Regulatory Effects of Gastrin and Secretin on Carcinomas of the Stomach and Colon

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Gastrin has been established as an important trophic hormone for various normal gastrointestinal tissues and it stimulates the growth of normal digestive tract epithelia (Johnson 1977). This study was designed to elucidate whether gastrin affects the metabolism and growth of human carcinomas having arisen from the gastrointestinal mucosa.

Protein synthesis. Stomach carcinomas obtained at surgery and colon carcinomas transplanted serially into nude mice were minced into small pieces in culture medium containing a leucine-free Eagle's medium, 10% fetal calf serum, penicillin (100U/ml), kanamycin (100 µg/ml) and 14C-labelled leucine (5 µCi/ml) with or without tetragastrin (10 µg/ml), and were incubated at 37°C for 6 hr. The tumor tissues and the media were separated by centrifugation. 14C-labelled protein produced in medium and the incorporation of 14C-leucine into the tumor tissues were determined in a liquid scintillation system.

Assessment of tumor growth. Two stomach and 3 colon carcinomas transplanted serially into nude mice were inoculated into the subcutaneous tissue of the backs. Administrated hormones were pentagastrin (250 µg/kg), secretin (100U/kg), a combination of pentagastrin and secretin in the same doses mentioned above, and 0.1 ml of saline was given to a control. Tumor size was measured twice a week for 4-5 weeks. The formula

\[ \text{Weight} = \frac{\text{length} \times \text{width}^2}{2} \]

was used. The weight doubling time of the tumor was calculated at a logarithmic phase of the tumor growth curve.

In 5 of 17 stomach carcinomas, gastrin enhanced 14C-leucine uptake into the tumor.
Fig. 1. In vivo stimulation of amino acid incorporation and protein production in human stomach carcinomas by gastrin. Values are expressed as percentages of control values.
○, amino acid incorporation; ●, protein production.

Table 1. Tumor weight doubling time of transplanted carcinomas in nude mice treated with gastrointestinal hormones (days)

<table>
<thead>
<tr>
<th></th>
<th>Pentagastrin</th>
<th>Secretin</th>
<th>Pentagastrin + secretin</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stomach</td>
<td>AST-1 (n = 9)</td>
<td>4.1** ± 0.64</td>
<td>5.0* ± 0.53</td>
<td>5.0 ± 0.91</td>
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<td></td>
<td>AST-7 (n = 5)</td>
<td>5.5 ± 0.42</td>
<td>5.3 ± 0.46</td>
<td>6.9 ± 0.47</td>
</tr>
<tr>
<td>Colon</td>
<td>ACL-1 (n = 7)</td>
<td>4.4** ± 0.26</td>
<td>5.0* ± 0.26</td>
<td>6.4 ± 0.27</td>
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<tr>
<td></td>
<td>ACL-5 (n = 6)</td>
<td>5.3 ± 0.53</td>
<td>5.5 ± 0.24</td>
<td>5.0 ± 0.29</td>
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<tr>
<td></td>
<td>ACL-6 (n = 8)</td>
<td>5.2 ± 0.53</td>
<td>4.6 ± 0.31</td>
<td>5.3 ± 0.23</td>
</tr>
</tbody>
</table>

Values are means ± s.e.
* p less than 0.05 compared with control; ** p less than 0.01 compared with control.

In 4 of 13 stomach carcinomas, gastrin increased the production of 14C-labelled protein. All of the cases in which protein synthesis was enhanced by gastrin were histologically poorly differentiated adenocarcinoma (Fig. 1). Gastrin also enhanced the protein synthesis of 2 colon carcinomas. One of 2 stomach and one of 3 colon carcinomas were enhanced in growth by gastrin. The weight doubling time was significantly shortened by pentagastrin. On the other hand, secretin inhibited the trophic action of pentagastrin (Table 1).

These data presented here indicate that the metabolism and growth of carcinomas having arisen from gastrointestinal mucosa are regulated in part by gastrin and/or secretin. Gastrointestinal hormone therapy might be useful for the treatment of some gastrointestinal carcinomas.

Reference