1. Abstract

Gastric cancer is one of the most common human cancers. Early detection remains the most promising approach to improving long-term survival of patients with gastric cancer. We previously performed Serial Analysis of Gene Expression (SAGE) on 4 primary gastric cancers and identified several gastric cancer-specific genes including Reg IV and olfactomedin 4. We assessed serum Reg IV and olfactomedin 4 levels in gastric cancer patients by enzyme-linked immunosorbent assay (ELISA). In patients with stage I gastric cancer, the sensitivity of serum Reg IV (35%) and olfactomedin 4 (25%) was superior to that of CEA (3%) or CA19-9 (5%). Furthermore, in patients with stage I gastric cancer, the combination of Reg IV and olfactomedin 4 elevated the diagnostic sensitivity to 52%. These results suggest that serum olfactomedin 4 in combination with Reg IV has utility in the early detection of gastric cancer.

2. Market & Needs

Gastric cancer is the most common malignancies worldwide, with 870,000 new cases every year. Mortality from gastric cancer is second only to lung cancer. Patients with gastric cancer are often diagnosed with advanced disease and five-year survival rates are poor, usually less than 30%. Therefore, early detection is the most promising approach to improving long-term survival of patients with gastric cancer. Assessment of tumor markers in serum is useful for early detection of gastric cancer.

3. Issues of current technology

There are 2 available tumor markers for gastric cancer, carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9 (CA19-9). However, only 11 to 50% of patients with gastric cancer are positive for serum CEA before surgery, and 16–35% are positive for CA19-9. Moreover, CEA and CA19-9 are not suitable for early screening because preoperative positivity for these markers depends on the tumor stage at the time of detection.

4. Outline of technology

Serum olfactomedin 4 in combination with Reg IV has utility in the early detection of gastric cancer. We show the results of measurement of serum Reg IV and olfactomedin 4 levels in gastric cancer patients by enzyme-linked immunosorbent assay (ELISA).

Detection of Reg IV protein in serum samples by ELISA. A high concentration (1000 ng/mL) of Reg IV was detected in 22 serum samples from patients with gastric cancer. The sensitivity and specificity of Reg IV for detection of gastric cancer were 37% and 97%, respectively.

* Yellow bar indicates the cutoff levels defined in this study. Red bars indicate the means +/- SE. Differences in the serum concentration of Reg IV between two groups were tested by nonparametric Mann–Whitney U-test.
Detection of olfactomedin 4 protein in serum samples by ELISA. A high concentration (44.3 ng/mL) of olfactomedin 4 was detected in 38 serum samples from patients with gastric cancer. The sensitivity and specificity for detection of gastric cancer were 31% and 95%, respectively.

* Yellow bar indicates the cutoff levels defined in this study. Red bars indicate the means +/- SE. Differences in the serum concentration of olfactomedin 4 between two groups were tested by nonparametric Mann–Whitney U-test.

Immunostaining of olfactomedin 4 in primary gastric cancer tissue samples. Strong and extensive olfactomedin 4 staining (brown) was observed in Cases 38, which also showed high concentrations of olfactomedin 4 in serum samples by ELISA.

The specificities and sensitivities of serum olfactomedin 4 combined with Reg IV with respect to tumor stage.

<table>
<thead>
<tr>
<th>Stage</th>
<th>olfactomedin 4 (n)</th>
<th>Reg IV</th>
<th>olfactomedin 4 in combination with Reg IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I</td>
<td>(n = 60)</td>
<td>25%</td>
<td>35%</td>
</tr>
<tr>
<td>Stage II</td>
<td>(n = 8)</td>
<td>63%</td>
<td>50%</td>
</tr>
<tr>
<td>Stage III</td>
<td>(n = 15)</td>
<td>40%</td>
<td>53%</td>
</tr>
<tr>
<td>Stage IV</td>
<td>(n = 40)</td>
<td>30%</td>
<td>33%</td>
</tr>
<tr>
<td>Specificity</td>
<td></td>
<td>95%</td>
<td>97%</td>
</tr>
</tbody>
</table>

5. Difference from currently available technology

There are 2 available tumor markers for gastric cancer, carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9 (CA19-9). We measured serum CEA and CA19-9 levels in gastric cancer patients by enzyme-linked immunosorbent assay (ELISA). In stage I gastric cancer, the sensitivities for detection of gastric cancer were 3% and 5%, respectively. Therefore, serum olfactomedin 4 combined with Reg IV is suitable for early screening for gastric cancer detection.

6. Current state of technology

Patent pending JP 2008-005023

7. Collaboration opportunities

Collaborative research, Research funds

8. Reference


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