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A number of studies of HLA expression after IFN treatment have been done by immunofluorescence analysis, using the fluorescence-activated cell sorter and the monoclonal antibody W6/32. As shown in figure 2, the accumulation of HLA surface protein increases steadily and roughly linearly for up to 6 days. By continuous sorting of cells with the highest content of HLA after the interferon treatment, we have derived a population of cells that show an enhanced response to interferon treatment relative to the original Molt 4 cells. From this population, a clone was isolated, and the time response to interferon treatment in comparison with the wild-type Molt 4 cells is also shown in figure 2. It can be seen that both curves start at the same point. The increases in the amount of HLA-A, B and C on the surface of the mutant clone is about twice the rate of wild-type Molt 4. The maximum value at 6 days in the mutant cells is about twice than in the wild-type cells.

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5. Analysis of antiviral state in RD114 and A204 cells after interferon treatment

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Interferon exerts antiviral and various non-antiviral activities on cells. For the development of the antiviral state in cells against exogenous infection of cytolytic viruses such as vesicular stomatitis virus and encephalomyocarditis virus (EMCV), induction of 2′–5′-oligo(A) synthetase or double-stranded (ds)-RNA-dependent protein kinase, or both, has been shown to have a crucial role (Revel 1979). However, in some cases, the antiviral effects of interferon are virus-specific (Nilsen *et al.* 1980; Samuel & Knutson 1981). Recently, different effects of mouse interferon on retrovirus production and on EMCV replication in a clonal cell line from NIH/3T3 cells were reported (Czarniecki *et al.* 1981). The inhibition of retrovirus production by interferon occurs at a late stage of virus growth before maturation and release of the virus from the cell surface (Friedman 1977; Billiau 1977). It may be correlated with some non-antiviral actions of interferon on cell membrane such as the inhibition of cell fusion induced by inactivated retrovirus (Tomita & Kuwata 1979) or Sendai virus (Tomita & Kuwata 1981). In the present study, we compared the effects of interferon on retrovirus and EMCV replication, and cell fusion in rhabdomyosarcoma cells chronically infected with retrovirus. Productions of [^{3}H]uridine-labelled retrovirus from HuIFN-α treated and untreated control cells were estimated by sucrose gradient centrifugation. As shown in figure 1, productions of baboon endogenous retrovirus (M7) from A204 cells and feline endogenous retrovirus (RD114) from RD114 and RD114-C1 cells (a subclone of RD114 cells) were in each case highly sensitive to the antiviral action of HuIFN-α. ^{3}H-labelled viruses released from interferon-treated A204 and

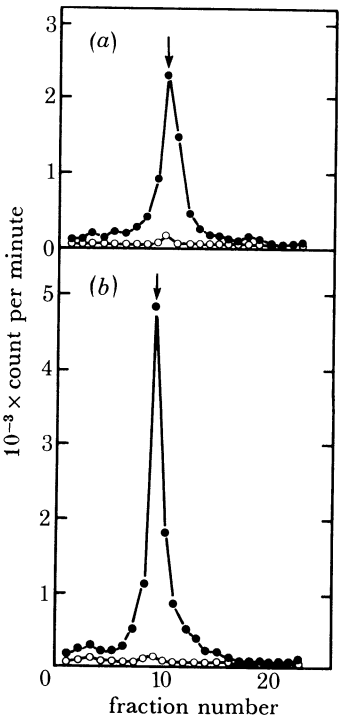

FIGURE 1. A204 (*a*) and RD114-C1 (*b*) cells were treated with HuIFN-α at 100 units ml^{-1} for 20 h, then washed twice with serum-free medium and cultured for 16 h in the presence of [^{3}H]uridine (15 μCi ml^{-1}) and HuIFN-α (100 units ml^{-1}). After partial clarification, the culture fluid was centrifuged on a linear gradient (150–600 g l^{-1}) of sucrose at 90000 *g* for 5 h. ●, Control; ○, HuIFN-α-treated cells. Arrows indicate the position of the density of 1.16 g ml^{-1}.

TABLE 1. ANTIVIRAL EFFECTS OF HuIFN-α AGAINST EMCV IN A204 AND RD114-C1 CELLS

cells	HuIFN-α ml^{-1}	EMCV (log t.c.i.d.$_{50}$/0.2 ml) virus yield	decrease
A204	0	6.3	—
	100	4.5	1.8
RD114-C1	0	7.3	—
	100	7.5	0

Cells were treated with HuIFN-α for 20 h, then challenged with EMCV at 1 t.c.i.d.$_{50}$ per cell. After 20 h, virus was harvested and the titres were determined by infecting VERO cells.

RD114-C1 cells were about 3.9 and 2.8 % of the control, respectively. Similar results were obtained by the assay of reverse transcriptase of released virus in the culture medium: namely, 100 units ml^{-1}† of HuIFN-α reduced retrovirus production to less than 10 % of control cells. However, replication of EMCV in RD114 and RD114-C1 cells was resistant compared with A204 cells (table 1). Both 2′–5′-oligo(A) synthetase and ds-RNA-dependent protein kinase, which were assayed according to the methods described by Minks *et al.* (1979) and Hovanessian & Rivière (1980), respectively, were examined in both A204 and RD114-C1 cells. In A204 cells,

† Units with reference to G-023-901-527 standard.

both 2′–5′-oligo(A) synthetase and protein kinase were markedly increased after HuIFN-α treatment but no significant increase of these enzyme activities was observed in RD114-C1 cells. On the other hand, in both A204 and RD114-C1 cells, a non-antiviral action of interferon, the inhibition of syncytium formations induced by u.v.-inactivated Sendai virus, was efficiently expressed by pre-treatment of cells with HuIFN-α at 100 units ml^{-1}. Furthermore, HuIFN-γ, kindly supplied by Dr K. Cantell, also showed these different effects on retrovirus production and EMCV replication in RD114-C1 cells. These results suggest that the mechanisms underlying the anti-retrovirus and the anti-cell fusion activities of interferon may be closely related, and that they are different from those of antiviral action against exogenous infection with EMCV.

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6. Interferon restriction of target organs for lymphocytic choriomeningitis virus-induced T lymphocytes may be lethal

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It is generally held that interferons play a role in recovery from acute primary viral infections. One of the most direct ways that this can be demonstrated is by use of anti-interferon serum. Rapid evolution of lethal disease in a number of murine infections (encephalomyocarditis, herpes simplex, Newcastle disease, Semliki Forest viruses) was observed when interferon liberated from virus-infected cells was neutralized by injection of anti-interferon serum. The neutralization suppressed the normal interferon effect, allowing unchecked dissemination of