helps in disease diagnosis; knocking down CEP55 expression or applying inhibitors and targeted therapies is expected to become a new target for disease treatment. CEP55, Centrosomal protein 55.

inflammatory disorders and repair developmental abnormalities, demonstrating broad application prospects. In autoimmune diseases, CEP55 mediates the massive secretion of inflammatory cytokines such as IL-6 and IL-1 β by activating the NF- κ B and PI3K/AKT/mTOR inflammatory signaling pathways, thereby driving chronic inflammation and immune dysfunction in the human body (117-119). Targeted inhibition of CEP55 can effectively block downstream inflammatory amplification reactions, alleviate tissue inflammatory damage in SLE, psoriasis and UC, and provide a novel molecular target for the precision anti-inflammatory treatment of autoimmune diseases (116-118). In reproductive system diseases, targeted regulation of the CEP55-mediated PI3K/AKT signaling pathway can ameliorate abnormal spermatogonial cell development, repair spermatogenesis disorders, and alleviate the infertility phenotype of male azoospermia (121,122); meanwhile, CEP55 participates in the regulation of the oocyte meiosis process and endometrial receptivity, providing new research insights for the auxiliary treatment of reproductive disorders such as endometriosis (123,124). In neurological

diseases, CEP55 is involved in neural stem cell proliferation and differentiation as well as embryonic brain development. Precise regulation of its expression helps promote neural injury repair, offering a new direction for targeted intervention of neurological developmental abnormalities and traumatic neurological diseases (15,137). In addition, CEP55 participates in the regulation of centrosome homeostasis and mitochondrial function remodeling. Targeted intervention of CEP55 can ameliorate pathological damage associated with metabolic disorders, providing a potential novel target for the precision treatment of metabolic diseases such as diabetic cardiomyopathy and CKD (134,135). The clinical translational applications of CEP55 are summarized in Fig. 5 and Table IV.

5. Summary and outlook

As a mammal-specific core centrosomal protein that regulates cytokinesis, CEP55, with its conserved structural features, participates in diverse physiological processes including embryonic development, germ cell differentiation, and immune

Table IV. Summary of clinical translational applications of CEP55.

Authors, year	Classification	Disease	Mechanism	Method	Clinical trial	(Refs.)
Fu <i>et al</i> , 2020	Diagnosis	Lung cancer	-	Tissue expression detection	CEP55 protein/mRNA detection	(70)
Xu <i>et al</i> , 2023; Deng <i>et al</i> , 2025		Hepatocellular carcinoma	-	Tissue expression AFP combined detection	CEP55 (AUC>0.9)	(48,49)
Singh <i>et al</i> , 2015;		Bladder cancer	-	Tissue urine mRNA detection	CEP55 mRNA (non- invasive urine test)	(16,103)
Huang <i>et al</i> , 2021		Gastric cancer	-	Tissue expression detection	CEP55 (meet the clinical diagnostic criteria)	(39)
Hajibabaie <i>et al</i> , 2025		Gastrointestinal cancer	-	Multigene panel testing	CEP55 + AURKA + DTL + TTK	(140)
Inoda <i>et al</i> , 2009; Kalimutho <i>et al</i> , 2018		Breast cancer	-	HLA-A24 peptide immunoassay	CEP55 restrictive peptide	(17,83)
Wangmo <i>et al</i> , 2024	Treatment	Colorectal cancer	-	Tumor microenvironment detection	CEP55 expression level	(33)
Xu <i>et al</i> , 2025; Peng <i>et al</i> , 2017		Pancreatic neuroendocrine tumor	PI3K/AKT/ mTOR	Small molecule targeted inhibition	mTOR inhibitor	(60,61)
Wolter <i>et al</i> , 2017		Triple-negative breast cancer	MEK1/2- MYC	Downregulation of pathway targets	MEK1/2-PLK1 pathway drugs	(21)
Su <i>et al</i> , 2019		Bladder cancer	-	Natural extracts combined with radiotherapy	Mulberry fruit water extract ion radiation	(104)
Sinha <i>et al</i> , 2018; Shen <i>et al</i> , 2022		Male azoospermia	PI3K/AKT	Targeted downregulation	CEP55 expression level	(121,122)
Huang <i>et al</i> , 2023		Gallbladder cancer	AKT/ERK	RNA interference	CEP55 knockdown (siRNA)	(144)
Chen <i>et al</i> , 2015		Head and neck cancer	Aurora-A- CEP55- PI3K	Combined targeting	Aurora-A inhibitor CEP55 targeted drug	(145)

homeostasis by precisely regulating cytokinesis at the end of cell division, centrosome homeostasis, and genomic stability. As research advances, the biological functions of CEP55 have transcended the single category of traditional cell-cycle regulation. Through multiple mechanisms such as PTM, ceRNA regulation and PPI, CEP55 modulates core pathways including PI3K/AKT, NF- κ B, JAK/STAT and MEK1/2-MYC, broadly mediating the onset and progression of multi-system diseases, including malignant tumor progression, immune-inflammatory disorders, reproductive-developmental malformations and chronic metabolic diseases. It serves as a key hub molecule connecting cell-cycle dysregulation to pathological processes across multiple diseases. Existing studies have fully demonstrated that CEP55 possesses multiple values in disease diagnosis, prognostic stratification, therapeutic prediction and targeted intervention. It represents a high-quality biomarker

and therapeutic target for both oncological and non-oncological conditions. Moreover, it shows substantial basic-research value and clinical-translational potential.

