Meta-analysis of the prognostic value of IncRNA DANCR for cancer patients in China

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Background: Abnormal expression of long non-coding RNA anti-differentiation noncoding RNA (IncRNA DANCR) can frequently be detected in cancer. Because of this, it is of vital necessity to perform a meta-analysis to clarify the value of IncRNA DANCR as a prognostic marker in malignant tumors.

Methods: Related studies were retrieved from electronic databases including Web of Science, PubMed, and OVID, from inception to November 21, 2018. The HRs and corresponding 95% CIs were also calculated to explore the relationship of IncRNA DANCR expression with patient survival. Moreover, ORs were computed to assess the association of IncRNA DANCR expression with the pathological parameters.

Results: A total of 14 studies involving 1,117 patients were included in this meta-analysis. The pooled HR suggested that high IncRNA DANCR expression was correlated with poor overall survival (OS; HR =1.85, 95% CI: 1.56–2.18) and disease-free survival (DFS; HR =2.49, 95% CI: 1.75–3.56) in cancer patients. Beside, High IncRNA DANCR expression was related to poor histological grade (PHG; OR =2.01, 95% CI: 1.08–3.75), high tumor stage (HTS; OR =3.52, 95% CI: 1.67–7.43), lymph node metastasis (LNM; OR =3.47, 95% CI: 1.42–8.49), and distant metastasis (DM; OR =3.76, 95% CI: 2.39–9.51). However, no evidence of obvious asymmetry was found for DFS (Pr>|z|=0.308), PHG (Pr>|z|=0.707), LNM (Pr>|z|=0.174), and DM (Pr>|z|=0.734) using Begg’s funnel plot.

Conclusion: Our findings suggest that high IncRNA DANCR expression can predict poor OS, DFS, PHG, HTS, LNM, and DM in cancer patients, implying that high IncRNA DANCR expression may potentially serve as a new indicator for poor prognosis and metastasis in cancer.

Keywords: IncRNA, DANCR, neoplasms, prognosis, metastasis

Introduction
Recent report demonstrates that, the US has witnessed about 1.7 million new cancer cases and 600,000 cancer-related deaths in 2017.1 Nevertheless, the 5-year survival of most cancers remains dismally low, and a large number of scientists are devoting themselves to looking for new biomarkers to determine or diagnose cancer prognosis.

IncRNA, which lacks a meaningful open reading frame, is defined as the transcribed RNA molecule that is >200 nucleotides in length, which has possessed many important functions in disease, such as posttranscriptional, transcriptional, and epigenetic regulation.2,3 In addition, abnormal IncRNA expression is currently recognized to be related to various cancer types.4–7 For instance, some IncRNAs play crucial parts in metastasis, invasion, and proliferation of cancer cells, indicating that IncRNA may serve be a useful marker for predicting cancer prognosis.8–10
Typically, the IncRNA DANCR was discovered by Kretz et al in 2012, which was originally deemed to be essential for the dedifferentiation of epidermal cells.\(^1\) Besides, recent studies reveal that DANCR plays a crucial role in the differentiation of periodontal ligament stem cells into osteoblasts, which can also promote tumor cell dissemination and metastasis formation.\(^2\)\(^-\)\(^4\) Moreover, IncRNA DANCR is also suggested in some studies to be correlated with different tumor biological parameters, such as tumor growth, metastasis, and progression.\(^5\)\(^-\)\(^7\) Metastasis and prognosis may be affected by IncRNA DANCR; nonetheless, a majority of existing studies are limited by their small sample sizes and discrete outcomes. As a consequence, an updated meta-analysis was performed in this study to determine the prognostic value of IncRNA DANCR in cancer patients.

## Materials and methods

### Literature collection

In accordance with the standard guidelines for meta-analyses,\(^8\)\(^,\)\(^9\)\(^,\)\(^1\)\(^9\) related articles that served IncRNA DANCR as a prognostic biomarker for the survival of cancer patients were systematically retrieved from some online databases by two authors independently from inception to November 21, 2018. Meanwhile, text words and Mesh strategies were adjusted based on the databases in this retrieval, including the following terms (“Long non-coding RNA differentiation antagonizing non-protein coding RNA” or “IncRNA DANCR” or “IncRNA ANCR”) and (“recurrence” or “outcome” or “survival”, “cancer” or “neoplasm” or “tumor” or “carcinoma”, “prognosis” or “prognostic”). Moreover, the reference lists of relevant articles were also manually retrieved during retrieval, so as to avoid missing any potentially eligible studies.

