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Claudin 18.2: A Promising Biomarker in Gastric Cancer

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Abstract

Gastric cancer remains a significant global health challenge, necessitating the identification of novel biomarkers for improved diagnosis and treatment. Claudin 18.2 (CLDN18.2), a tight junction protein predominantly expressed in the gastric mucosa, has emerged as a promising biomarker in gastric cancer research. Aberrant CLDN18.2 expression has been observed in gastric cancer tissues, with minimal expression in normal gastric epithelium. This aberration renders CLDN18.2 a potential diagnostic biomarker, offering utility in distinguishing gastric cancer from benign lesions or healthy tissue. Moreover, high CLDN18.2 expression levels have been associated with adverse clinicopathological features and poor prognosis in gastric cancer patients, indicating its prognostic significance. Additionally, CLDN18.2 presents an attractive therapeutic target, with monoclonal antibodies targeting CLDN18.2 showing promising results in clinical trials. Despite these advancements, challenges such as assay optimization and validation of CLDN18.2-targeted therapies remain. Further research is warranted to fully elucidate the clinical utility of CLDN18.2 and its integration into routine clinical practice for the management of gastric cancer.

Keywords: Claudin 18.2; Biomarker; Gastric cancer; Antibody-Dependent cellular cytotoxicity

Introduction

Gastric cancer represents a significant global health burden, with high incidence rates and often poor prognosis, particularly in advanced stages. Early detection and effective treatment strategies are critical for improving patient outcomes. In recent years, the identification of biomarkers has gained considerable attention as they offer potential solutions for early diagnosis, prognostic evaluation, and targeted therapy in gastric cancer. Among these biomarkers, Claudin 18.2 (CLDN18.2) has emerged as a promising candidate.

CLDN18.2 is a member of the claudin family, which plays a crucial role in the formation of tight junctions and the maintenance of epithelial barrier integrity. Initially identified as a tissue-specific protein predominantly expressed in the gastric mucosa, CLDN18.2 has garnered significant interest due to its dysregulated expression in gastric cancer. Aberrant CLDN18.2 expression patterns have been observed in gastric cancer tissues, with elevated levels compared to normal gastric epithelium. This differential expression profile underscores the potential of CLDN18.2 as a diagnostic biomarker for gastric cancer.

Beyond its diagnostic implications, mounting evidence suggests that CLDN18.2 may hold prognostic significance in gastric cancer. High expression levels of CLDN18.2 have been associated with aggressive tumor behavior, advanced disease stage, and poor patient survival outcomes. Such findings highlight the potential utility of CLDN18.2 as a prognostic indicator, aiding in risk stratification and treatment decision-making for gastric cancer patients.

Moreover, CLDN18.2's selective overexpression in gastric cancer cells makes it an attractive target for therapeutic intervention. Monoclonal antibodies targeting CLDN18.2 have shown promising results in preclinical studies and early-phase clinical trials, offering a targeted approach to treatment with potentially improved efficacy and reduced toxicity compared to conventional chemotherapy regimens [1].

Despite these promising prospects, several challenges remain in the clinical translation of CLDN18.2 as a biomarker and therapeutic target in gastric cancer [2]. Optimization of diagnostic assays, validation of CLDN18.2-targeted therapies, and elucidation of associated signaling pathways are critical areas for further investigation. Nonetheless, the evolving landscape of CLDN18.2 research holds great promise for advancing the management of gastric cancer, potentially leading to more personalized and effective treatment strategies. This review aims to explore the current understanding of CLDN18.2 in gastric cancer and its implications for clinical practice.

CLDN18.2 in Gastric Cancer

Claudin 18.2 (CLDN18.2) has garnered significant attention in the realm of gastric cancer research due to its distinct expression patterns and potential implications for diagnosis, prognosis, and targeted therapy. CLDN18.2, a tight junction protein primarily expressed in the gastric mucosa, plays a pivotal role in maintaining epithelial barrier integrity [3]. However, in gastric cancer, aberrant expression of CLDN18.2 has been observed, with elevated levels detected in tumor tissues compared to normal gastric epithelium.

The differential expression of CLDN18.2 in gastric cancer holds promise as a diagnostic biomarker. Immunohistochemical analysis has revealed high CLDN18.2 expression levels in gastric cancer tissues, making it a potential tool for distinguishing malignant lesions from benign or healthy gastric tissue. Moreover, the specificity of CLDN18.2 expression in gastric cancer cells presents an opportunity for targeted imaging approaches, facilitating non-invasive detection and staging of the disease [4].

