Dean&Francis

ISSN 2959-409X

# The Role of ZNF292 in Breast Cancer

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**Abstract:**

Breast cancer as one of the most malignant tumors in the world numbered sixth in all cancer-related deaths. In China, breast cancer has become one of the most seriously fatal malignant tumors. Etiologically, breast cancer can be classified as basal-like breast cancer (BLBC), of which about ninety percent of BLBC patients are Chinese. The absence of precise mechanisms underlying the pathogenesis and aggressive progression of BLBC has greatly hindered the search for effective targeted therapeutic agents. Therefore, the search for better intervention and therapeutic options in terms of molecular mechanisms is an excellent approach. There is growing evidence that ZNF292 has an inhibitory role in cancer, but its function and exact mechanism in breast cancer are unknown. This paper explores the impact of ZNF292 on breast cancer by combining important findings on the role of ZNF292 in cancer over the past year, and the results of taz-driven human breast cancer via inhibition of SKP2-P27 targeting.

**Keywords:** ZNF292, Breast cancer, Tumor Suppressor Gene, Gene Expression

## 1. Introduction

Breast Cancer (BC) is the most frequently cancer in females in worldwide. Over 2.3 million new cases of diagnosis each year, and is the secondary reason cause of cancer deaths in women. Internationally, breast cancer the rate of incorporation and mortality have increased in the last three decades, which has been associated with changes in risk factors, better cancer registries, and cancer detection. Breast cancer incidence and mortality are on the rise on a global scale. About 80 percent of breast cancer patients are older than 50 years of age. The survival is determined by the phases and molecular sub-types of the cancer. Based on the level of mRNA gene expression, breast cancer can be categorized into varieties of molecular sub-types including Luminal B, Luminal A, HER2-enriched. These molecular sub-types provide the insights for new therapeutic strategies and stratification of patients, which influences the treatment of breast cancer patients.[1]

The Skp2-p27 signaling pathway is an essential segment of cell cycle regulation and plays an essential role in tumor development in particular. Skp2 (S-phase kinase-associated protein 2), an element of the SCF (Skp1-Cul1-F-box) E3 ubiquitin ligase complex, is known to control the cell cycle process by recognizing and promoting the ubiquitination and subsequent degradation of a variety of ubiquitina-

tion and subsequent degradation of cell cycle inhibitory proteins, such as p21, p27, and p57, which control cell cycle progression during the G1-S transition [2].Thus, it prevents the cell cycle from entering the S phase from the G1 phase.[2] In breast cancer, Skp2 over-expression is implicated in tumor progression, and p27 degradation is one of the key mechanisms by which Skp2 promotes the proliferation of breast cancer cells. skp2 promotes cell cycle progression by ubiquitinating p27, leading to its degradation and thus deregulation of the inhibitory effect on CDK2-Cyclin E complexes[2]

Zinc finger protein 292 (ZNF292) is a strongly conserved zinc finger protein, which works as a transcription factor. These zinc fingers specifically bind to the growth hormone (GH) promoter and synergistically activate transcription in conjunction with the POU-family transcription factor, POU1F1. Initially identified as an enhancer of growth hormone expression in a rat pituitary gland model, ZNF292 has since been implicated in tumorigenesis and disease progression.[3]

In the present study, we aimed to determine the role of ZNF292 in the development and malignant progression of BLBC. We postulate that ZNF292 blocks breast cancer cell growth by interfering with the SKP2 and P27 signaling axis. Through unpacking this mechanism, our study offers fresh theoretical foundations and potential targets for breast cancer prevention and therapy.

