TYPE C VIRAL POPULATIONS IN NORMAL C57BL/6 MOUSE AND IN RadLV-Rs RELATED LEUKEMIA

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The activation of leukemogenic viruses in C57BL mice upon X-irradiation was suggested by the emergence of C-type viruses in radio-induced tumors. These were termed RadLV for radio-induced leukemia viruses. The particular RadLV isolate investigated in our laboratory (RadLV-Rs) induces lymphoreticulosarcomas localised to the spleen and lymph nodes. Our previous attempts to isolate the leukemogenic component revealed a high complexity of the viral content of the RadLV-Rs isolate. In addition to the RadLV-Rs itself and to non-leukemogenic endogenous retroviruses (N- and X-tropic) several non-endogenous B-tropic viruses (BL^1) were isolated, but none displayed the same leukemogenic activity as that of the RadLV-Rs. The B tropism of the RadLV-Rs and of the BL^1 as well as the proteic structure of the latter strongly support their emergence through rounds of recombinations between the endogenous N- and X-tropic viruses. Such a mechanism (activation of the expression of endogenous viruses followed by recombinational events) is proposed as an hypothesis for leukemia induction upon X-irradiation. Our preliminary investigations have already evidenced favors this model for a number of facts which support this model. (1) New retroviruses (BL^1) do arise by genetic recombination between endogenous retroviruses as observed in the RadLV-Rs complex; this proposal was further confirmed in *in vitro* reconstruction experiments in which SCI mouse cells were coinfected with N- and X-tropic endogenous viruses. (2) Some, if not all, of the genetically reassorted viruses were found to be leukemogenic, this was found true for three different clones of BL^1 viruses although the latency period was much longer than that of RadLV-Rs itself. (3) If it is assumed that the outbreak of these late leukemias would depend on the spontaneous late expression of the xenotropic virus (as it is known in the C57BL/6 mouse) by a new recombinational event involving BL^1 viruses, then the latency period would largely depend on the age at inoculation. Our observation showed that the age at leukemia outbreak remained the same (600 days) whether the animals were infected when 30 or 400 days old (Table 1). (4) If late leukemias are induced via a recombination between BL^1 and X viruses, and because recombination may lead to different antigenic reassortments one may expect the leukemias induced to be polymorph and the tumorial tissues to contain *de novo* generated viruses able to induce by themselves rapid leukemias as in this case of RadLV-Rs infection. In agreement with this assumption, our experiments, although incomplete, have shown that leukemias induced by cloned BL^1 viruses are of different types: most of them are B-type leukemias affecting the spleen and lymph nodes but in addition more than 10% are either null or T.

TABLE 1. 1223-B VIRUS (L^1) INDUCED LEUKEMOGENESIS LATENCY ACCORDING TO AGE AT INOCULATION

Age at inoculation (days)	Latency (days)	Age at death (days)
30	580	610
390	260	650

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TUMOR INDUCTION IN RATS BY SIMIAN SARCOMA ASSOCIATED (HELPER) VIRUS AND RESCUED MURINE SARCOMA VIRUS

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Three groups of newborn rats were injected intraperitoneally and subcutaneously with three different cultures of human A204 cells productively infected with various amounts of rescued sarcoma virus. These virus producing A204 cells were obtained by serial dilution of the culture supernatant of rat cells nonproductively transformed by the Kirsten strain of murine sarcoma virus superinfected with the simian sarcoma/helper virus complex from SiSV/SiSAV producing NC 37 cells. Sarcoma genome containing viral particles could be demonstrated by a positive focus assay at a dilution of 10^{-4} of the original rescued virus preparation and to a lesser extent at a dilution of 10^{-5}. No focus formation was observed with a dilution of 10^{-6}. Injection of 1 million A204 cells infected with a dilution of 10^{-4} led to subcutaneous sarcomas at the site of inoculation and a hyperplastic and neoplastic proliferation especially of erythroblasts. Injection of A204 cells infected with a dilution of 10^{-6} induced a malignant proliferation of hemopoietic cells, some of which were of myeloid origin and others of unknown origin. No sarcomas were observed in this group. The mean latency period for lesions to develop in the first group (dilution, 10^{-4}) was 90 days while that in the last group was 175 days. The induced tumors were of host cell origin and replicating virus could be detected in the diseased animals. Inoculation of uninfected A204 cells never led to local or generalized tumors nor did the animals show any other signs of disease. These results are suggestive for an oncogenic potential of the woolly monkey (simian) type C helper virus in rats.