Stimulating Effect of Mouse Sarcoma Virus on the Multiplication of Newcastle Disease Virus

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Chany & Robbe-Maridor (1968) have reported that the multiplication of murine hepatitis virus was stimulated in tissue cultures infected with murine sarcoma virus, MOLONEY strain MSV (M) and suggested that this was caused by MSV (M) blocking the biological action of interferon. Hermodsson (1963) and Maeno et al. (1966) reported that some parainfluenza viruses enhance the multiplication of Newcastle disease virus (NDV) and that this effect must be due to a suppression of the production and antivirus action of interferon.

The present report describes the stimulating effect of MSV (M) on the multiplication of Newcastle disease virus (NDV), KANSAS strain, adapted to grow in mouse cells. Results suggest that this effect is related only to a decrease in the cellular sensitivity to the antivirus action of interferon.

Swiss mice embryo cells (SMEC) were grown in 30 ml. plastic tissue culture flasks, each seeded with 1.5×10⁶ cells. Half of these cultures were inoculated with about 1 f.f.u./cell of MSV (M). The remaining cultures were not infected. At 48 hr later the infected cells showed a general morphological conversion (Bernard et al. 1968) and the two series were inoculated with NDV at a multiplicity of about 10 embryo infectious doses (EID₅₀) per cell. After adsorption for 2 hr at 22 ° with occasional agitation, the infected monolayers were washed 3 times and overlaid with fresh medium. The cultures were incubated for 24 hr at 37 °. The flasks were then frozen and thawed three times in an alcohol-solid CO₂ mixture and their contents centrifuged at 3,500 g for 10 min. Supernatant fluids were stored at −80 ° until titrated for NDV by inoculation of 0.1 ml. of each dilution into the allantoic cavities of five eggs. After incubation at 37 ° for 2 days the allantoic fluid was collected from each egg and all samples were tested for haemagglutinating activity using 0.5 % chicken red blood cells in physiological saline. The 50 % embryo infectious dose (EID₅₀) was calculated by the method of Reed & Muench (1938).

From the results of 4 experiments (Table 1) it appears that about 100 times more NDV was produced in cultures previously inoculated with MSV (M) than in normal cultures, suggesting that MSV (M) blocks the action of the interferon produced by NDV. The results of further experiments supported this hypothesis. Cells infected by MSV (M), which does not induce interferon (J. Peries and M. Canivet, unpublished results) behaved like uninfected cells in the production of interferon when treated with u.v. inactivated NDV. Thus, when

<table>
<thead>
<tr>
<th>Experiment</th>
<th>Control cells</th>
<th>MSV (M) pre-infected cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.8</td>
<td>320</td>
</tr>
<tr>
<td>2</td>
<td>3.2</td>
<td>320</td>
</tr>
<tr>
<td>3</td>
<td>3.2</td>
<td>180</td>
</tr>
<tr>
<td>4</td>
<td>5.6</td>
<td>560</td>
</tr>
</tbody>
</table>

Table 1. Stimulation by MSV (M) of NDV yield from mouse embryo cells
Short communications

SMEC were inoculated with MSV (M) and treated with u.v. inactivated NDV, interferon production was the same as that in uninfected cells used as controls. The interferon activity in the supernatant fluids of both types of culture showed titres of about 1/40 to 1/80. In view of the twofold uncertainty of the assay method, this difference is not significant.

On the other hand, cells inoculated with MSV (M) and treated with irradiated NDV were not protected against the cytopathogenic effect of vesicular stomatitis virus (VSV, INDIANA strain). In these experiments SMEC cultures were prepared in small test tubes and treated with MSV (M) and NDV as in cultures prepared to demonstrate the stimulating effect of MSV (M) on the multiplication of NDV. The supernatant fluids from all cultures were harvested and tested for interferon; cells were challenged with 250 CEPI 90 of vesicular stomatitis virus (VSV). As noted in previous experiments, interferon was present at the same activity in the supernatant fluids of MSV (M) pre-inoculated cultures as in those of cells treated only with NDV. Despite this fact, the latter cells were protected against the cytopathic effect of VSV whereas the former were destroyed entirely by the challenge virus.

Thus the mechanism of interferon induction seems to be unhindered by the presence of MSV (M) despite inhibition of the antivirus effect of interferon. It is possible therefore that MSV (M) interferes with the mechanism of action of interferon and thereby improves the infective yield of NDV.

Laboratory of Experimental Haematology
Institut de Recherches sur les Leucémies
Hôpital Saint-Louis
Paris-10ème.

REFERENCES

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