### Study selection

All the included studies were then evaluated, and data were extracted by two scholars independently. Typically, the study inclusion criteria were as follows: 1) studies in which all tumors were confirmed by histological or pathological examinations; 2) studies in which the IncRNA DANCR expression levels in human tumor tissues were measured; 3) studies in which patients were grouped in accordance with different IncRNA DANCR expression levels, and the cutoff values of high and low DANCR expression might be the median or mean of all samples in their study; and 4) studies with sufficient original data for statistical analyses of pathological or patient survival parameters with IncRNA DANCR expression.

In addition, the study exclusion criteria were shown below: non-human studies and non-English studies; editorials, reviews, expert opinions as well as letters; database analysis without original data; and studies mentioning functions and molecular structure of IncRNA DANCR only.

### Date extraction

Data from the original articles were independently examined and extracted by two reviewers, and any disagreement between them during the process of literature assessment was settled by the consensus with a third reviewer. A series of data were collected in this meta-analysis, including surname of the first author, publication year, country, tumor type, sample size, number of patients with LTS, PHG, HTS, LNM and DM, reference gene and detection method of IncRNA DANCR, as well as HRs and 95% CIs of elevated IncRNA DANCR expression for OS and DFS.

### Statistical methods

The Stata version 12.0 software was adopted for all statistical analyses. In addition, the heterogeneity was also measured in this meta-analysis using Q and I\(^2\) tests. The test results had indicated the presence of significant heterogeneity in this research (\(I^2 ≥50\%), and \(P<0.1\));\(^2\)\(^0\) therefore, the random effect model should be adopted. Besides, the potential publication bias was also assessed by Egger’s test and Begg’s funnel plot. The pooled ORs and HRs should be extracted from the published data; typically, the crude data should be adopted if the HRs could not be obtained directly from the publications. Besides, the survival information extracted from Kaplan–Meier curves should be adopted to estimate the HRs when they were not directly reported in the studies. To make a summary about the outcomes of survival, both SE and the log HR should be collected.\(^2\)\(^1\) Moreover, 95% CIs and ORs should be combined to assess the relationship of clinicopathological parameters with IncRNA DANCR.

### Results

#### Study characteristics

Details about the screening process are shown in Figure 1. In accordance with the exclusion and inclusion criteria, 14 studies involving 1,117 patients were enrolled into this meta-analysis.\(^2\)\(^2\)\(^-\)\(^5\)\(^5\) Characteristics of the 14 studies included in this meta-analysis are summarized in Table 1. As could be observed, the sample size in the 14 studies ranged from 34 to 135, with an average of 79.57. Besides, all the enrolled studies were published between 2015 and 2018 and were carried out in China. Among these studies, respectively, one study had focused on CVR,\(^2\)\(^5\) TNBC,\(^2\)\(^9\) RB,\(^3\)\(^0\) HCC,\(^3\)\(^4\) and BC,\(^3\)\(^5\) three concentrated on GC;\(^2\)\(^2\)\(^,\)\(^2\)\(^7\)\(^,\)\(^2\)\(^8\) two focused
on OSC; two on glioma; and two on CRC. All clinical pathological parameters were dependent on the pathology. Moreover, it was found that the reference genes of lncRNA DANCR were different among these studies, which had included GAPDH, β-actin, and small nuclear RNA U6. Moreover, the thresholds of high and low lncRNA DANCR expression levels, including the median and average lncRNA DANCR expression, were also different among these studies.

