



# The Clinical Value of Cancer Stem Cell Markers in Gastric Cancer

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## Editorial

Nowadays, gastric cancer remains the life-threatening complaint in spite of advanced surgical procedures and other methods, such as radiotherapy and chemotherapy, having improved the overall survival of patients dramatically. According to the statistics, gastric cancer ranks the fifth most common cancer, meanwhile the third leading cause of cancer patients. To further improve the prognosis of patients with gastric cancer, investigations of mechanisms towards gastric carcinogenesis and invasion appear in full swing. Hereinto, several genetic biomarkers have been regarded as prognostic factors of gastric cancer and might be helpful to individual treatment.

Accumulating evidence has suggested that cancer is hierarchically organized, with only a rare subpopulation of cancer cells termed cancer stem cells (CSCs). CSC has been identified to play vital roles in the initial, dissemination and recurrence of numerous solid tumors, including gastric cancer. The identification of CSC is still controversial, the most common method is labeling the special markers expressing on the tumor cell surface by Immunohistochemistry.

Recently, CD44 and CD133 present the novel and the most robust CSC markers in many solid tumors, such as colon cancer, breast cancer. However, the evidence to determine the clinical value of CD44 and CD133 remains insufficient, partially because much existing evidence is conflicting. We performed a meta-analysis to elucidate whether CD44 or CD133 overexpression would correlate with gastric cancer clinicopathology and prognosis, and to explain which of these markers would have more clinical value based on the meta-analysis evidence. 26 Studies included in this meta-analysis with a total of 4729 involved patients. The eligible studies were published between 1993 and 2015. The results demonstrated that high expression of CD44 was associated with Lauren type (intestinal type) and lymphatic vessel invasion. CD133 over-expression was related to high TNM stage (III/IV), high depth of invasion (T3/T4), lymph node metastasis, vascular invasion, and distant metastasis. In addition, survival analysis demonstrated a significant association between CD44, as well as CD133 and poor 5-year overall survival. Based on our results, combined detection of CD44 and CD133 expression can be an especially effective tool for pathological diagnosis and prognostic prediction of gastric cancer patients in clinical applications.

As one of the variant of CD44, CD44v6 has been extensively studied in many tumors and its prognostic value has been reported. Moreover, the monoclonal antibodies of CD44v6 have been identified their target-therapy potential. Despite, several clinical studies were carried out to evaluate the relationship of CD44v6 expression with clinicopathology and prognosis of gastric cancer, no consistent finding was available. Hence, a meta-analysis of published data was performed to systematically elucidate whether CD44v6 overexpression would have correlations with the diagnostic and prognostic value in patients with gastric cancer. 16 eligible articles with 2177 gastric cancer patients were included in this meta-analysis, the publication years of all studies ranged from 1995 to 2015. Among this study, Five studies including 913 patients were assessed for the correlation between CD44v6 and 5-year overall survival (OS). The results showed that the upregulated CD44v6 was associated with lymph node metastasis, distant metastasis, high TNM stage, lymphatic vessel invasion and vascular invasion. Pooled HR indicated that CD44v6 positive expression was correlated poor 5-year OS. Taken together, CD44v6 overexpression was correlated to the characteristics of tumor metastasis in gastric cancer, consisting with many mechanism studies. Thus, clinicians should closely follow up the gastric cancer patients with CD44v6 upregulation in consideration of their high risk for metastasis.

There also many other CSC markers in gastric cancer, such as SOX-2, Lgr-5, ALDH1. The Clinical value of these markers may need more research to support, meanwhile, the detail mechanism of CSC in tumor invasion and metastasis of gastric cancer also need further research.

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