Expression and significance of matrix metalloproteinases and their tissue inhibitors in the infiltration and metastasis of lung cancer  WANG Xinyun, YANG Jiahong, MA Ying, ZHENG Haigen, CHENG Bo, ZHENG Hongwei, ZHU Congzhong. Department of Pathology, Tianjin Medical University, Tianjin 300070, P. R. China

【Abstract】Objective To determine the expression of matrix metalloproteinases (MMPs) and tissue inhibitors of metalloproteinases (TIMPs) in lung cancer specimens, and to find out the possible roles of MMPs and TIMPs in the infiltration and metastasis of lung cancer. Methods The expression of MMP-1, MMP-2, MMP-9, MMP-13, TIMP-1, TIMP-2 were detected in 104 lung cancer tissues by immunohistochemical method. Results The expressions of MMPs and TIMPs were up-regulated in lung cancer tissues. The expression of MMP-2 was related to differentiated degree of tumor cells. MMP-9 correlated with lymph node metastasis of lung cancer. The positive rate of TIMP-1 was related to TNM stage and lymph node metastasis. In lung cancer tissues, there was positive correlation between MMP-2 and TIMP-2, and between MMP-9 and TIMP-2. Conclusion MMPs and TIMPs may play the important roles in the development of lung cancer. MMP-9 and TIMP-1 might promote the infiltration and metastasis of lung cancer.

【Key words】Lung neoplasms  Matrix metalloproteinases  Tissue inhibitors of matrix metalloproteinases

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\[ \text{MMPs} \] \[ \text{TIMPs} \] \[ \text{MMPs} \] \[ \text{TIMPs} \] \[ \text{MMPs} \] \[ \text{TIMPs} \] \[ \text{MMPs} \] \[ \text{TIMPs} \]
1

1.1 1994～1999 104 72 32 27～79 57.76
1999 (WHO)

1.2 10% 5 μm 80 C 3 h

SABC-DS 0.01% PBS

SABC-AP, BCIP/NBT AEC, AEC

SP, SABC-DS, SABC-AP, SABC-POD

(BCIP/NBT) 60 min

AEC 10～30 min

1.3 (1,2) 4 100 10～20% 10%～40% (+), 41～70% (++), >70% (+++)

1.4 MMPs TIMPs χ² Fisher Spearman

Fig 1 Immunohistochemical staining of MMP-2 protein was located in cytoplasm and cell membrane of pulmonary adenocarcinoma with moderate differentiation SP method × 400

Fig 2 Immunohistochemical staining of TIMP-2 protein was located in cytoplasm and cell membrane of pulmonary squamous cell carcinoma with poor differentiation SP method × 400

<p>| Tab 1 MMPs expression in lung cancer tissues |</p>
<table>
<thead>
<tr>
<th>Degree</th>
<th>MMP-1 (%)</th>
<th>MMP-2 (%)</th>
<th>MMP-9 (%)</th>
<th>MMP-13 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>−</td>
<td>19(18.5)</td>
<td>24(23.1)</td>
<td>25(25.0)</td>
<td>48(46.2)</td>
</tr>
<tr>
<td>+</td>
<td>21(20.2)</td>
<td>14(13.5)</td>
<td>31(29.8)</td>
<td>29(27.9)</td>
</tr>
<tr>
<td>++</td>
<td>31(29.8)</td>
<td>23(22.1)</td>
<td>24(23.1)</td>
<td>19(18.3)</td>
</tr>
<tr>
<td>+++</td>
<td>33(31.7)</td>
<td>43(41.3)</td>
<td>23(22.1)</td>
<td>8(7.7)</td>
</tr>
</tbody>
</table>

Positive rate % 81.7 76.9 75.0 53.8
2.2 TIMPs

![Image]

2.3

![Image]

2.4

![Image]

2.5

![Image]

2.6

![Image]
Tab 6 Correlation of MMPs and TIMPs expressions with each other in lung cancer tissues

<table>
<thead>
<tr>
<th>Index</th>
<th>Correlation coefficient ($r_\text{s}$)</th>
<th>MMP-1</th>
<th>MMP-2</th>
<th>MMP-9</th>
<th>MMP-13</th>
<th>TIMP-1</th>
<th>TIMP-2</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMP-1</td>
<td>1.000</td>
<td>0.277</td>
<td>0.226</td>
<td>0.210</td>
<td>0.221</td>
<td>0.204</td>
<td></td>
</tr>
<tr>
<td>MMP-2</td>
<td>2.077</td>
<td>1.000</td>
<td>0.145</td>
<td>0.063</td>
<td>0.147</td>
<td>0.310</td>
<td></td>
</tr>
<tr>
<td>MMP-9</td>
<td>2.226</td>
<td>0.226</td>
<td>1.000</td>
<td>0.049</td>
<td>0.236</td>
<td>0.330</td>
<td></td>
</tr>
<tr>
<td>MMP-13</td>
<td>2.210</td>
<td>0.210</td>
<td>0.063</td>
<td>1.000</td>
<td>0.149</td>
<td>0.107</td>
<td></td>
</tr>
<tr>
<td>TIMP-1</td>
<td>2.221</td>
<td>0.221</td>
<td>0.147</td>
<td>0.236</td>
<td>1.000</td>
<td>0.397</td>
<td></td>
</tr>
<tr>
<td>TIMP-2</td>
<td>2.024</td>
<td>0.204</td>
<td>0.310</td>
<td>0.330</td>
<td>0.107</td>
<td>1.000</td>
<td></td>
</tr>
</tbody>
</table>

3

MMPs, TIMPs, ECM

MMPs

TIMPs

ECM

BM

V

N

(MMP-2, MMP-9)

MMP-2 (76.9%), MMP-9 (75.0%)

MMP-1 (81.7%)

MMP-2 (76.9%)

MMP-9 (75.0%)

MMP-1 (81.7%)

MMP-2, MMP-9

TIMPs

MMPs

TIMPs

ECM

Hofmann

MMP-2

TIMP-2

MMPs

TIMPs

MMP-2

TIMP-1

MMPs

TIMPs

MMP-2

TIMP-1

MMPs

TIMPs

MMP-2

TIMP-1

MMPs

TIMPs

MMP-2

TIMP-1

MMPs

TIMPs

MMP-2

TIMP-1

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TIMP-1

MMPs

TIMPs

MMP-2

TIMP-1

MMPs

TIMPs

MMP-2

TIMP-1

MMPs

TIMPs

MMP-2

TIMP-1

MMPs

TIMPs

MMP-2

TIMP-1

MMPs

TIMPs

MMP-2

TIMP-1