**Association between the lncRNA DANCR expression level and survival**

To assess the role of lncRNA DANCR in OS for cancer patients, cumulative meta-analysis was carried out in this research. As shown, the relationship of OS with lncRNA DANCR was reported in ten studies enrolling 839 patients (Table 2). Meanwhile, the fixed effects model was adopted since there was no significant heterogeneity ($I^2=0.0\%$, $P=0.728$). The results suggested that the OS in cancer patients was markedly related to the lncRNA DANCR expression (pooled HR = 1.85, 95% CI: 1.56–2.18; Figure 2A). Besides, sensitivity analysis was also carried out, which had confirmed the robustness of these results (Figure 2B). Subsequently, subgroup analyses stratified by cancer type, sample size, NOS score, and HR statistic method were also carried out (Table 3, Figure 3).

Moreover, cumulative meta-analysis was also performed to determine the role of lncRNA DANCR in DFS among the 330 cancer patients recruited into the eligible studies (Figure 4). The results revealed that lncRNA DANCR was correlated with DFS (pooled HR = 2.49, 95% CI: 1.75–3.56) in cancer patients upon statistical analyses. Similarly, the
**Table 1** The basic information and data of all included studies in the meta-analysis

<table>
<thead>
<tr>
<th>Reference</th>
<th>Year</th>
<th>Country</th>
<th>Tumor type</th>
<th>Sample size (n)</th>
<th>Low IncRNA DANCR expression (n)</th>
<th>High IncRNA DANCR expression (n)</th>
<th>Total LTS PHG</th>
<th>HTS LNM DM</th>
<th>Q</th>
<th>P</th>
<th>I²</th>
<th>I² (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hao et al 22</td>
<td>2017</td>
<td>China</td>
<td>gC</td>
<td>118</td>
<td>24</td>
<td>18</td>
<td>46</td>
<td>12</td>
<td>6</td>
<td>1</td>
<td>79.4</td>
<td>0.000</td>
</tr>
<tr>
<td>Fan et al 23</td>
<td>2017</td>
<td>China</td>
<td>OsC</td>
<td>46</td>
<td>23</td>
<td>23</td>
<td>46</td>
<td>12</td>
<td>12</td>
<td>2</td>
<td>24.2</td>
<td>0.024</td>
</tr>
<tr>
<td>Yuan et al 24</td>
<td>2018</td>
<td>China</td>
<td>glioma</td>
<td>86</td>
<td>23</td>
<td>23</td>
<td>46</td>
<td>12</td>
<td>12</td>
<td>2</td>
<td>61.4</td>
<td>0.024</td>
</tr>
<tr>
<td>Mao et al 25</td>
<td>2018</td>
<td>China</td>
<td>CRC</td>
<td>104</td>
<td>24</td>
<td>24</td>
<td>46</td>
<td>12</td>
<td>12</td>
<td>2</td>
<td>83.5</td>
<td>0.000</td>
</tr>
<tr>
<td>Liu et al 26</td>
<td>2018</td>
<td>China</td>
<td>CRC</td>
<td>65</td>
<td>23</td>
<td>23</td>
<td>46</td>
<td>12</td>
<td>12</td>
<td>2</td>
<td>24.2</td>
<td>0.024</td>
</tr>
<tr>
<td>Wang et al 27</td>
<td>2018</td>
<td>China</td>
<td>gC</td>
<td>60</td>
<td>23</td>
<td>23</td>
<td>46</td>
<td>12</td>
<td>12</td>
<td>2</td>
<td>79.4</td>
<td>0.000</td>
</tr>
<tr>
<td>Wang et al 28</td>
<td>2017</td>
<td>China</td>
<td>gC</td>
<td>65</td>
<td>23</td>
<td>23</td>
<td>46</td>
<td>12</td>
<td>12</td>
<td>2</td>
<td>24.2</td>
<td>0.024</td>
</tr>
<tr>
<td>Jiang et al 29</td>
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<td>China</td>
<td>OsC</td>
<td>34</td>
<td>23</td>
<td>23</td>
<td>46</td>
<td>12</td>
<td>12</td>
<td>2</td>
<td>79.4</td>
<td>0.000</td>
</tr>
<tr>
<td>Liu et al 30</td>
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<td>China</td>
<td>CRC</td>
<td>104</td>
<td>24</td>
<td>24</td>
<td>46</td>
<td>12</td>
<td>12</td>
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<td>61.4</td>
<td>0.024</td>
</tr>
<tr>
<td>Wang et al 31</td>
<td>2018</td>
<td>China</td>
<td>CRC</td>
<td>47</td>
<td>23</td>
<td>23</td>
<td>46</td>
<td>12</td>
<td>12</td>
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<td>24.2</td>
<td>0.024</td>
</tr>
<tr>
<td>Wang et al 32</td>
<td>2018</td>
<td>China</td>
<td>OsC</td>
<td>95</td>
<td>23</td>
<td>23</td>
<td>46</td>
<td>12</td>
<td>12</td>
<td>2</td>
<td>79.4</td>
<td>0.000</td>
</tr>
<tr>
<td>Yang et al 33</td>
<td>2018</td>
<td>China</td>
<td>glioma</td>
<td>82</td>
<td>23</td>
<td>23</td>
<td>46</td>
<td>12</td>
<td>12</td>
<td>2</td>
<td>79.4</td>
<td>0.000</td>
</tr>
<tr>
<td>Yuan et al 34</td>
<td>2016</td>
<td>China</td>
<td>hCC</td>
<td>135</td>
<td>23</td>
<td>23</td>
<td>46</td>
<td>12</td>
<td>12</td>
<td>2</td>
<td>79.4</td>
<td>0.000</td>
</tr>
<tr>
<td>Zhan et al 35</td>
<td>2018</td>
<td>China</td>
<td>BC</td>
<td>106</td>
<td>23</td>
<td>23</td>
<td>46</td>
<td>12</td>
<td>12</td>
<td>2</td>
<td>79.4</td>
<td>0.000</td>
</tr>
</tbody>
</table>

