NONSPECIFICITY OF PHAGOCYTOSIS OF INFLUENZA VIRUSES BY MOUSE MACROPHAGES

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For a long time the view was held [1, 2, 7, 11, 15] that phagocytosis is not a factor in antiviral immunity, and this was regarded as one of its cardinal differences from antibacterial immunity. It has to be accepted that objectively there are several facts that are evidence of the exceptional nature of viruses as objects of phagocytosis, namely their extremely small size, their resistance to intracellular enzymes, their ability to integrate with the genome of the host's cells, and their prolonged persistence in them. A unique feature of the nature of viruses is their obligate parasitism on subcellular and molecular-genetic structures of the infected cell. However, as more recent investigations using methods of electron and luminescence microscopy, etc., have shown, cells of the macrophagal-microphagal system do carry out phagocytosis of viruses and disintegrate them [3-6, 8-10, 12-14]. Immune phagocytes in this case are much more able to disintegrate viruses than phagocytes of intact animals.

The writers showed previously [13] that cells of cultures of mouse perotoneal macrophages phagocytose and disintegrate influenza virus. However, no results of the study of the specificity of phagocytosis could be found in the literature.

The aim of this investigation was to study the immunologic specificity of this phenomenon. For this purpose cultures of mouse macrophages, immune to influenza virus with the antigenic formula HON1 were tested for their ability to disintegrate not only the homonymous virus, but also influenza virus widely different from it antigenically, namely virus H3N2.

EXPERIMENTAL METHOD

Influenza viruses of subtypes A, namely A/PR/8/34 (HON1) and A/England/42/72 (H3N2), subcultured in chick embryos, were used. The virus was purified and concentrated with formalized chick erythrocytes in order to prepare formol vaccine [8].

Male albino mice weighing 18-20 g were immunized with A/PR/8 formol vaccine with a titer of 1:5120/0.5 ml in the hemagglutination test (HAT). Each mouse received 0.5 ml of formol vaccine 5 times intraperitoneally (at intervals of 3-4 days). The antibody titer in the anti-PR8 sera on the 8th-10th day after immunization was 1:12,800 in the hemagglutination inhibition test (HIT) on the 8th-10th day after immunization against PR8 virus it was 1:12,800, and in the complement fixation test (CFT) it was 1:640-1:1280. These sera reacted in the HIT with A/England/42/72 virus in a dilution of 1:160-1:320, just like normal mouse sera.

Cultures of peritoneal macrophages were obtained from immune and intact mice [8]. After monolayer formation the macrophages were infected with allantoic virus with a multiplicity of 20 EID_{50} per cell. The infected cells were incubated for 30 min at 4°C and 1 h at 37°C, washed, and treated with maintenance medium. The cells were then kept for 24 h at 37°C, frozen and thawed five times, and dilutions of the cell extracts were used to infect chick embryos. After incubation for 2 days at 37°C, virus was detected in the allantoic cavity of the embryos by the HAT.

EXPERIMENTAL RESULTS

In intact macrophages both viruses reproduced equally: PR8 virus was found in 3 and England virus in 4 of the 20 infected embryos.

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TABLE 1. Nonspecific Modification of Macrophages during Immunization of Mice with Influenza Virus

Mouse macrophages	Virus for infection	Dilutions of extract of macrophages injected into embryos				Number of embryos in virus/total number of infected embryos
		10^{-1}	10^{-2}	10^{-3}	10^{-4}	
Intact	PR8 (H0N1)	0	320	320	0	
		10*	80	160	0	7/12
		40	40	0	0	
	England (H3N2)	10	160	0	0	
		40	320	0	0	6/12
		20	80	0	0	
Immune to PR8	PR8	80	0	20	0	
		320	0	0	0	
		0	0	0	0	3/20
		0	0	0	0	
		0	0	0	0	
	England	160	0	40	0	
		80	0	0	0	
		20	0	0	0	4/20
		0	0	0	0	
		0	0	0	0	

Legend. *) Titers of virus in HAT expressed in reciprocal values; 0) virus absent according to HAT.

Macrophages immune to influenza virus HON1 thus disintegrated influenza virus H3N2, widely different from it antigenically, to an equal degree. In the immune animal, nonspecific functional modification of the phagocytes evidently takes place, accompanied by activation of the lysosomal apparatus of the cell. This enhanced enzymic function of the immune cells of the phagocytic system, it must be supposed, is of fundamental importance for overcoming the viremia and for destruction of the viral proteins. Protection of the cell against foreign viral genetic inflammation penetrating inside it, and inhibition of reproduction of the virus constitute one of the cardinal features of antiviral immunity.

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