LETTERS

The LDH Virus: An Interfering Biological Contaminant

The lactate dehydrogenase-elevating virus (LDH virus) is widely distributed in nature, having been found in wild and laboratory mice in North America, Australia, England, and Europe (*1-4*).

Of special relevance to the biological research community is the inconspicuous and thus unappreciated presence of this "silent" virus in many of the mouse-passaged materials used in biomedical research. Known contaminations have occurred in more than 100 transplantable mouse tumors, many of the oncogenic virus preparations, and other viral, bacterial, and *Bartonella*-like materials that have been or are being serially passed in mice (*1-4*).

We wish to call attention to the interpretative hazards associated with the wide variety of physiological alterations that this ubiquitous agent is capable of inducing in experimental mice. Some of the host alterations that are known to be associated with this viral infection have been erroneously ascribed to implanted tumors, oncogenic viruses, or to other experimentally imposed factors or conditions. Thus, certain immunological changes or manifestations observed in mice after tumor transplants or inoculation with other oncogenic materials may result, either largely or in part, from the concomitant LDH viral infection. The presence of the LDH virus is therefore capable of modifying and compromising otherwise carefully acquired biological data.

Following is an abridged list of host alterations and influences that are associated with the LDH viral infection and have caused or are capable of causing distortion, misinterpretation, or confusion of experimental data:

1) Immunological effects: lymphocyte trapping; thymus involution; changes in T cells, B cells, and macrophages; moderate splenomegalia and lymph node enlargement; enhancement or depression of humoral immunity; depression of cellular immunity; and production of virus-antibody complexes (*1-6*).

2) Endocrinological alterations: two- to tenfold increases in plasma corticosterone levels during the acute phase of viral infection (*1, 6, 7*).

3) Host enzyme changes: two- to hundredfold increases in plasma LDH and some other plasma enzymes, some of lifelong persistence (*1-4*).

4) Modifications of cancer therapy: potentiation of asparaginase and glutaminase effectiveness (*8*).

5) Alterations of host clearance capabilities: decreases in the rate of clearance of many naturally occurring or injected enzymes and other proteins and two- to tenfold increases in their half-life (*9*).

6) Changes in tumor behavior: increases in the incidence and growth rates of certain tumors and reduction of the percentage of regressions and of host survival times (*6, 10*).

7) Alterations in oncogenic viral expression: increases in tumor incidence; reduction of spontaneous regressions; increases in the number of spleen foci; and production of interferon (*6, 11*). Suppression of the incidence of mouse mammary tumor viruses or of tumors induced by the Moloney sarcoma virus under special conditions (*12*).

Investigators working with biological materials that have a high probability of carrying this silent virus are urged to establish its presence or absence. Editors and reviewers charged with monitoring the accuracy of published material should challenge submitted manuscripts that are appropriately suspect. As a minimum, the presence or absence of the virus in recipient mice and in mouse-passaged preparations should be clearly stated in all reports of research in which such materials were used.

However, to cope most effectively with this problem, it is also necessary to remove the passenger LDH virus, when present, from the classical, as well as newer, transplantable mouse tumors, from oncogenic and other virus preparations, and from miscellaneous mouse-passaged materials such as experimental murine pathogens and *Eperythrozoon coccoides*. Protective housing, quarantine procedures, and appropriate sanitary safeguards should also be used to prevent uncontrolled reinfection (*12, 13*).

The LDH virus produces a lifelong persisting viremia in infected animals. There is no known therapeutic means capable of eliminating the virus from the host. It is possible, however, by utilizing either special tissue culture techniques or appropriate heterotransplantation procedures to delete the LDH virus from specific tumors, mouse-passaged bacterial and viral materials, or other contaminated preparations, and then to transplant such virus-free materials back into "clean" mice (*2, 4*).

While it is possible for each laboratory to test and "purify" their own contaminated preparations, in practice this is time-consuming and requires special expertise and appropriate research facilities. Since LDH viral contamination will be a continuing problem for the foreseeable future because of recontaminations, individual solutions to the problem

are not consistent with realistic research economics. Such a special technical need of a significant section of the biological and biomedical research community could be more effectively accomplished by establishing a central laboratory within or sponsored by the National Institutes of Health or an appropriate institute or foundation. The establishment of such a center for both the detection and elimination of the virus would provide greater assurance that costly research studies in which mice are used would not be subject to misinterpretation as a consequence of the presence of an uncontrolled agent that alters immunological and other basic physiological parameters.

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Xeroxing Life

Barbara J. Culliton's excellent summary of the burgeoning controversy over human cloning (News and Comment, 24 Mar., p. 1314) suggests that once it is full-blown, this one will be dominated by arguments even more specious than those advanced (on both sides) by recombinant DNA research extremists. I am concerned here with only one of the possibilities: doubtless there will be opportunity in the future for ventilation of the others. At issue is the false notion, thus far undisputed by scientists responding to the press, that the product of a single successful nuclear transplantation is a "clone," that is, an *identical copy* (I avoid Jeremy Rifkin's plug for Xerox) of the individual donating the transplanted nucleus. My concern with this specific point is that, more than any other, the idea of mass production of identical persons is repugnant to the laity, perhaps because it is so obvious a departure from the organic way of doing things.

There is, however, no possibility in principle of making copies identical to an individual donor by the method being discussed. All animal ova studied so far, including those of mammals, contain a population of "maternal" messenger RNA molecules, laid down in the egg cytoplasm during oogenesis, and functioning in protein synthesis during development proper (*1*, *2*). Protein synthesis is indispensable for development, and a