**Note:** The dashes represent no data.

**Abbreviations:** BC, colorectal cancer; CRC, cervical cancer; CVR, cervical cancer; DM, distant metastasis; HTS, high tumor stage; hTs, high tumor stage; LN, Lymph node metastasis; LNM, lymph node metastasis; LTS, larger tumor size; OsC, osteosarcoma; PHG, poor histological grade; RB, retinoblastoma; TnBC, triple negative breast cancer.

These results suggested that the shorter OS and DFS in cancer patients might be associated with higher *IncRNA DANCR* expression. As a result, it could be concluded that *IncRNA DANCR* was an independent factor of the survival for cancer patients.

**Association between the *IncRNA DANCR* expression level and LTS**

Figure 5A shows the association between LTS and *IncRNA DANCR* expression from ten studies involving 757 patients. Specifically, the random-effects model was adopted due to the presence of a significant heterogeneity among the eligible studies ($F=79.4\%, P_{Q}=0.000$). Our results had revealed a pooled OR of 1.63 (95% CI: 0.80–3.31; high vs low *IncRNA DANCR* expression). Moreover, sensitivity analysis of all included studies was also performed, and the OR of high to low expression groups was 2.10 (95% CI: 1.25–3.54) after the study by Hao et al 22 was excluded ($F=56.6\%, P_{Q}=0.018$) (Figure 5B and C).

Conforming to the abovementioned results, no significant difference was detected in the LTS incidence between two groups, but additional studies were needed to confirm the association between *IncRNA DANCR* and LTS in cancer patients.

**Association between the *IncRNA DANCR* expression level and PHG**

In this research, data regarding the association between the *IncRNA DANCR* expression and PHG had been collected from six eligible studies involving 503 cancer patients, and the random-effects model was adopted as a result of the significant heterogeneity ($F=61.4\%, P_{Q}=0.024$). Besides, the OR of high to low *IncRNA DANCR* expression groups was 2.10 (95% CI: 1.08–3.75, Figure 6A). Typically, the heterogeneity had disappeared ($F=24.2\%, P_{Q}=0.266$) after two studies were removed in sensitivity analysis, with the OR of high to low expression groups of 3.14 (95% CI: 1.95–5.05) (Figure 6B and C).

In accordance with these results, a significant difference was noted in the incidence of PHG between two groups, indicating that the risk of PHG was remarkably correlated with high *IncRNA DANCR* expression.