Beyond its diagnostic utility, CLDN18.2 expression has prognostic implications in gastric cancer. Studies have shown that elevated levels of CLDN18.2 are associated with adverse clinicopathological features, including advanced tumor stage, lymph node metastasis, and poor overall survival rates. Consequently, CLDN18.2 expression status may serve as a prognostic indicator, aiding in risk stratification and treatment decision-making for gastric cancer patients [5].

Diagnostic Potential

The diagnostic potential of Claudin 18.2 (CLDN18.2) in gastric cancer stems from its distinct expression patterns, with elevated levels observed in tumor tissues compared to normal gastric epithelium. This aberrant expression makes CLDN18.2 an attractive biomarker for the detection and diagnosis of gastric cancer [6].

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Immunohistochemical analysis has been the primary method used to assess CLDN18.2 expression levels in gastric cancer tissues. High levels of CLDN18.2 expression have been consistently detected in gastric cancer samples, while minimal to no expression is observed in normal gastric mucosa. This stark contrast in expression levels between cancerous and healthy tissues underscores the potential utility of CLDN18.2 as a diagnostic marker for gastric cancer.

Furthermore, CLDN18.2 expression status has shown promise in distinguishing gastric cancer from benign gastric lesions or healthy tissue. Studies have reported high sensitivity and specificity of CLDN18.2 immunohistochemistry in differentiating malignant gastric lesions from non-malignant ones, highlighting its potential as a diagnostic tool [7].

In addition to its application in tissue-based diagnosis, CLDN18.2 holds promise for non-invasive detection and staging of gastric cancer. The development of CLDN18.2-targeted imaging probes offers opportunities for molecular imaging techniques, such as Positron Emission Tomography (PET) or magnetic resonance imaging (MRI), to detect CLDN18.2-expressing tumors in vivo. This non-invasive approach could facilitate early detection, staging, and monitoring of gastric cancer, potentially improving patient outcomes.

Overall, the diagnostic potential of CLDN18.2 in gastric cancer is underscored by its selective overexpression in cancerous tissues and its ability to distinguish malignant lesions from benign ones with high sensitivity and specificity. Further research and validation studies are warranted to optimize CLDN18.2-based diagnostic assays and integrate them into routine clinical practice for the early detection and management of gastric cancer.

Prognostic Implications

The prognostic implications of Claudin 18.2 (CLDN18.2) expression in gastric cancer are significant, offering valuable insights into disease progression and patient outcomes. Several studies have demonstrated a correlation between CLDN18.2 expression levels and adverse clinicopathological features, as well as overall survival rates in gastric cancer patients.

High levels of CLDN18.2 expression have been consistently associated with advanced tumor stage, lymph node metastasis, and other aggressive clinicopathological characteristics. This suggests that CLDN18.2 expression status may serve as a prognostic indicator for gastric cancer patients, aiding in risk stratification and treatment decision-making [8].

Moreover, CLDN18.2 expression has been linked to poorer overall survival outcomes in gastric cancer patients. Patients with tumors exhibiting high levels of CLDN18.2 expression tend to have shorter survival times compared to those with lower CLDN18.2 expression levels. This highlights the potential utility of CLDN18.2 as a prognostic biomarker, enabling clinicians to identify patients at higher risk of disease progression and poor outcomes [8].

The prognostic significance of CLDN18.2 in gastric cancer underscores the importance of incorporating its assessment into clinical practice. By stratifying patients based on CLDN18.2 expression status, clinicians can tailor treatment strategies and surveillance protocols to optimize patient outcomes. Furthermore, CLDN18.2 may serve as a valuable adjunct to traditional prognostic factors, enhancing the accuracy of prognostic assessments in gastric cancer patients.

Therapeutic Target

The selective overexpression of Claudin 18.2 (CLDN18.2) in gastric cancer cells makes it an attractive therapeutic target for the development of novel treatment strategies. CLDN18.2-targeted therapies offer the potential for more precise and effective treatment options, with the aim of improving patient outcomes while minimizing systemic toxicity [9].

Monoclonal antibodies directed against CLDN18.2 represent one approach in CLDN18.2-targeted therapy. Zolbetuximab, a monoclonal antibody targeting CLDN18.2, has shown promising results in preclinical studies and early-phase clinical trials. By specifically binding to CLDN18.2-expressing tumor cells, zolbetuximab mediates Antibody-Dependent Cellular Cytotoxicity (ADCC) and Antibody-Dependent Cellular Phagocytosis (ADCP), leading to the destruction of cancer cells. Additionally, zolbetuximab may inhibit tumor growth and metastasis through immune-mediated mechanisms, such as activation of Natural Killer (NK) cells and enhancement of antitumor immune responses [8-9].

