INTERFERON AND THE ANTIBODY RESPONSE.

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SUMMARY.

(1) The effect of mouse interferon on the primary *in vitro* antibody response of mouse spleen cells against sheep erythrocytes was studied. Concentrations of interferon greater than 8 units/ml significantly inhibited the antibody response while low concentrations of 0.08 - 0.8 units/ml were mildly enhancing. No effect on cell viability was observed with any of the interferon concentrations. The effects were specific for mouse interferon as human interferon had no effect on the antibody response of mouse spleen cells.

(2) The immunosuppressive activity of crude and partially-purified interferon preparations correlated with the interferon titres. The antiviral and immunosuppressive activities of interferon preparations were equally sensitive to trypsin, heat and periodate treatments and insensitive to nuclease and low pH treatments. These results strongly indicated that both activities were functions of similar molecules with the properties of glycoproteins.

(3) The polyclonal response of mouse spleen cells to the B cell mitogen lipopolysaccharide was suppressed by interferon while the proliferative response to the T cell mitogen phytohemagglutinin was unaffected.

(4) Suppression was most marked when interferon was present from the beginning of the culture period. Addition of interferon at later times had progressively less inhibitory effect. Interferon had no effect when added after 48 hours.

(5) Suppression of the antibody response was observed when spleen cells were pretreated for four hours at 37°C before antigenic challenge.

No suppression resulted following pretreatment at 4°C. No measurable quantity of interferon was taken up by the cells during pretreatment.

(6) Although interferon appeared to act during the first few hours of the antibody response no suppression of the early response was observed. The suppressive effect was not apparent for at least 50 hours. The kinetic data has been interpreted in terms of interferon-sensitive and interferon-resistant clones of antibody-forming cells.

(7) The presence of interferon-sensitive and interferon-resistant antibody-forming cell precursors was demonstrated using a culture system which permitted individual clones to be studied. Interferon had no effect on the division of B cells but suppressed the antigen-induced activation of some B cell precursors. The effect was an "all-or-nothing" phenomenon. Precursors which were suppressed by interferon were completely suppressed while interferon-resistant precursors were able to develop normally into clones of antibody-forming cells in the presence of interferon.

(8) A mechanism for interferon-induced antibody suppression has been proposed. Interferon only suppresses the activation of non-dividing B cell precursors. Once precursors have become activated and entered cell cycle they are refractory to suppression by interferon. This mechanism adequately explains all the observations.

(9) Three theories, which are not mutually exclusive, have been proposed to explain the significance of interferon-induced suppression of the antibody response during viral infections. These theories

suggest that suppression might function as a protective mechanism which operates at a time when an active antibody response would in some way be harmful to the host. The first theory concerns non-specific immunologically-mediated tissue damage which may result if antibody production was not suppressed by interferon during viral infections. The other two theories deal with conservation of the immune system. Interferon may either prevent virus-mediated destruction of activated lymphocytes or protect the immune system against the possible induction of specific tolerance to viral antigens.

ABBREVIATIONS.

AFC	antibody-forming cell
ALS	antilymphocyte serum
B cell	a cell of the antibody-forming cell lineage
BCG	Mycobacterium tuberculosis (strain BCG)
Ci	curie
CMI	cell-mediated immunity
con A	concanavalin A
CS	calf serum
CV	Chikungunya virus
Dimethyl POPOP	1,4-bis [2(4-methyl-5-phenyl-oxazolyl)] benzene
DNA	deoxyribonucleic acid
DTH	delayed-type hypersensitivity
EDTA	ethylenediamine tetraacetic acid
EMC	encephalomyocarditis
FCS	foetal calf serum
g	grammes or times gravity
GVH	graft-versus-host
HEPES	N-2-Hydroxyethylpiperazine-N'-2-ethanesulphonic acid
HSV	herpes simplex virus
JMM	Joklik-modified medium
Kg	kilogramme
LCM	lymphocytic choriomeningitis
LPS	lipopolysaccharide
M	molar
MEM	minimum essential medium
MIF	macrophage migration inhibition factor
mg	milligramme

ml.	millilitre
mm	millimetre
m.o.i.	multiplicity of infection
mRNA	messenger RNA
NDV	Newcastle disease virus
nm	nanometer
PBS	phosphate-buffered saline
PFC	plaque-forming cell
PFU	plaque-forming unit
PHA	phytohemagglutinin
poly I:C	polyriboinosinic-polyribocytidilic acid
poly U	polyribouridylic acid
PPD	purified protein derivative from tuberculin
PPO	2,5-Diphenyloxazole
PWM	poke weed mitogen
RES	reticuloendothelial system
RNA	ribonucleic acid
SBSS	Shortman's balanced salts solution
SFV	Semliki forest virus
SIRS	soluble immune response suppressor
SRBC	sheep red blood cells
SV 40	simian virus 40
T cell	thymus-derived cell
TRIC	trachoma-inclusion conjunctivitis
tRNA	transfer RNA
µg	microgramme
µl	microlitre
UV	ultraviolet
VSV	vesicular stomatitis virus