VACCINATION OF LEUKEMIC MICE
WITH VIABLE DRUG-ALTERED LEUKEMIC CELLS *

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A strong host reaction induced by specific tumour antigens is a primary goal for
immune therapy of cancer. However, in most instances, host immunity exerted little
therapeutic effect against the tumour and sometimes an enhancement of the rate of
tumour growth was observed 1,4.

Therefore, in a few laboratories it has been attempted to alter tumour cell im-
munogenicity in order to elicit a valuable host immune response. Despite numerous
approaches to increase the immunogenicity of cancer cells, there have not been
definite results 3,9,20.

Our and other laboratories 2,6,16 reported that treatment of tumour-bearing
animals with anti-neoplastic compounds can lead to modifications of tumour cell
immunogenicity as evidenced by the prolonged or indefinite survival of syngeneic
hosts challenged with the drug-treated neoplasms. An immune response to the drug-
modified cells has been observed both in in vivo 14 and in vitro experiments 12. As the
drug-induced alteration persisted indefinitely after the withdrawal of the chem-
therapeutic treatment, the antigenic sublines are considered of interest for cancer
cell biology and for experimental immunotherapy.

Previous studies have shown that drug-induced antigens are strongly immunogenic
and would appear to be in excess 15 of any pre-existing transplantation antigens, in
common with parental untreated cells.

In this study, mice challenged with parental tumour cells have been vaccinated
with viable, drug-altered syngeneic cells. As animals react to drug-induced antigens

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and to tumour-associated transplantation antigens (TATA), an inoculum of viable altered cells should elicit host immune response to TATA stronger than a similar inoculum of non-viable parental cells.

MATERIALS AND METHODS

Animals and tumours

Male DBA/2 Cr C3Hf, C57Bl/6J and (Balb/cCrxDBA/2Cr)F1 mice (hereafter called CDF1) 8- to 10-week-old, obtained from Charles River Breeding Laboratories and maintained in standard conditions, were used.

Stock tumours were kindly furnished by Roswell Park Memorial Institute, Buffalo, N.Y. (L1210Ha), National Cancer Institute, NIH, Bethesda, Md (L1210Cr) and National Cancer Institute, Milan, Italy (EL4 and C3H-GL). Experimental lymphomas were maintained by weekly i.p. injection of 10^6 ascites cells in DBA/2Cr mice (L1210Ha-L1210Cr), 15 x 10^6 ascites cells in C57Bl/6J mice (EL4) and 10^5 spleen cells i.v. in C3Hf mice (C3H-GL). Sublines L1210Ha/DTIC and L1210Cr/DTIC, originated from parental tumours following in vivo 5-(3,3-dimethyl-1-triazeno)-imidazole-4-carboxamide (DTIC) treatment for 3-5 transplant generations as previously described, were maintained by weekly i.p. inoculum of 10 x 10^6 ascites cells in immunosuppressed (cyclophosphamide i.p. 200 mg/kg/24 h before tumour challenge) CDF1 mice.

Cell viability was checked microscopically by dye exclusion, and no inocula with less than 95% viability were used. An autopsy was performed on all dead animals as well as on those killed at the end of the 60-day observation period.

Drugs

Cyclophosphamide (Cy-NSC 26271) dissolved in chilled saline, BCNU (NSC-409962) dissolved in a few drops of ethyl alcohol and the volume adjusted with saline were used immediately. The DTIC was solubilized with citric acid in distilled water. Drugs were obtained from Dr. H. B. Wood, Jr. (Drug Research and Development Program, Division of Cancer Treatment, National Cancer Institute, USA).

Immunization

Single i.p. injections of 10 x 10^6 DTIC-modified cells were given to CDF1 mice; in the case of parental, host-compatible L1210Ha and L1210Cr leukemias, 40 x 10^6 X-inactivated cells (5000R-Securix Compact CGR-200 KW, 12 mA, 0.5 mm copper, aluminum filter, rate 98R/min) were inoculated i.p. For the EL4 and C3H-GL lymphomas, a single i.p. injection of 10 x 10^6 viable cells was given to CDF1 mice.

RESULTS

On the basis of transplantation experiments in CDF1 animals previously performed, the L1210Ha leukemia appeared highly immunogenic in contrast with the poor immunogenicity of the L1210Cr leukemia. The immunogenicity of non-viable L1210Ha and L1210Cr in respect to the immunogenicity of the correspondent viable