## 2. Literature review

### 2.1 Research results of ZNF292 and SKP2-P27signaling pathway

According to one study, ZNF292 blocks esophageal squamous cell carcinoma (ESCC) cell growth by interfering with the SKP2 and P27 signaling axis. The results of this study showed that the expression of ZNF292 was higher in normal tissues than in tumor tissues, and the low expression of this protein was associated with poor prognosis in ESCC patients. ZNF292 knockdown significantly increased s-phase entry and proliferation of ESCC cells, whereas SKP2 knockdown lead to the increased in P27 expression and shortened P27 half-life.[4]

### 2.2 The role of ZNF292 in breast cancer

We found that ZNF292 expression was higher in neighboring and normal tissues. Besides, it's lower in tumor tissues. Knockdown of ZNF292 increased cell the rate of proliferation, colony forming ability and cell cycle progression. In mechanism, deletion of ZNF292 promoted SKP2 expression at the transcriptional level, which stimulated P27 ubiquitin-degradation and finally promoteing cell cycle progression. Hence, our findings suggest a novel ZNF292-skp2-p27 transcriptional regulatory pathway, which deepens our comprehension of how ZNF292 inhibits BLBC cell proliferation.

### 2.3 The role of ZNF292-SKP2-P27 Signaling pathway

ZNF292 binds to the area that codes for SKP2, and ZNF292 knockouts raise the levels of SKP2 expression. As a result, ZNF292 inhibited SKP2 transcriptional expression, reduced ubiquitinated degradation of P27, increased P27, and prevented ESCC cell multiplication and cell cycle G1/S phase shift. With these results, we suggest that ZNF292 could be related to tumor growth and raise the possibility that the ZNF292/SKP2/P27 signaling axis may have a similar function in other cancer types.[5] Despite the fact that they do not directly correlate with breast cancer. Further studies are needed to investigate the exact role of ZNF292 in breast cancer, and more specific studies may be needed to confirm the role of ZNF292 in breast cancer cells and its impact on SKP2 and P27.

### 2.4 Interactions between ZNF292 and other signaling pathways

ZNF292 may be participated in the regulation of various signaling pathways such as Wnt/β-catenin, which affects the biological behavior of breast cancer cells. For example, it has been suggested that cZNF292 regulates the Wnt/β-catenin signaling pathway and influence the proliferation and apoptosis of hepatocellular carcinoma cells.[6]

## 3. Mechanism

ZNF292 is a transcription factor ,which may be crucial for the growth and advancement of breast cancer cells via the cell cycle by controlling the expression of genes downstream ,like SKP2,which in turn influences the quantity of P27,a protein linked to the cell cycle. Therefore, a new target for the therapy of breast cancer may be ZNF292 and the signaling pathway it controls.

p27 protein is a cyclin kinase inhibitor that regulates cell cycle and is directly involved in cell proliferation and differentiation. P27mRNA is constant during the normal cell cycle, while P27 protein levels are highly expressed in the G0 phase, decline in the G1 phase, and reach their lowest in the S phase. It is believed that the change of p27 protein level is caused by SKP2-mediated counterproteasome degradation.[7] P27 expression and half-life were reduced by ZNF292 loss, while the P27 expression was increased by SKP2 knockdown.ZNF292 can bind to the SKP2 pro-

ISSN 2959-409X

moter region, and ZNF292 knockdown can increase SKP2 expression levels. These results suggest that ZNF292 inhibits SKP2 transcriptional expression, decreases P27 ubiquitination and degradation, and accumulates P27 to prevent cell proliferation and the G1/S phase transition of the cell cycle.ZNF292 may control the transcriptional level of SKP2 expression, which in turn may impact P27 stability and cell cycle regulation.[4]In ESCC studies, ZNF292 was found to be highly expressed in normal tissues surrounding tumors, but lowly expressed in tumor tissues.[4]

