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7. Fatty acid desaturation–promoting factor (DPF) induced by interferon

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Interferon (IFN) induces changes in the saturation of the long-chain 18 carbon fatty acids (C_{18} fatty acids). After pulse treatment of human and bovine cells with HuIFN-α and with HuIFN-β there was a drastic but reversible increase in the saturation of the C_{18} fatty acids (Apostolov & Barker 1981). The increase in saturation peaked at 10–12 h and was followed by a

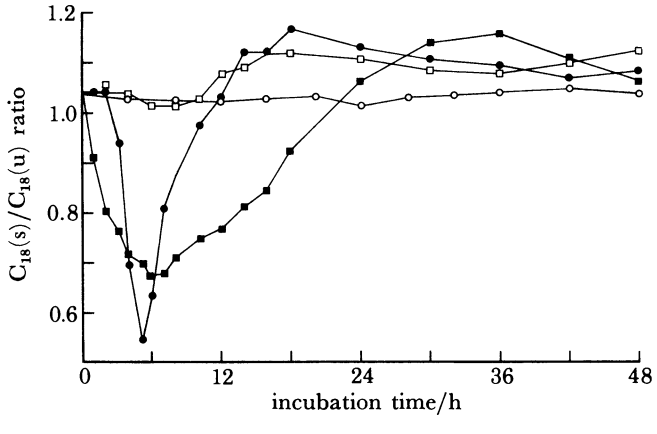

Figure 1. Desaturation-promoting factors: kinetic response. Baby hamster kidney (BHK/C13) and rabbit kidney (RK13) cells were pulse-treated with HuIFN-α (Ly) as previously described (Apostolov & Barker 1981), and the supernatants of these cells harvested 8 hours after this treatment. The supernatants were concentrated and partly purified by zinc acetate precipitation according to the method of Lampson *et al.* (1963) and used to treat BHK cells in the same manner as for IFN. The kinetic changes in the fatty acid profile of these cells were subsequently followed over a 48 h period. As the changes observed in the fatty acid profiles of the cells were concerned almost entirely with the C_{18} fatty acids, only these results are presented here, in the form of a ratio of fully saturated C_{18} to unsaturated C_{18} fatty acids ($C_{18}(s):C_{18}(u)$ ratio). ○, Untreated BHK cells; □, BHK cells treated with tenfold concentrated tissue culture medium; ●, BHK cells treated with tenfold concentrated supernatant from RK13 cells; ■, BHK cells treated with tenfold concentrated supernatant from BHK cells.

rebound effect at 24 h, with an increase in unsaturation that lasted until 72 h. These results suggested that the saturation of the C_{18} fatty acids is under strong cellular control. The overlay medium of IFN-treated cells was harvested at 8 h, and partly purified and concentrated as described for IFN (Lampson *et al.* 1963).

The putative polypeptide material was used to pulse-treat uninfected cells as for IFN. The material produced an effect on the saturation of the C_{18} fatty acids that was a mirror image of the effect of IFN (figure 1). There was a reversible increase in desaturation that peaked at 8–10 h, again followed by a noticeable rebound effect towards an increase in C_{18} fatty acid saturation. As discussed previously (Apostolov 1980; Apostolov & Barker 1981) changes in the saturation of fatty acids affect their melting points and indirectly the fluidity of cell membranes. An increase in the saturation of the C_{18} fatty acids, which make up 40–50 %

of the total of extractable fatty acid from the cell, leads to an increase in membrane rigidity. The capacity of IFN to increase the saturation of C_{18} fatty acids could be the effector mechanism for the following effects of IFN:

(1) increased cell membrane buoyant density (Chang *et al.* 1978) owing to higher density of stearic acid (18:0, m.p. 69 °C) over the unsaturated C_{18} fatty acids (for example, oleic acid, 18:1, m.p. 14 °C);

(2) inhibition of maturation and release by budding of retroviruses (Chang *et al.* 1977) due to reduced membrane mobility;

(3) inhibition of syncytia formation by Sendai virus-infected cells (Tomita & Kuwata 1981) (same reason as for (1) and (2));

(4) inhibition of cell division, for the same reasons as (1) and (2) but also possibly due to inhibition of cell metabolism by inhibition of lipid (membrane)-dependent enzymes (Sandermann 1978);

(5) inhibition of virus replication, mainly for reasons (1), (2) and (4);

(6) the decrease of the effects of IFN after repeated exposure of the host to IFN (refractoriness to IFN (Borden *et al.* 1975)) due to induction of desaturation promotion factor and increased membrane fluidity.

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8. Altered Natural Killer cell response in patients with malignant lymphoma

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Natural Killer (NK) cells may be an important anti-tumour mechanism (Herberman & Holden 1978). Furthermore, interferon and interferon inducers potentiate NK-mediated cytotoxicity (Einhorn *et al.* 1978) and may constitute a mechanism whereby interferon mediates its anti-tumour effect. Patients with malignant lymphomas have long been acknowledged to have marked defects in immunity, particularly cell-mediated immunity (Hancock *et al.* 1977). NK cell function in such patients has not, however, yet been assessed.