Influence of Sarcoma 180 on Adenocarcinoma 755 in the Mouse*

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The growth rates of tumors, although influenced in part by local vascular conditions, appear to depend on the genetic endowments and the metabolic states of both the tumor and the host. There is abundant evidence which indicates that the host-tumor relationship embraces more than local phenomena, and that, in addition to competition for metabolites, both tumor and host exert reciprocal influences on each other. The generalized effects of tumors of endocrine glands which elaborate hormonal substances, particularly those of pituitary, adrenal, and pancreatic islets, are well known. The possibility that tumors of an apparently nonendocrine nature may also produce systemic effects remains to be explored. It is not improbable that some of the determinant properties of malignancy are to be found in the systemic effects of tumors as well as in their local cellular pattern. As a corollary to this, various tumors will affect a host in different ways, possibly antithetical, and two different tumors in the same host might well affect each other.

This paper reports observations on the growth of both Carcinoma 755 and Sarcoma 180 in the same host. Sarcoma 180 is insensitive as to host strain, growing readily in all stocks of mice. Adenocarcinoma 755 is strain-fixed to C57 black mice. The differences between these two tumor types are demonstrated also by their individual responses to 8-azaguanine, which is markedly inhibitory to Carcinoma 755, but wholly without effect on Sarcoma 180 (2).

EXPERIMENTAL

Approximately 300 mice, 4-5 months of age, both male and female, of the C57 strain inbred in these laboratories for many generations, were used in these experiments. Animals in a single experiment received simultaneous (by trocar) implants of approximately equivalent fragments from a single freshly dissected tumor free of necrosis. Carcinoma 755 was implanted in the right axilla, and, 12-15 days later, Sarcoma 180 was implanted in the left axilla. Additional control animals received implants of only one of the tumors. The animals were killed 7-10 days after the last implantation and the freshly dissected tumors weighed individually. The timing of operations is especially important because of the rapid rate of growth of Sarcoma 180 as compared to that of Carcinoma 755. In order to observe the activity of the drug in a situation where both a susceptible and a resistant tumor were present, half the animals in one experiment were treated with 8-azaguanine, 2 mg/day, from the time of the second implantation to the conclusion of the experiment.

The tumor weights from the several experiments cannot be compared to one another, since the experiments were carried out at different times and with different donor tumors. The sex differences from one experiment to another have no significance, it having been observed previously that each of the tumors grew equally in both sexes after implantation from the same batch of donor tumor.

DISCUSSION

The tumor weights in the several experiments (Table 1) consistently show that Sarcoma 180 inhibits the growth of Carcinoma 755. Conversely, the growth of Sarcoma 180 appears to be enhanced by the co-existence of Carcinoma 755. This apparent stimulatory effect of the carcinoma on the sarcoma is not abolished by treatment with 8-azaguanine, indicating that it does not involve the mechanism susceptible to interference by azaguanine. On the other hand, the inhibitory effects of Sarcoma 180 and of 8-azaguanine on Carcinoma 755 are additive. 8-Azaguanine did not affect Sarcoma 180 even in the mice in which Carcinoma 755 was also present.

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That the growth rate of Carcinoma 755 is not limited by the capacity of the host reservoir to supply essential nutrients had been previously demonstrated by the finding that the same host can support at least three implants of Carcinoma 755 at different sites, the individual tumors growing at the same rate as corresponding singly implanted controls.

The data suggest the possibility that Sarcoma 180 elaborates a substance to which Carcinoma 755 is sensitive; conversely, Carcinoma 755 might elaborate a substance beneficial to Sarcoma 180 or alter the host so as to favor the growth of Sarcoma 180. That the proliferative influences which are accelerated in regenerating liver are blood-borne has been demonstrated by Bucher, Scott, and Aub (1). Whether or not the sarcoma-stimulatory effect of Carcinoma 755 is of a similar nature is yet to be explored. Whatever the course of events, these findings provide further evidence of the fundamental biological differences between the two tumors and illustrate again the humoral or systemic factors in neoplastic processes.

The histology of the visceral organs of the experimental animals is under study and will be reported elsewhere.

SUMMARY

Two different experimental tumors, adeno-carcinoma 755 and Sarcoma 180, have been grown in the same host and some of their reciprocal effects observed.

Sarcoma 180 appears to inhibit the growth of Carcinoma 755, but Carcinoma 755 enhances the growth rate of Sarcoma 180.

### TABLE 1

**Influence of Sarcoma 180 on Carcinoma 755**

<table>
<thead>
<tr>
<th>No.</th>
<th>Tumor</th>
<th>Sex</th>
<th>No. of mice</th>
<th>Weight of Sarcoma 180 (gm.)</th>
<th>Weight of Carcinoma 755 (gm.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>180</td>
<td>F</td>
<td>20</td>
<td>0.999 ± 0.245</td>
<td>1.599 ± 0.339</td>
</tr>
<tr>
<td></td>
<td>755</td>
<td>F</td>
<td>20</td>
<td>1.539 ± 0.290</td>
<td>0.668 ± 0.307</td>
</tr>
<tr>
<td></td>
<td>180/755</td>
<td>M</td>
<td>20</td>
<td>1.782 ± 0.217</td>
<td>0.550 ± 0.444</td>
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<tr>
<td>II</td>
<td>180</td>
<td>M</td>
<td>20</td>
<td>0.985 ± 0.185</td>
<td>1.416 ± 0.325</td>
</tr>
<tr>
<td></td>
<td>755</td>
<td>M</td>
<td>19</td>
<td>1.463 ± 0.286</td>
<td>0.498 ± 0.270</td>
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<tr>
<td></td>
<td>180/755</td>
<td>M</td>
<td>20</td>
<td>1.398 ± 0.215</td>
<td>0.490 ± 0.220</td>
</tr>
<tr>
<td>III</td>
<td>180</td>
<td>F</td>
<td>17</td>
<td>0.876 ± 0.305</td>
<td>0.763 ± 0.390</td>
</tr>
<tr>
<td></td>
<td>755</td>
<td>F</td>
<td>17</td>
<td>1.398 ± 0.215</td>
<td>0.400 ± 0.220</td>
</tr>
<tr>
<td></td>
<td>180/755</td>
<td>M</td>
<td>20</td>
<td>0.800 ± 0.225</td>
<td>1.638 ± 0.118</td>
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<tr>
<td>IV</td>
<td>180</td>
<td>M</td>
<td>20</td>
<td>0.818 ± 0.182</td>
<td>1.080 ± 0.160</td>
</tr>
<tr>
<td></td>
<td>755</td>
<td>M</td>
<td>10</td>
<td>1.400 ± 0.325</td>
<td>0.951 ± 0.160</td>
</tr>
<tr>
<td></td>
<td>180/755</td>
<td>M</td>
<td>8</td>
<td>1.265 ± 0.259</td>
<td>0.327 ± 0.165</td>
</tr>
</tbody>
</table>

* Treated with 8-azaguanine.

REFERENCES

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