**Association between the *IncRNA DANCR* expression level and HTS**

In this meta-analysis, the correlation between HTS and *IncRNA DANCR* expression was detected in ten eligible
Table 2  Survival data of studies included in the meta-analysis

<table>
<thead>
<tr>
<th>Reference</th>
<th>Year</th>
<th>Country</th>
<th>Tumor type</th>
<th>Sample size (n)</th>
<th>Method</th>
<th>OS, HR (95% CI)</th>
<th>DFS, HR (95% CI)</th>
<th>HR statistic</th>
<th>NOS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hao et al22</td>
<td>2017</td>
<td>China</td>
<td>GC</td>
<td>118</td>
<td>Multivariate</td>
<td>1.66 (1.0363–2.6590)</td>
<td>NA</td>
<td>Survival curve</td>
<td>8</td>
</tr>
<tr>
<td>Li and Zhou24</td>
<td>2018</td>
<td>China</td>
<td>Glioma</td>
<td>86</td>
<td>Multivariate</td>
<td>1.85 (1.0844–3.1562)</td>
<td>NA</td>
<td>Survival curve</td>
<td>7</td>
</tr>
<tr>
<td>Liang et al25</td>
<td>2019</td>
<td>China</td>
<td>CRC</td>
<td>104</td>
<td>Multivariate</td>
<td>2.06 (1.0683–3.9724)</td>
<td>2.397 (1.385–7.279)</td>
<td>Data in paper</td>
<td>8</td>
</tr>
<tr>
<td>Liu et al26</td>
<td>2015</td>
<td>China</td>
<td>CRC</td>
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<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>7</td>
</tr>
<tr>
<td>Mao et al27</td>
<td>2017</td>
<td>China</td>
<td>GC</td>
<td>60</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>7</td>
</tr>
<tr>
<td>Pan et al28</td>
<td>2018</td>
<td>China</td>
<td>GC</td>
<td>65</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>7</td>
</tr>
<tr>
<td>Sha et al29</td>
<td>2017</td>
<td>China</td>
<td>TnBC</td>
<td>63</td>
<td>Multivariate</td>
<td>1.56 (1.02–2.38)</td>
<td>NA</td>
<td>Survival curve</td>
<td>8</td>
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<tr>
<td>Wang et al30</td>
<td>2018</td>
<td>China</td>
<td>RB</td>
<td>57</td>
<td>Multivariate</td>
<td>2.26 (1.694–4.0238)</td>
<td>2.84 (1.3068–6.1721)</td>
<td>Data in paper</td>
<td>6</td>
</tr>
<tr>
<td>Wang et al31</td>
<td>2018</td>
<td>China</td>
<td>CRC</td>
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<td>Wang et al32</td>
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<td>China</td>
<td>OSC</td>
<td>95</td>
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<tr>
<td>Yang et al33</td>
<td>2018</td>
<td>China</td>
<td>Glioma</td>
<td>82</td>
<td>Multivariate</td>
<td>1.783 (1.121–3.4821)</td>
<td>2.288 (1.359–3.653)</td>
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<td>6</td>
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<td>2018</td>
<td>China</td>
<td>HCC</td>
<td>135</td>
<td>Multivariate</td>
<td>2.757 (1.379–5.514)</td>
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<td>6</td>
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<tr>
<td>Zhan et al35</td>
<td>2018</td>
<td>China</td>
<td>BC</td>
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<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>7</td>
</tr>
</tbody>
</table>

Note: NA represents no data.

Abbreviations: BC, bladder cancer; CRC, colorectal cancer; CVR, cervical cancer; DFS, disease-free survival; GC, gastric cancer; hCC, hepatocellular carcinoma; NOS, Newcastle–Ottawa Scale; OS, overall survival; OsC, osteosarcoma; RB, retinoblastoma; TnBC, triple negative breast cancer.

Figure 2  Forest plot (A) and sensitivity analysis (B) showed the relationship between IncRNA DANCR expression level and OS in cancer.