Currently, basic research on CEP55 has formed a relatively complete theoretical system. Its molecular structure, core signaling pathways, regulatory mechanisms and expression characteristics in multiple diseases have been gradually clarified. Non-invasive detection models, multi-dimensional prognostic scoring systems, and various targeted intervention strategies have been validated by basic experiments, laying a theoretical foundation for clinical translation. However, existing research still presents obvious shortcomings, and a substantial gap remains before standardized clinical application can be realized. First, current studies are mainly based on basic experiments, small-sample single-center clinical observations, and bioinformatics analysis. Large-sample,

multi-center, prospective clinical cohort studies are lacking. In addition, the diagnostic cut-off values, prognostic evaluation standards, and positive determination systems for CEP55 across different diseases and detection samples have not been unified, which fails to support standardized clinical detection and application. Second, the targeted therapy system for CEP55 remains immature. At present, the types of specific CEP55 small-molecule inhibitors are limited, and their targeting precision requires further optimization. Novel agents including siRNA and peptide vaccines face multiple problems such as low delivery efficiency, poor stability and undefined off-target toxicity, and no mature-targeted drugs are available for routine clinical application. Third, an obvious imbalance exists in the research scope. Existing studies are highly concentrated on tumors, whereas research on CEP55 in non-tumor diseases, including autoimmune diseases, reproductive genetic diseases, and chronic metabolic diseases, remains insufficient. The specific molecular regulatory mechanisms, clinical intervention targets, and therapeutic windows of CEP55 in these diseases have not yet been clarified, and the cross-correlation mechanisms of regulatory networks among different diseases lack systematic elaboration. Fourth, the clinical application system is imperfect. The combined medication regimens, optimal dosing strategies, indication screening criteria, long-term drug resistance mechanisms, and safety evaluation systems for CEP55 targeted therapy have not been established, restricting its clinical promotion and application. In addition, research samples of CEP55 in rare tumors and rare genetic diseases are scarce, and the underlying mechanisms remain unclear. These issues require further supplementation and improvement in future studies.

Based on the current research status and existing shortcomings, future clinical translation can be advanced from four dimensions: Deepening basic mechanisms, expanding clinical research, optimizing targeting systems, and broadening application scenarios. First, researchers should carry out large-sample, multi-center prospective studies to unify CEP55 detection thresholds and evaluation criteria, optimize non-invasive detection protocols, and construct standardized precision diagnosis and treatment models. Second, advance the research and development of targeted drugs, optimize delivery systems for small-molecule inhibitors, siRNA, and peptides, explore optimal regimens for targeted combinations with radiotherapy, chemotherapy, and immunotherapy, and address clinical drug-resistance issues. Third, deepen mechanistic research on non-tumor diseases and the multi-disease regulatory network of CEP55, and broaden its clinical application boundaries. Fourth, strengthen basic-mechanism research. This work should focus on dynamic regulatory patterns of CEP55 involving PTM, RNA-based regulation, and PPI, analyze its functional differences and dynamic regulatory mechanisms across different disease pathological stages, and elucidate disease-specific functional characteristics to provide theoretical support for individualized precision diagnosis and treatment.

In summary, CEP55 overcomes the application limitations of traditional single biomarkers and single therapeutic targets. It enables comprehensive coverage for the diagnosis and treatment of multisystem diseases under both tumor and non-tumor conditions, and shows prominent advantages

in early-disease screening, precise subtyping, prognostic prediction, drug-resistance reversal, and targeted therapy. As the relevant research system continues to improve, CEP55 is expected to become a core molecular target for precision medicine and individualized diagnosis and treatment of multi-system diseases. It provides new ideas and a theoretical basis for mechanistic exploration of intractable clinical diseases and the development of novel therapeutic strategies.

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Authors' contributions

SN put forward ideas, designed the framework of the article, initiated discussions, and was responsible for the revision of the article. QH participated in the discussion, collected information, and was responsible for the preparation of the article. KH and XL participated in the discussion of the article. YH and WZ were committed to providing theoretical knowledge related to clinical medicine and clinical trials. WH and ZL were responsible for reviewing the article and providing funding. All authors read and approved the final version of the manuscript. Data authentication is not applicable.

Ethics approval and consent to participate

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Competing interests

The authors declare that they have no competing interests.

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