

In selected experiments we titrated various ratios of effector to target cells. Figure 2 shows that interferon-mediated enhancement of CML activity at 39°C was more pronounced with high than with low ratios of effector to target cells. This was not so at 37°C. When the cultures were assayed for CML activity at different times after initiation, the peak of activity was always found at day 6, regardless of the temperature of incubation or the presence of interferon. Thus trivial kinetic differences can be excluded as the explanation of our operations.

The lymphoblastoid human B-cell line Daudi has been shown to be highly sensitive to the growth-inhibitory effect of interferon¹³. Daudi cells (given by H. Strander and J. Zeuthen) were cultured in microtitre plates using RPMI 1640 medium with antibiotics and 10% fetal calf serum as described elsewhere¹⁴. Interferon was added to the cells at the beginning of cell propagation, and proliferation was measured by the uptake of ¹⁴C-thymidine or by counting viable cells on days 3–4 (ref. 14). In this system growth inhibition is not due to cell killing because it is reversible¹⁴. The relative inhibition of growth

killer cells and increased inhibition of growth occur *in vivo*. If so, fever during virus infections would potentiate host defence mechanisms. The fact that (1) the defence against viral disease is particularly dependent on cell-mediated immunity, (2) viruses are particularly good interferon inducers and (3) interferon is produced *in vivo* at elevated temperature leads us to suggest that interferon besides its antiviral role, is a normal immunoregulatory molecule leading the immune response in a 'more' cell-mediated direction at elevated body temperature.

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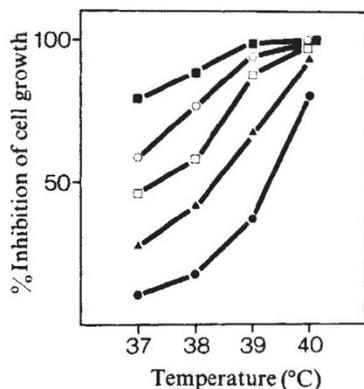


Fig. 3 Relative inhibitory effect of different interferon concentrations on the propagation of Daudi cells at different incubator temperatures. The results of quadruplicate cultures, each containing 2×10^4 Daudi cells in 0.2 ml of culture medium, with and without interferon in the doses were determined. DNA synthesis was quantified by addition of 0.02 μ Ci of ¹⁴C-thymidine per culture for the last 16 h of a 96-h culture period. Mean c.p.m. \pm s.d. of the control cultures without interferon at the four temperatures were 20,340 \pm 570, 26,890 \pm 450, 26,370 \pm 790 and 3,180 \pm 190, respectively. The inhibition of thymidine uptake by a certain interferon concentration at a certain temperature has been calculated in percentage of the control at that temperature. ●, 1 partially purified human leukocyte interferon per ml.; ▲, 2 U ml⁻¹; □, 3 U ml⁻¹; ○, 5 U ml⁻¹; ■, 10 U ml⁻¹.

obtained by different concentrations of interferon at four temperatures is shown in Fig. 3. A pronounced increase in the inhibitory activity was found with increasing temperatures.

Our experiments show that the antiviral and two non-antiviral properties of interferon are temperature-dependent, but at different levels.

The antiviral effect was not increased until 40°C was reached. Increase in temperature itself is known to inhibit viruses. This was overcome by adding more virus at the higher temperatures. The mechanisms by which interferon potentiates the alloreactive killer T-cells generated⁶ are unknown. Possibly interferon acts by inhibiting suppressor cells or by enhancing the expression of histocompatibility antigens on the cells¹⁵. The inhibition of the multiplication of Daudi cells (a B-cell line) might be analogous to the inhibitory effects of mouse interferon on B-cell functions *in vivo*⁵. We do not know whether a similar 'fever'-induced interferon-augmented generation of

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Errata

In the letter 'Electron microscopic location of protein thiol residues' by M. Stewart and V. Diakiw, *Nature* **274**, 184, line 21 in Fig. 3 legend should read: Tris-HCl, pH 8 at 4°C. Samples for electron microscopy were . . .

In the review article 'Handedness of atoms and parity non-conservation' by G. Feinberg, *Nature* **271**, 509, line 11 on page 510 should read: approximately $|\delta| \approx 10^{-11}$.

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