Acquired Immunity to a Specific Antibody and Its Inheritance in Paramecium aurelia

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An animal infected with a pathogenic microorganism responds, as is well known, by the development in its blood of an antibody which acts specifically on the invading parasite. This is the natural defense mechanism of the animal against injury by the parasite. Many researches (1) during more than 30 years indicate the less well known fact that the parasite may respond to the host's antibody by developing heightened resistance or complete immunity to it. Such a response appears as an increased virulence of the pathogenic organism and becomes an important medical problem. The mechanism of this apparent increase in virulence is not thoroughly understood and three interpretations have been suggested: (1) The initial infection included more than one strain of pathogens and the initially predominant form alone was killed off by the antibody, thus permitting another strain to develop predominance; this is then a theory of selection. (2) The antibody produced by the host acts as a mutation inducing agent and produces mutations altering the antigenic properties of the parasite. (3) The antibody produces changes in the antigenic properties of the parasite, but these are not true mutations; they are merely long-lasting modifications or temporarily inherited changes which invariably revert to the original condition. The third interpretation is so fundamentally out of harmony with knowledge of heredity in other organisms that one or the other of the first two interpretations has been most generally accepted by workers in this field. However, the pathogenic organisms are unsuitable for critical analysis of the problem because (1) purity of the strain is difficult to establish in pathogenic organisms; and (2) the absence of sexual processes makes impossible genetic tests of the mutation hypothesis.

I have therefore attempted to analyse the problem in *Paramecium aurelia*, a single-celled animal particularly favorable for such studies. A race known to be entirely pure (homozygous) for all its genes was injected into rabbits. The antibody formed in the rabbit's blood is specifically active on the race of paramecia used for the injections even when the antiserum is diluted 1 part to 4,000 parts of salt solution. Its activity consisted in quickly paralyzing the paramecia and in killing them when applied in concentrations greater than 1:1000. Although occasional individuals of this race of paramecium show temporary increases in resistance to the antiserum, none of these differences persisted for even a single day during reproduction by fission. The race is thus hereditarily uniform and the first hypothesis, selection, cannot be invoked as an explanation of acquired immunity.

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When the temporarily resistant paramecia were subjected to the antiserum they acquired complete immunity to the antiserum: they were no longer affected by even undiluted antiserum. Further, this induced immunity was inherited during reproduction by fission in culture media entirely free from antiserum. In some lines of descent the immunity was suddenly and completely lost after a short period (a week or so; 25 to 30 cell generations); in others it lasted for various longer periods, still existing in some after a period of more than 75 days of rapid multiplication (more than 279 cell generations). In all immune cultures, however, the hereditary immunity was invariably lost suddenly and completely after fertilization. This result occurred regardless of the combinations brought together at fertilization: in crosses of immune by susceptible cultures; in crosses of immune by reverted cultures; in crosses between two different immune cultures; and in self-fertilization within a single immune culture. These results demonstrate that the acquired immunity is not an ordinary persistent mutation, but is only temporarily inherited for long periods during vegetative reproduction, as maintained by the third hypothesis above.

Finally it was demonstrated that the loss of immunity was not due to induction of reverse mutations by the serum-free culture medium, for it also occurred in the absence of fertilization in media containing dilute antiserum. When immune cultures underwent fertilization in this dilute antiserum culture medium, many lost their immunity at once; but others retained it for variable periods, as in the original inductions.

This study demonstrates that, in Paramecium, the persistence of acquired immunity to a specific antibody is due neither to selection nor to ordinary mutations. It is a case of *temporary* though long inheritance of an acquired character. This is a form of inheritance not recognized by modern, generally accepted canons of genetics, but was extensively studied by its discoverer, Jollos (2). Further investigations designed to bring such temporary inheritance under experimental control will doubtless be of great value both theoretically and in the control of infectious disease.

Literature Cited

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