59

2'5' Oligoadenylate Synthetase and Effects of Interferon on Retrovirus-Producing Murine Lymphoma Cells

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Antiviral effects of murine interferon (IFN) on the originally established murine lymphoma cell line ON-1 producing endogenous retrovirus were studied using the methods for assaying 2'5'oligoadenylate (2'5'A) synthetase activity and analysing the synthesized oligonucleotides. In spite of continuous production of retrovirus the endogenous IFN in culture medium was not detected and only the baseline activity of 2'5'A synthetase was measured. Treatment of ON-1 cells with murine IFN resulted in reversible dose dependent reduction of virus yield judging by the reverse transcriptase activity, with accompanying 50-fold increase of 2'5'A synthetase activity above the baseline level when assaying the product of reaction by chromatography on the PEI-cellulose plates. The 2'5'oligoadenylates were further analysed by polyacrylamide gel electrophoresis in the presence of urea since this technique provides the opportunity to separate both phosphorylated oligonucleotides and core species. The development of antiviral state was shown to be accompanied by the induction of 2'5'A synthetase resulting in the synthesis of 2'5'A of various chain length. This approach proved to be useful in evaluation of the response of virus-infected cells to IFN treatment.

60

A Stromal Cell Line From LP-BM5 Infected Long-Term Bone Marrow Cell Cultures (LTBMC) Inhibits Hematopoiesis *In Vitro*.

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Murine acquired immunodeficiency syndrome (MAIDS) induced by defective LP-BM5 murine leukemia virus (MuLV) is a disease with many similarities to human AIDS. Recent studies indicated that the depressed hematopoiesis observed in LP-BM5 MuLV-infected long-term bone marrow cultures (LTBMCs) may be attributable to a defect of hematopoietic stroma. We report here the generation of two permanent murine stromal cell lines derived from normal and virus-infected marrow cultures. LTBMCs were established from normal and viral infected animals and maintained for 9 months. After 9 months in culture, adherent cells from LTBMC flasks were passaged weekly. Upon further selection we established one normal and one virus-infected stromal cell line of primarily fibroblastic morphology. The ability of these stromal cell lines to support the reconstituting hematopoietic progenitors was studied. Stromal cells were cocultured with normal and viral infected low density-nonadherent cells (LNC). Additional control LNC cultures without stromal cells were established and produced no detectable stromal cells after 3 weeks in culture. Results indicated that when cocultured with normal LNC, the normal stromal cell line efficiently supported the production of myeloid, megakaryocyte, and erythroid precursors. However, the supportive ability was reduced when infected LNC was cocultured. In contrast, infected cell line induced inhibition of both normal and virus-infected reconstituting progenitors produced up to a 40-fold decrease in hematopoietic precursors. These findings suggest that stromal cell line derived from viral infected LTBMCs exhibits defective characteristics of the hematopoietic stroma as observed in parental counterpart and restricts the support of hematopoiesis *in vitro*.