Are Bone Marrow-Derived Fibroblastoid Colony-Forming Cells Involved in Viral Leukemogenesis?

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ARE BONE MARROW DERIVED FIBROBLASTOID COLONY-FORMING CELLS INVOLVED IN VIRAL LEUKEMOGENESIS?

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Haemopoietic tissues contain cells capable of forming fibroblastoid colonies *in vitro*. It has been suggested that these cells belong to the stromal component of the haemopoietic tissue and that they induce specific haemopoietic microenvironment[1]. We assayed the incidence of bone marrow derived fibroblastoid colony-forming cells in the BALB/c, C3H, C57BL and (BALB/c x DBA/2)F1 (CD2) mouse strains. The number of colony-forming cells declined from 82 $\pm$ 19 per 10^6 bone marrow cells at birth, to 27 $\pm$ 5 per 10^6 bone marrow cells in 3 week old mice and 19 $\pm$ 6 per 10^6 in 6 week old mice (fig. 1). The above mentioned strains are all characterized by low spontaneous leukaemia rates. Inoculation of Soule tumour virus into 5 day old BALB/c mice induced high lymphosarcoma incidence with an average latency of 4 months. As early as 2 weeks following virus inoculation, a reduction in the number of bone marrow derived fibroblastoid colony-forming cells was observed (fig. 1). In contrast, the total cellularity and the number of CFU-s and CFU-c in the bone marrow did not differ significantly from the numbers in control animals.

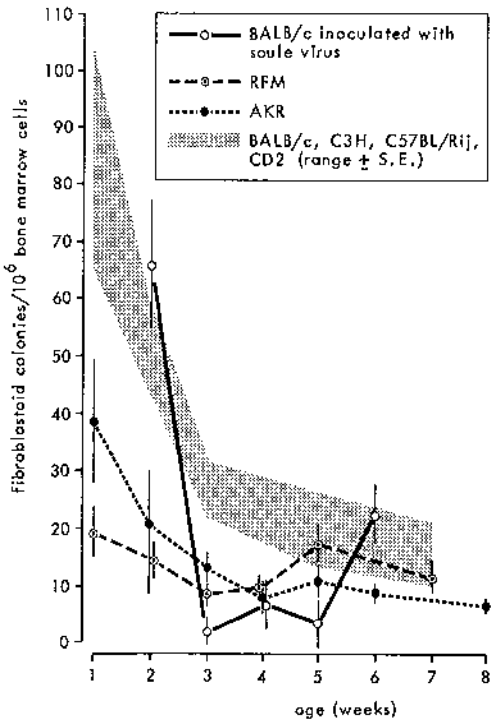

Fig. 1. Incidence of fibroblastoid colony forming cells in mouse bone marrow.

A low incidence of bone marrow derived fibroblastoid colony-forming cells was also observed in AKR mice which are characterized by a high spontaneous leukaemia rate. Using a modified XC plaque assay we found that fibroblastoid colonies from both AKR mice and from Soule virus inoculated BALB/c mice harboured an ecotropic virus. In the latter mouse strain budding C type particles were observed in electron microscope preparations of cells from fibroblastoid colonies. The presence of ecotropic virus in fibroblastoid cells did not seem to be part of a generalized infection of the bone marrow, since

cells in CFU-c colonies assayed under similar conditions had very low XC transforming activity (Table 1).

The results presented here demonstrate a correlation between high leukaemia incidence in mice (AKR and Soule virus infected BALB/c) and ecotropic virus producing fibroblastoid cells in the bone marrow. RFM mice were also found to have a low incidence of fibroblastoid colony forming cells early in life (fig. 1). This mouse strain shows a high incidence of lymphoreticular tumours in old age[2]. However, no evidence was obtained so far for early expression of virus in the bone marrow of this mouse strain.

If fibroblastoid colony-forming cells and their progeny participate in the regulation of haemopoiesis, their infection by leukaemia viruses could be the cause of pre-leukaemic pertubations of haemopoiesis. Moreover, these cells may serve as a site for malignant transformation of haemopoietic cells by simultaneously providing differentiation signals and oncogenic viruses.

TABLE 1.

PRESENCE OF XC SYNCYTIA INDUCING VIRUS IN BONE MARROW DERIVED FIBROBLASTOID COLONIES FROM AKR MICE

mouse strain	number of cells/plate	CSF	number of colonies /plate and colony type	number of XC syncytia/plate*	number of XC syncytia/colony (calculated)
AKR	5×10^4	+	60 ± 10 (CFU-c)	20 ± 10	0.3
	5×10^4	-	0	17 ± 5	-
	6×10^5	-	10 ± 5 (fibroblastoid)	500 ± 50	50.0
BALB/c	5×10^4	+	70 ± 15 (CFU-c)	0	0
	5×10^4	-	0	0	-
	6×10^5	-	35 ± 11 (fibroblastoid)	0	0

* XC cells were plated on top of preformed fibroblastoid or CFU-c colonies and syncytia scored 4 days later.

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2. Zurcher, C., van Zwieten, M.J. and Hollander, C.F. (1976) in REP Annual Report, pp. 280-281.

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