Abbreviations: IncRNA DANCR, long non-coding RNA anti-differentiation noncoding RNA; OS, overall survival.
Table 3 Subgroup analysis of OS by tumor type, sample size, NOS score, and HR statistic method

<table>
<thead>
<tr>
<th>Subgroup analysis</th>
<th>No. of studies</th>
<th>No. of patients</th>
<th>Pooled HR (95% CI)</th>
<th>Heterogeneity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>10</td>
<td>839</td>
<td>1.85 (1.56–2.18)</td>
<td>0.0</td>
</tr>
<tr>
<td>Cancer type</td>
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<td></td>
</tr>
<tr>
<td>Digestive system cancer</td>
<td>3</td>
<td>357</td>
<td>1.98 (1.38–2.83)</td>
<td>0.0</td>
</tr>
<tr>
<td>Non-digestive system cancer</td>
<td>7</td>
<td>482</td>
<td>1.81 (1.50–2.19)</td>
<td>0.0</td>
</tr>
<tr>
<td>Sample size</td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>Number &gt;90</td>
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<td>452</td>
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</tr>
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<td>Number ≤90</td>
<td>6</td>
<td>387</td>
<td>1.90 (1.50–2.40)</td>
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<td>NOS score</td>
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</tr>
<tr>
<td>NOS &gt;7</td>
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<td>1.65 (1.23–2.23)</td>
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<tr>
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<td>554</td>
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<tr>
<td>HR statistic</td>
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<td></td>
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<tr>
<td>Survival curve</td>
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<td>0.0</td>
</tr>
<tr>
<td>Data in paper</td>
<td>4</td>
<td>355</td>
<td>2.31 (1.59–3.37)</td>
<td>0.0</td>
</tr>
</tbody>
</table>

**Abbreviations:** NOS, Newcastle–Ottawa Scale; OS, overall survival.

Figure 3 Forest plots of subgroup analysis for OS of patients with cancer.

**Notes:** Subgroup analysis by tumor type (A), sample size (B), NOS score (C), and HR statistic method (D).

**Abbreviations:** NOS, Newcastle–Ottawa Scale; OS, overall survival.
As far as cancer patients were concerned, high IncRNA DANCR expression was markedly correlated with greater susceptibility to LNM.

Association between the IncRNA DANCR expression level and DM

In this meta-analysis, the correlation of DM with the IncRNA DANCR expression level was examined in four eligible studies including 241 patients, and the fix effects model was adopted due to the limited heterogeneity ($I^2=0.0\%$, $P_{I^2}=0.666$). The OR of high to low IncRNA DANCR expression groups was $>4.76$ (95% CI: 2.39–9.51, Figure 9). Consistent with these results, the DM incidence was significantly different between two groups, revealing that high IncRNA DANCR expression could remarkably predict a higher tendency to develop DM in cancer patients.

Publication bias

Subsequently, the Begg’s funnel plot was conducted in this study to evaluate the potential publication bias. Figure 10 shows no evidence of obvious asymmetry for DFS (Pr>|z|=0.308), LTS (Pr>|z|=0.283), PHG (Pr>|z|=0.707), LNM (Pr>|z|=0.174), and DM (Pr>|z|=0.734). However, significant publication bias was detected for OS (Pr>|z|=0.004) and HTS (Pr>|z|=0.007).

Discussion

Cancer still poses a serious threat to human health, which is gradually increased in recent years in terms of morbidity. Nonetheless, the exact metastasis mechanism in cancer patients remains unclear despite that metastasis is an important indicator of poor prognosis. Therefore, it is necessary to identify new molecular markers to predict tumor metastasis at present, since they may play critical roles in treating and predicting cancer. lncRNAs, one of these molecular markers, can affect tumor initiation, progression, and occurrence, which can easily collect the useful biomarkers for cancer monitoring and diagnosis.
IncRNA DANCR has been verified in previous studies to be an important oncogene in various human cancers, including GC, glioma, CVR, OSC, CRC, RB, HCC, and BC. Additionally, IncRNA DANCR expression has been confirmed in recent study to be upregulated in CRC tissues, which is correlated with poor survival for CRC patients. Moreover, according to Li et al, DANCR could positively promote the proliferation and migration of glioma through activating the Wnt/β-catenin signaling pathway. Besides, Mao et al also reported that DANCR was upregulated in GC tissues, which could enhance the migration and invasion of GC cells. Additionally, Wang et al found that DANCR could strongly suppress HCC proliferation via targeting miR-216a-5p and KLF12. Furthermore, Lu et al demonstrated that DANCR...