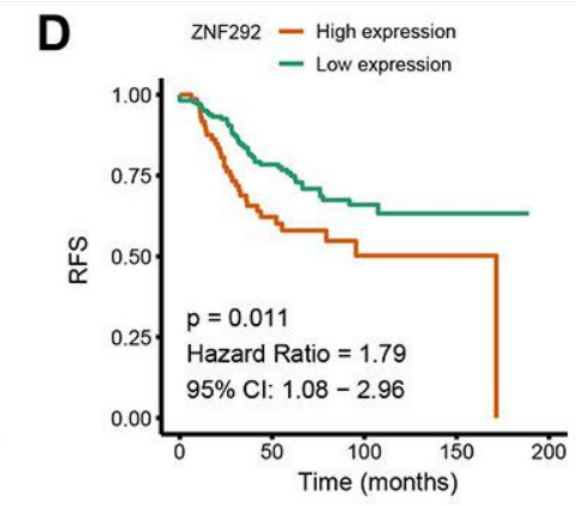


**Figure 1**

Immunohistochemistry (IHC): This is a commonly used method to detect the level of protein expression, which can be applied to paraffin-embedded tissue sections to detect the expression of ZNF292 protein by specific antibodies. The IHC method is easy to operate and can directly display the expression and location of the protein at the histomorphological level.

Real-time quantitative PCR (RT-qPCR): This is a sensitive technology to detect the expression level of mRNA. By designing specific primers for ZNF292 gene, the expression of ZNF292 mRNA in breast cancer tissues can be quantitatively analyzed. With high sensitivity and accuracy, RT-qPCR is an important means to study the changes of gene expression.

Western Blot: This method can detect the expression level of a specific protein in a tissue sample. Proteins were separated by electrophoresis and then transferred to a membrane and detected using a specific antibody against ZNF292.Western Blot is able to provide semi-quantitative information on protein size and quantity119.

Fluorescence in situ hybridization (FISH): If copy number changes in the ZNF292 gene need to be detected, FISH technology can be used. By using probes specific to the ZNF292 gene sequence, the copy number of the gene can be directly observed in the nucleus, which is of great significance for the study of gene amplification or deletion120.

Gene chip or high-throughput sequencing technology: For example, multi-gene expression profiling for breast cancer can be used to detect the expression level of multiple genes including ZNF292 at the same time. These methods can provide more comprehensive gene expression information and help to understand the molecular mechanism of breast cancer.

ELISA: Although ELISA is usually used to detect antibodies or proteins, it can also be used to detect the expression level of some specific proteins interacting with ZNF292, for example, by detecting proteins interacting with ZNF292 to indirectly understand its functional status119.

There is evidence that ZNF292 may have predictive significance for breast cancer as low expression of the protein is linked to a poor prognosis in esophageal squamous cell carcinoma.ZNF292 expression may develop into a biomarker to forecast a patient ‘s prognosis if it may indicate the severity of the illness or the likelihood that it will progress.

## 4. Application of ZNF292 in breast cancer

The clinical applications of ZNF292 include, but are not limited to, as a new therapeutic target and as a diagnostic biomarker for prognostic assessment and disease monitoring, and its clinical applications in existing cancer treatments are mainly in the areas of acting as a tumor suppressor, cell cycle regulation, prognostic biomarker, and a potential radiotherapy sensitizer, but to achieve its specific functioning mechanism and clinical applications in cancer treatment, it needs to overcome a variety of challenge including technology, ethics, economy and the need to verify its effectiveness and safety through large-scale clinical trials.

### 4.1 The Role of ZNF292 in Esophageal Squamous Cell Carcinoma

Firstly, ZNF292 is described to be a tumor suppressor that plays an inhibitory role in a variety of cancers. Studies have shown that ZNF292 low expression is linked to poor prognosis in individuals with esophageal squamous cell carcinoma (ESCC). ZNF292 is over-expressed nearby and normal tissues of ESCC, but not tumor tissues[4]

### 4.2 ZNF292 and cerebral ischemic injury

Secondly, The prior patent provides an siRNA for target

silencing of a cZNF292 gene, and the siRNA can significantly inhibit the expression of cZNF292 in a human lung adenocarcinoma cell, effectively silence the cZNF 292 in the lung adenocarcinoma cell, and significantly reduce the expression of the circular RNA, thereby achieving the purpose of treating lung adenocarcinoma. The patent also provides a medicine for treating lung adenocarcinoma and lung cancer comprising the siRNA.

