Letters to the Editor


Letter

In a recent study, Biemer-Huttmann et al. (1) reported that the expression of both MUC2 and MUC5AC mucins is significantly associated with sporadic colorectal carcinomas with MSI-H.1 Because the coexpression of both MUC2 and MUC5AC was observed in 68% of a series of 22 MSI-H cancers and this mucin expression pattern is identical to that observed in serrated polyps of the colorectum (2), the authors hypothesize that serrated polyps may represent precursors of MSI-H cancers (1).

The data reported by Biemer-Huttmann et al. (1) are in accordance with our own results on sporadic gastric carcinomas that show a significantly higher frequency of MUC5AC expression in carcinomas with the MSI-H phenotype (Table 1). In our series, 56.8% of the cases expressing MUC5AC are of the MSI-H phenotype, whereas only 22.2% of the cases with no expression of MUC5AC display the MSI-H phenotype (Table 1). A similar association was observed between MUC5AC expression and the presence of instability for tetranucleotide STR markers (Table 2). No relationship between MUC2 expression and the MSI-H phenotype or instability for tetranucleotide STR markers was observed in our series of gastric carcinoma (Tables 1 and 2).

In previous studies, our group has shown that MSI is associated with gastric carcinomas of the intestinal/atypical subtypes (3). At variance with this, expression of MUC5AC was predominantly observed in diffuse gastric carcinomas (4), and MUC2 expression was predominantly observed in mucinous gastric carcinomas (5). The results we have obtained recently identify a subgroup of carcinomas that shows high levels of instability for different markers (3, 6) and maintains a gastric type differentiation with MUC5AC expression.

Together with the results of Biemer-Huttmann et al. (1) on colorectal cancer, our data on gastric cancer suggest that there is a consistent parallel between genetic instability and MUC5AC expression. This is particularly interesting in colorectal tumours because MUC5AC is not expressed in the normal colon mucosa. Further studies should be undertaken to clarify the mechanisms underlying the widespread association of MUC5AC and MSI in tumors of the digestive tract.

Table 1

<table>
<thead>
<tr>
<th>Microsatellite instability</th>
<th>MUC2 expression (n = 33)</th>
<th>MUC5AC expression (n = 46)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MSI-H</td>
<td>Positive n (%)</td>
<td>Positive n (%)</td>
</tr>
<tr>
<td></td>
<td>9 (52.9)%</td>
<td>21 (56.8)%</td>
</tr>
<tr>
<td>MSI-L</td>
<td>2 (11.8)</td>
<td>8 (21.6)%</td>
</tr>
<tr>
<td>MSS</td>
<td>6 (35.3)</td>
<td>8 (21.6)%</td>
</tr>
<tr>
<td>Total</td>
<td>17 (100)</td>
<td>37 (100)%</td>
</tr>
</tbody>
</table>

1 P = not significant.
2 P = 0.0048. Microsatellite instability: high (MSI-H); low (MSI-L); no MSI, microsatellite stable (MSS).

Table 2

<table>
<thead>
<tr>
<th>Tetranucleotide instability</th>
<th>MUC2 expression (n = 41)</th>
<th>MUC5AC expression (n = 64)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive n (%)</td>
<td>Negative n (%)</td>
<td>Positive n (%)</td>
</tr>
<tr>
<td>Present</td>
<td>11 (47.8)%</td>
<td>23 (54.8)%</td>
</tr>
<tr>
<td>Absent</td>
<td>12 (52.2)</td>
<td>19 (45.2)%</td>
</tr>
<tr>
<td>Total</td>
<td>23 (100)</td>
<td>42 (100)%</td>
</tr>
</tbody>
</table>

1 P = not significant.
2 P = 0.00141.

References

5. Reis, C. A., David, L., Carvalho, F., Mandel, U., de Bolós, C., Mirgorodskaya, K., Clausen, H., and Sobrinho-Simões, M. Immunohistochemical study of the expression of MUC6 mucin and coexpression of other secreted mucins (MUC5AC and MUC2) in...
The finding that MUC5AC expression is associated with MSI-H cancer in stomach as well as colon is intriguing. However, the proposed serrated pathway to MSI-H cancer in the colon lacks a well-defined counterpart in the stomach. Therefore, a shared mechanism may not necessarily apply but is certainly worthy of further investigation. Our recent experience with hyperplastic polyposis of the colorectum reinforces the suggested role for hyperplastic polyps and serrated adenomas in the histogenesis of sporadic MSI-H colorectal cancer (1). By contrast, colorectal cancers developing in subjects with hereditary nonpolyposis colorectal carcinoma arise in traditional adenomas (2) and show a relative lack of mucinous differentiation and expression of MUC5AC. This invites further caution in considering mechanisms that could link MUC5AC expression with DNA microsatellite status.

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References

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1 The abbreviation used is: MSI-H, high level(s) of microsatellite instability.

2 Unpublished personal observations.
Reply
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