Host Cell Species Specificity of Mouse and Chicken Interferons

Abstract. *Three thousand units of mouse interferon and 2000 units of chicken interferon were assayed on the respective heterologous species cell cultures. No antiviral activity was observed in the heterologous systems, suggesting a virtually complete species barrier to the action of these interferons.*

Following the original observation that interferon exerted greatest antiviral action in cells of the homologous species (*1*), it was reported that interferon may exert a substantial antiviral effect in heterologous cells (*2*). In our laboratory, 50 to 100 units of mouse, chicken, or guinea pig interferons were observed to be completely species specific (*3*). With the availablity of high potency mouse interferon (*4*) and the ability to concentrate chicken interferon, it became feasible to test large amounts of interferon on heterologous cells.

Mouse serum interferon was prepared by the intravenous injection of undiluted Newcastle disease virus, followed by exsanguination 6 hours later and maintenance of the serum at *p*H 2 for at least 4 days. The titers of interferon in mouse serums were 20,000 to 50,000 units per 3 ml. Interferon titers were expressed as the reciprocal of the greatest dilution which caused 50 percent reduction of vesicular stomatitis virus plaques (plaque-forming units) on primary chicken embryo or mouse embryo cell cultures (*4*).

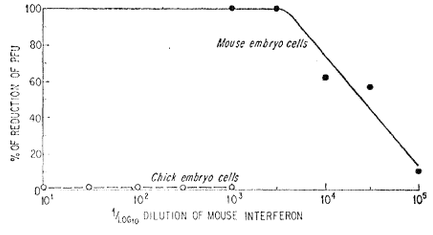

Fig. 1. Antiviral activity of mouse interferon on mouse and chicken embryo cell cultures. (PFU, plaque-forming units.)

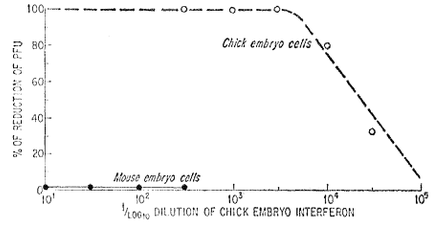

Fig. 2. Antiviral activity of chicken interferon on chicken and mouse embryo cell cultures. (PFU, plaque-forming units.)

Chicken interferon was prepared by allantoic infection of 11-day embryonated eggs with the neurotropic WS strain of influenza A virus. Allantoic fluids were harvested after 2 days and treated with 0.15*M* perchloric acid (*5*). After centrifugation the supernatant was neutralized with 1*N* sodium hydroxide, and then ammonium sulphate was added to 40 percent saturation. The resulting supernatant contained the interferon activity which was precipitated by the addition of ammonium sulphate to 60 percent saturation. The active precipitate was dialyzed against distilled water, and concentrated with Aquacide II (*6*). The concentrate was finally dialyzed against Eagle's medium without serum before assaying. The final titer, which was 20,000 units per 3 ml, was 150 times the concentration of the original material.

The chicken and mouse interferons (50 units/3 ml) were characterized by their activity against heterologous virus, by inactivation with crystalline trypsin, by their capacity to remain in suspension when centrifuged at 105,000*g* for at least 2 hours, and by their stability at *p*H 2. The possibility of residual infectious virus in the undiluted interferons was eliminated by the fact that interferons digested by trypsin showed no infectivity for embryonated eggs.

The mouse and chicken interferons were assayed for antiviral activity on both mouse and chicken embryo cell cultures. As indicated in Figs. 1 and 2, no antiviral activity of interferon was detected on heterologous cells when as much as 3000 units of mouse interferon and 2000 units of chicken (1/10 dilution) were employed. In other experiments similar results were obtained after the interferons were treated with as much as 1000 hemagglutination inhibition units of the appropriate rabbit antiviral antibody, indicating the absence of interfering virus at the highest concentrations of interferon. Merigan has independently observed similar species specificity when using as much as 1000 units of chicken and mouse interferon in heterologous cell cultures (*7*).

Our results suggest an almost complete barrier to the antiviral action of chicken and mouse interferons in the heterologous cells in vitro. The difference between these results and previous reports of activity of interferon in heterologous mouse or chicken cells is probably not due to different interferons produced by the same species. In our laboratory, interferons induced by Chikungunya, Sindbis, and vaccinia viruses in chicken and mouse cell cultures exhibited appropriate species specificity when 20 to 100 units of interferon were used. Since the genetic information for interferon is believed to reside in the host cell genome (*8*), it is not surprising that interferons induced by various viruses manifest species specificity. This holds true even when encephalomyocarditis virus is used as the challenge virus in the mouse cell culture assay system. Perhaps some of the cross reacting interferon preparations contained an additional antiviral component which was not interferon (for example, interfering virus and cell receptors). It has been reported, however, that at least one interferon may cross a particular species barrier. Rhesus monkey interferon has been observed in several laboratories to have some activity on human cells (*9*). In agreement with these observations preliminary experiments indicate that mouse interferon can exert a small fraction of its activity on hamster or rat embryo cell cultures.

The virtually complete species barrier between mouse and chicken interferons suggests that this striking property should be more generally applied for characterizing interferons.

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References and Notes

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25 May 1964