### 4.3 Circulating and circular RNA cZNF292 and clinical information based on machine learning

Thirdly, cZNF292 combined with clinical information (CM), consisting of age, sex, body mass index, heart rate, and diastolic blood pressure, was effective in predicting AMI. CM+CzNF292 distinguished between patients with AMI and non-AMI, unstable angina and AMI, and acute cor pulmonale syndrome (ACS) and non-ACS. The expression of cZNF292 in endothelial or cardiomyocyte cells was down-regulated and had an anti-oxidative glucose deprivation/re-oxidative apoptotic effect; RNA stability studies showed that CZNF292 was stable. Circulating CZNF292 was experimentally identified as a potential biomarker for AMI, and a " CM+CZNF292" prediction model was established.
[8]

### 4.4 The role of ZNF292 in the neuroprotective effect

In a cerebral ischemia-reperfusion injury model, it was found that knocking down circRNA ZNF292 can reduce oxidative damage, inhibit apoptosis and proliferation of cells. This suggests that ZNF292 may have a potential therapeutic role in nerve injury diseases such as cerebral ischemia[9]

## 5. Discussion

Although the precise function of ZNF292 in breast cancer remains unknown, its impact on ESCC has led to speculation that the protein may influence the expression of SKP2 and P27, thereby potentially regulating the cell cycle and proliferation of breast cancer cells [4]. Additionally, ZNF292 may be involved in various processes such as proliferation, apoptosis, migration, and invasion of breast cancer cells.
However, further research is required to elucidate its specific role and mechanism in breast cancer. It is also important to note that the role of ZNF292 may vary among different subtypes of breast cancer; therefore, comprehensive analysis for each subtype is necessary. This will help us understand the potential significance of the ZNF292 gene in prognosis and therapy for breast cancer. The discussion here explores the potential utility of ZNF292 as a therapeutic target or prognostic marker for breast cancer. Furthermore, it examines the feasibility and challenges associated with integrating it into an assessment system for diagnosis, treatment, or prognosis.
For instance, one approach could involve detecting proteins interacting with ZNF292 to indirectly assess its functional status119. When designing experiments related to ZNF292 detection methods should consider factors such as experimental purpose, sample type specificity required information level detail conditions experiment accuracy reliability results ensure recommended referring relevant guidelines literature.

## 6. Conclusion

Although these findings come from the ESCC model, they provide clues to understanding the possible mechanisms of ZNF292 in breast cancer. Besides, ZNF292 may regulate SPK2P27 signaling axis through the similar way in ESCC, which help to affect cell cycle progression and cell proliferation. If there is similarities of the role of ZNF292 in ESCC or breast cancer, then its expression level may become a key factor affecting breast cancer cell proliferation and cell cycle regulation. Further research will help clarity the specific role of ZNF292 in breast cancer development and may reveal new treatment strategy.
Whereas there is no direct evidence for breast cancer, ZNF292, as a transcription factor, may play a role in the proliferation and cell cycle regulation of breast cancer cells by regulating the SKP2/P27 signaling axis. If the role of ZNF292 in breast cancer is similar to that in ESCC, its expression level may become an important prognostic factor. Further studies will help to confirm the specific role of ZNF292 in breast cancer and may lead to the discovery of new therapeutic targets or prognostic biomarkers.
In order to fully assess the potential of ZNF292 as a therapeutic target or prognostic marker for breast cancer, further studies are needed to investigate its specific mechanism of action in breast carcinogenesis and development, as well as its expression patterns and functional differences in different breast cancer subtypes. In addition, we need to explore the treatment strategy of ZNF292 and how to accurately evaluate its clinical application value.

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