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Letters

"Outbreak of Hind Limb Paralysis in Young CFW Swiss Webster Mice"

A recent article in *Comparative Medicine* (1) described an outbreak of hind limb paralysis in CFW Swiss mice, and presumptively attributed the outbreak to infection with Abelson's murine leukemia virus (A-MuLV) although the authors show no proof that Abelson's leukemia virus was the cause. Incorporation of such a claim in the abstract and emphasis in the Discussion fosters inaccuracy in the scientific literature. A-MuLV is an experimental acute transforming defective retrovirus that contains a viral oncogene (v-onc) that was usurped from the host genome. A-MuLV was originally isolated from prednisolone-treated BALB/c mice that were experimentally infected with exogenous Moloney murine leukemia virus (Mo-MuLV). A-MuLV rapidly transforms cells, but is replication-defective, and requires a replication competent "helper" virus to reproduce itself. Viruses containing v-onc genes do not contribute significantly to the incidence of naturally occurring retrovirus-induced tumors in mice, as oncogene capture is an exceedingly rare event. These defective viruses are experimental phenomena with a low frequency of horizontal spread and with rapid and lethal (a few weeks) consequences. Thus, the likelihood of barrier-maintained CFW Swiss mice becoming infected with a replication-defective, experimental acute transforming retrovirus is, to say the least, exceedingly unlikely. Furthermore, the possibility that A-MuLV is maintained as a provirus in CFW Swiss mice is even more remote, as its genetic origins come from Mo-MuLV, which is of exogenous origin. Exogenous retroviruses are not endogenous proviruses, and exist in wild mice, but not in laboratory mice. The only portion of the A-MuLV that is of mouse origin is the non-retrovirus related proto-oncogene (*abl)*. The murine *abl* host gene is not a proviral element.

The article promulgates other inaccuracies. Most notable is the statement that A-MuLV "is suspected to be the cause of parosteal lymphoma reported in man (2)." The reference that the authors cite makes no such claims. For reasons discussed above, that is an impossibility. Indeed, the cited reference compares the human syndrome with the experimental disease in mice induced by A-MuLV, but makes no such claim of common etiology. Finally, the authors imply that it would be desirable to obtain mice free of endogenous retroviruses. Although the authors rightly state that screening for retroviruses is not a routine practice and doing so would increase the cost of animals, the very notion is naïve. Mice harbor numerous replication competent and replication defective endogenous proviruses (both leukemia and mammary tumor viruses), as well as literally thousands of retrovirus-like elements. These comprise the genetic characteristics of the laboratory mouse, and indeed contribute significantly to the very characteristics for which mice were selectively bred. It would take an international effort, larger in scale than the human genome project, to eliminate retroviruses from the genome of the mouse (or any other species for that matter) and the resultant "retrovirus-free" mouse wouldn't be a mouse.

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References

1. **Ceccarelli, A. V. and N. Rozengurt.** 2002. Outbreak of hind limb paralysis in young CFW Swiss Webster mice. Comp. Med. **52(2):**171-175.
2. **Smith, R.** 1984. Parosteal lymphoblastic lymphoma. A human counterpart of Abelson virus-induced lymphosarcoma in mice. Cancer **54(3):**471-476.

Authors' Response

We are responding to the letter written by Dr. Barthold pertaining to our manuscript "Outbreak of Hind Limb Paralysis in Young CFW Swiss Webster Mice" (1).

The sentence in the Abstract of the paper refers to "a presumptive diagnosis" based on the epidemiological, clinical and pathological features which are the facts that made this outbreak unique and worthy of reporting. The core of our discussion emphasizes the uniqueness of the symptoms and pathology of the case. We raised the possibility of a viral etiology because of the epidemiological features of the outbreak. This was supported by the existence of a report of another outbreak of lymphoma of proven viral origin, in mice from the same vendor, the same strain, same age, published on the same year, which together are, at the least, suggestive of a common etiology to the two cases. References to Abelson's murine leukemia virus (A-MuLV) are quoted because they are the only existing reports on lymphoma associated with these very unusual clinicopathological features. A debate about the viral biology would have been well beyond the scope of this case report. The reason for referring to this paper was to raise the awareness that a virus with some properties similar to A-MuLV could be responsible for a spontaneous outbreak of lymphoma. A clear and honest statement is made in our paper that a viral etiology could not be confirmed in this case. Moreover, the discussion includes a self-criticism on the point that appropriate material was not collected at the time of the outbreak.

We acknowledge that our reference to the report by Smith (2)

should have been worded "*…and to have many clinical and cell phenotype similarities with a parosteal lymphoma reported in man.*"

Dr. Barthold points out that the mouse genome harbors thousands of retrovirus-like elements and that a mouse without them would not be a mouse. Indeed, on page 175, we state "*…In addition, given the fact that MuLV fragments have been identified in the mouse genome (16, 24), the chances of clearing colonies of these infections are virtually nil at present.*" We did not proposed that a retrovirus-free mouse is achievable, but that recording and reporting outbreaks of this nature are a worthwhile endeavor. We indeed agree that a "retrovirus-free" mouse would probably not be a mouse. Neither is literally a mouse, one with human genes in it. We live in a strange and changing world; mice are not what they used to be.

The authors are very grateful to Dr. Barthold for his attentive and detailed inspection of their communication and for his valuable, clarifying comments.

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References

1. **Ceccarelli, A.V. and N. Rozengurt.** 2002. Outbreak of hind limb paralysis in young CFW Swiss Webster mice. Comp. Med. **52:**171-175.
2. **Smith, R.** 1984. Parosteal lymphoblastic lymphoma. A human counterpart of Abelson virus-induced lymphosarcoma of mice. Cancer **54(3):**471-476.