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Induction of Histiocytomas by Pristane Treatment of Mice Chronically Infected with Moloney Murine Leukemia Virus *

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Normally Moloney murine leukemia virus (M-MuLV) induces T-cell derived leukemia in mice after a latency period of several months. Recently this virus was shown to replicate in infected mice in a wide variety of cells of hemopoietic and non-hemopoietic origin without transforming these cells [1].

Here we report that histiocytic tumors were induced after pristane injection into the peritoneal cavity of mice chronically infected with M-MuLV. Two sets of viremic mice were used: At 8 weeks of age BALB/c mice were infected with M-MuLV and 2 and 4 weeks later they received 0.5 ml pristane intraperitoneally. In the second experiment BALB/Mo mice [2] were injected with pristane at 6 and 10 weeks of age. BALB/Mo mice carry the M-MuLV as an endogenous virus and are viremic from about 1 week of age on [3]. After a latency time of at least 2 months following the second pristane application, 6 of 14 M-MuLV infected BALB/c and 19 of 24 BALB/Mo mice developed abdominal tumors with massive hemorrhagic ascites. The surface of the peritoneum was covered with whitish solid layers of tumor tissue. The ascites fluid contained up to 10^8 cells/ml. In the thymus, spleen, and lymph nodes, growth of histiocytic tumor cells was not observed.

The tumors and the ascites fluid were characterized histologically and cytologically. The results are summarized in Table 1. The markers shown are characteristic for the monocyte/macrophage lineage; hence the tumors could be classified as histiocytomas.

Table 1. Histological and cytological characterization of tumors induced by pristane treatment of mice chronically infected with Moloney murine leukemia virus

Feature:	Intraperitoneal tumor	Ascites fluid/ tissue culture
Morphology:	Histiocytoma	Promonocytes/ monocytes/ Macrophage-Like cells
Reticuline	+	–[a]
α-*N*-esterase	+	+
Acid phosphatase	+	+
Lysozyme	+	+
α_1-antichymotrypsin	–	+
M-MuLV specific proteins	+	+

[a] Reticuline is only a consistuent of solid tissue

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When transplanted into syngeneic hosts most of the histiocytomas could be serially passaged. From nine tumors permanent tissue culture lines were established. With one exception all tissue culture lines release high titers of ecotropic M-MuLV.

The infection of mice with M-MuLV usually results in the induction of T-cell leukemia several months after the infection. M-MuLV lacks a transforming gene and the leukemia induction by this virus is still poorly understood. An abnormal proliferation of lymphocytes caused by the chronical virus infection is regarded as one of the possible mechanisms leading to leukemia [4]. In our case a similar chain of events may be responsible for the formation of histiocytic tumors. The application of pristane into the peritoneal cavity induces a constant proliferation of normal phagocytes. But virus infection is needed to set off the development of this specific tumor.

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References

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