Combination therapies involving CLDN18.2-targeted antibodies with conventional chemotherapy agents have also been explored. Preclinical studies have demonstrated synergistic effects between zolbetuximab and chemotherapy, leading to enhanced tumor cell killing and improved treatment outcomes. Clinical trials evaluating the efficacy and safety of zolbetuximab in combination with chemotherapy regimens are underway, with promising preliminary results reported in gastric cancer patients [10].

Challenges and Future Directions

The therapeutic targeting of Claudin 18.2 (CLDN18.2) in gastric cancer presents both opportunities and challenges, necessitating further research and strategic considerations for its effective implementation in clinical practice. One of the primary opportunities lies in the selective overexpression of CLDN18.2 in gastric cancer cells, making it an attractive therapeutic target. Monoclonal antibodies directed against CLDN18.2, such as zolbetuximab, have shown promising results in preclinical studies and early-phase clinical trials. These targeted therapies offer the potential for improved treatment outcomes and reduced systemic toxicity compared to conventional chemotherapy regimens. However, several challenges must be addressed to maximize the therapeutic potential of CLDN18.2-targeted therapies in gastric cancer. One such challenge is the optimization of treatment strategies to enhance efficacy and minimize resistance development. This may involve exploring combination therapies with other agents, such as chemotherapy, immune checkpoint inhibitors, or targeted agents against other molecular pathways implicated in gastric cancer progression.

Another challenge is the identification of predictive biomarkers for treatment response to CLDN18.2-targeted therapies. While CLDN18.2 expression status may serve as a potential biomarker, additional factors influencing treatment response need to be elucidated. Biomarkers related to tumor heterogeneity, immune microenvironment, and molecular subtypes of gastric cancer may provide valuable insights into patient selection and treatment optimization.

Conclusion

CLDN18.2 represents a promising biomarker in gastric cancer, offering diagnostic, prognostic, and therapeutic implications. Its selective overexpression in gastric cancer cells and association with aggressive tumor behavior make it an attractive target for personalized medicine approaches. Continued research efforts are essential to further elucidate the clinical utility of CLDN18.2 and its integration into routine clinical practice for the management of gastric cancer patients.

References

1. Hirose K, Niwa Y, Wakai K, Matsuo K, Nakanishi T, et al. (2007). Coffee consumption and the risk of endometrial cancer: Evidence from a case-control study of female hormone-related cancers in Japan. Cancer sci 98: 411-415.
2. Zamboni WC, Ramalingam S, Friedland DM, Edwards RP, Stoller RG, et al. (2009). Phase I and pharmacokinetic study of pegylated liposomal CKD-602 in patients with advanced malignancies. Clin

cancer res 15: 1466-1472.

3. Pellino A, Brignola S, Riello E, Niero M, Murgioni S, et al. (2021). Association of CLDN18 protein expression with clinicopathological features and prognosis in advanced gastric and gastroesophageal junction adenocarcinomas. J Pers Med 11: 1095.
4. Singh P, Toom S, & Huang Y. (2017). Anti-claudin 18.2 antibody as new targeted therapy for advanced gastric cancer. J hematol oncol 10: 1-5.
5. Niu Q, Liu J, Luo X, Su B, & Yuan X, et al. (2021). Future of targeted therapy for gastrointestinal cancer: Claudin 18.2. Oncol Transl Med 7: 102-107.
6. Wang H, Yuan Y, Lu C, Zhou S, Zhang Y, et al. (2021). Analysis of T-cell receptor repertoire in peripheral blood of patients with pancreatic cancer and other pancreatic diseases. J Cell Mol Med, 25: 3991-4000.
7. Angerilli V, Ghelardi F, Nappo F, Grillo F, Parente P, et al. (2024). Claudin-18.2 testing and its impact in the therapeutic management of patients with gastric and gastroesophageal adenocarcinomas: A literature review with expert opinion. Pathol Res Pract, 155145.
8. Wang X, Hang Y, Liu J, Hou Y, Wang N, et al. (2017). Anticancer effect of curcumin inhibits cell growth through miR-21/PTEN/Akt pathway in breast cancer cell. Oncol Lett 13:4825-4831.
9. Hatakeyama, M. (2004). Oncogenic mechanisms of the Helicobacter pylori CagA protein. Nat Rev Cancer 4: 688-694.
10. Matsuda Y, Semba S, Ueda J, Fuku T, Hasuo T, et al. (2007). Gastric and intestinal claudin expression at the invasive front of gastric carcinoma. Cancer sci 98: 1014-1019.

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