Brief Communication

Immunology of the Mouse Mammary Tumor Virus (MTV): Neutralization of MTV by Mouse Antiserum

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The antigenicity of the mouse mammary tumor virus (MTV) in species other than the mouse has been recognized for many years; antisera from rabbits, rats, and guinea pigs immunized with MTV-containing tissue extracts are capable of neutralizing the biologic activity of the virus (1, 2, 3, 6, 9). More recently, it has been demonstrated that MTV is also immunogenic in the mouse; antisera from immunized mice react with MTV antigen in immunodiffusion to produce a precipitate line specific for MTV (5, 11). The present communication reports that mouse antiserum is also capable of neutralizing the biologic activity of MTV.

MTV antigen for immunization of the mice was prepared by centrifugation of MTV in a sucrose density gradient, as previously described (7, 8). The source of virus was milk obtained from BALB/c CrGl mice that had been fostered on DBA/2 CrGl mice, and therefore were infected with the MTV carried by that strain.

Each of five I BiCrGl adult female mice received an intraperitoneal injection of saline containing the MTV derived from 0.01 ml milk on Days 1, 4, 8, and 22. The mice were bled 2 weeks after the last injection, and their sera were pooled and frozen in a commercial refrigerator. The pooled serum contained antibodies against MTV, as measured by the development of the precipitate line specific for MTV, when it was tested in immunodiffusion against MTV antigen (5).

Normal mouse serum for control purposes was obtained from normal adult BALB/c male mice. Serum from several donors was pooled and frozen until needed.

Biologically active MTV for the neutralization experiment was prepared from an extract of BALB/c CrGl lactating mammary gland tissue by sedimentation in the ultracentrifuge, as previously described (3).

The neutralization procedure was carried out in vitro at room temperature (3, 6). Equal amounts of undiluted mouse serum and saline, or saline alone, were combined in test tubes with the virus preparation so that 1 ml of solution contained MTV from 0.05 gm of lactating gland tissue. After 2 hours, 0.2-ml quantities were injected intraperitoneally into each test mouse. Each mouse thus received the amount of MTV contained in 0.01 gm (wet weight) of mammary tissue. The test mice were 4-week-old BALB/c females.

The efficacy of the neutralization was measured by the noduligenic assay for MTV (10), which involves hormonal stimulation of hyperplastic alveolar nodule development in the mammary glands of mice injected with MTV. Beginning at 8 weeks of age, the test mice received daily injections for 13 weeks of 1 μg estradiol 17β plus 500 mg deoxycorticosterone acetate. Five weeks after the last injection, the mice were killed and their mammary glands were removed and stained in whole mount preparations (6). The glands were then examined for the presence of hyperplastic nodules as indication of the biologic activity of the injected MTV.

MTV was neutralized by treatment with the antiserum obtained from immunized mice (Table 1). None of the 10 females injected with MTV combined with this antiserum developed nodules during the hormonal stimulation, whereas nodules did develop in 7 of 10 females injected with MTV in saline alone and in 7 of 9 females injected with MTV combined with normal mouse serum.

Attempts to detect specific immunologic responsiveness in the mouse against MTV were unsuccessful until recently (4). The present demonstration that mouse antibodies can neutralize the biologic activity of MTV seems to establish firmly that the mouse is, indeed, capable of developing a specific immune response against this virus. The immunogenicity of this virus can now be detected in animals of its natural host species by the resistance of immunized mice against transplants of MTV-

<table>
<thead>
<tr>
<th>BALB/c mice injected i.p. with MTV suspended in</th>
<th>No. of mice</th>
<th>No. of mice with nodules</th>
<th>Average no. of nodules per nodule-bearing mouse</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saline</td>
<td>10</td>
<td>7</td>
<td>5.9</td>
</tr>
<tr>
<td>Normal mouse serum</td>
<td>9</td>
<td>7</td>
<td>7.1</td>
</tr>
<tr>
<td>Immune mouse serum</td>
<td>10</td>
<td>0</td>
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Development of hyperplastic alveolar nodules in mice given injections of biologically active MTV suspended in saline or in mouse serum.

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infected mammary tissue (12), and also by the presence in the sera of immunized animals of specific antibodies capable both of precipitating the virus in immunodiffusion systems and of neutralizing its biologic activity.

REFERENCES

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