Figure 6 Forest plot (A), sensitivity analysis (B), and the forest plot of sensitivity analysis (C) showed the association between PHG and IncRNA DANCR expression level in cancer. Abbreviations: IncRNA DANCR, long non-coding RNA anti-differentiation noncoding RNA; PHG, poor histological grade.

Figure 7 Forest plot (A), sensitivity analysis (B), and the forest plot of sensitivity analysis (C) showed the association between HTS and IncRNA DANCR expression level in cancer. Abbreviations: HTS, high tumor stage; IncRNA DANCR, long non-coding RNA anti-differentiation noncoding RNA.
could drive cancer cell proliferation by targeting DANCR.\(^43\)

was elevated in a broad spectrum of human cancers, and MYC
noncoding RNA; LN M, lymph node metastasis.\(^43\)

correlation between LN M and the clinicopathological parameters, including PHG, HTS, DM, and
LNM. To sum up, findings of this meta-analysis indicated that IncRNA DANCR might serve as a valuable biomarker
for the poor prognosis of most cancers.

**Limitations**

Several limitations should be taken into consideration when interpreting the conclusion of this meta-analysis. First, data
in this meta-analysis might not be applicable for countries all over the world, since all the included studies were from
China. Second, in spite of the best effort made to search for all relevant studies only 14 studies were ultimately enrolled
in this study; the relatively small sample size might reduce the stringency of our conclusion. Third, the criterion of high
expression was not consistent among all articles, making it difficult to obtain the same value. Last but not least, there
were other factors that might affect cancer prognosis, such as comorbidities and therapies, but related information
was not available in the analyzed enrolled articles, which had therefore become an inherent shortcoming of this systematic
review and meta-analysis. As a consequence, the role of

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**Figure 8** Forest plot (A), sensitivity analysis (B), and the forest plot of sensitivity analysis (C) showed the association between LN M and IncRNA DANCR expression level in cancer.

**Abbreviations:** IncRNA DANCR, long non-coding RNA anti-differentiation noncoding RNA; LN M, lymph node metastasis.

In this research, related data collected from the 14 eligible studies involving 1,117 cancer patients were analyzed, and a fixed or a random effects model had been adopted based on the heterogeneity analysis results. For cancer patients, high IncRNA DANCR expression could potentially serve as an indicator of poor prognosis. Besides, significant differences were found in OS and DFS between the two groups after combining HRs from the Cox multivariate analyses, and it was found that poor OS and DFS in various cancer kinds were associated with high IncRNA DANCR expression. Moreover, high IncRNA DANCR expression in cancer patients was also remarkably related to some clinicopathological parameters, including PHG, HTS, DM, and LN M. To sum up, findings of this meta-analysis indicated that IncRNA DANCR might serve as a valuable biomarker for the poor prognosis of most cancers.

**Figure 9** Evaluation of the relationship between IncRNA DANCR expression level and DM in cancer.

**Abbreviations:** DM, distant metastasis; IncRNA DANCR, long non-coding RNA anti-differentiation noncoding RNA.
In conclusion, our findings suggest that high lncRNA DANCR expression in cancer should be further confirmed by more high-quality and well-designed studies.

**Conclusion**

To sum up, our findings suggest that high lncRNA DANCR expression in a series of cancers is remarkably correlated with poor OS, DFS, PHG, HTS, DM, and LNM. As a result, lncRNA DANCR may potentially serve as a biomarker to determine metastasis and predict the prognosis for cancer patients.

**Abbreviations**

BC, bladder cancer; CRC, colorectal cancer; CVR, cervical cancer; DFS, disease-free survival; DM, distant metastasis; GAPDH, glyceraldehyde-3-phosphate dehydrogenase; GC, gastric cancer; HCC, hepatocellular carcinoma; HTS, high tumor stage; lncRNA DANCR, long non-coding RNA anti-differentiation noncoding RNA; LNM, lymph node metastasis; LTS, larger tumor size; NOS, Newcastle–Ottawa Scale; OS, overall survival; OSC, osteosarcoma; PHG, poor histological grade; RB, retinoblastoma; TNBC triple negative breast cancer.

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**Disclosure**

The authors report no conflicts of interest in this work.

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