LETTER TO THE EDITOR

INHIBITORY EFFECT OF NOGALAMYCIN ON TUMOUR PROMOTION

Sir,

(Received on March 15, 1983)

Nogalamycin (NM), an anthracycline antibiotic, has been shown to inhibit RNA synthesis (1, 4), and induce tumour regression (2,3). In this communication, the effects of nogalamycin on the initiation and promotion of skin tumours in mice are discussed.

7,12-Dimethylbenz[*a*]anthracene (DMBA) and 12-0-tetradecanoylphorbol-13-acetate (TPA) were obtained from Sigma Chemical Co., St. Louis, MO, USA. Nogalamycin (NM) was obtained from Upjohn Co., Kalamazoo, MI, USA. All other chemicals were of analytical reagent grade.

TABLE I : Incidence of papillomas in mice at 12 weeks post treatment.

Groups	Treatment		No. of tumour-bearing mice / No. of mice studied
	Initiation agent(s)	Promotion agent(s)	
A	Isotonic saline	25 μg TPA	0/10
B	50 μg DMBA	Isotonic saline	0/10
C	50 μg DMBA	25 μg TPA	10/10
D	50 μg DMBA+10 μg NM	25 μg TPA	10/10
E	50 μg DMBA+25 μg NM	25 μg TPA	7/10
F	50 μg DMBA	25 μg TPA+10 μg NM	0/10
G	50 μg DMBA	25 μg TPA+25 μg NM	0/10

DMBA : 7, 12-Dimethylbenz[*a*]anthracene.
TPA : 12-0-tetradecanoylphorbol-13-acetate.

Female CD-1 mice, weighing 20-30 g, were obtained from Charles River Lab., Wilmington, MA, USA, and used in these studies. The mice were fed Charles River chow and water *ad libitum*, and maintained on a 12:12-hour light-dark schedule. The mice were shaved 2 days prior to the first treatment. The drug treatment scheme is presented

in Table I. Each mouse received a single topical dose of initiation agent(s). followed one week later by a single topical dose of promotion agent(s). The animals were examined weekly, and the incidence of tumours was recorded.

As shown in Table I, no papilloma was observed in the mice given either TPA (group A) or DMBA (group B) at 12 weeks post treatment, while papillomas developed at the site of application in mice treated with both DMBA and TPA (group C). Moreover, nogalamycin (NM) inhibited TPA-mediated promotion at a dose as low as 10 μg. On the other hand, the 10 μg dose of NM did not inhibit DMBA-induced initiation, and the 25 μg dose of NM produced 30% reduction of papilloma development. The study was terminated after 12 weeks when tumours were observed in all of the animals in the positive control group (group C).

In conclusion, the results of this study demonstrate that nogalamycin (NM) is an effective antineoplastic agent. Furthermore, these results reveal that NM specifically inhibits tumour promotion at low dose, while it is an effective inhibitor of both initiation and promotion at high dose.

MAKAU P. LEE* AND R. V. CHAUDHURI
Research Division,
Seragen Inc., Boston, MA 02122, U.S.A.

REFERENCES

1. Arrighi, F. E. Nucleolar RNA synthetic activity in Chinese hamster cells *in vitro* and the effects of actinomycin D and nogalamycin. *J. Cell. Physiol.*, **69** : 45–52, 1967.
2. Bempong, M. A. and R.A. Butts. Inhibition and regression of chemically induced tumour in rats by nogalamycin. *Sci. Biol. J.*, **1** : 138–143, 1975.
3. Bempong, M. A. Cytological effects of nogalamycin in mammals and regression of methylcholanthrene-induced and spontaneous tumors in rats. *Int. J. Clin. Pharmacol. Biopharm.*, **14** : 6–14, 1976.
4. Kersten, W., H. Kersten and W. Szybalski. Physiochemical properties of complexes between deoxyribonucleic acid and antibiotics which affect ribonucleic acid synthesis (actinomycin, daunomycin, cinerubin, nogalamycin, chromoycin, mithramycin and olivomycin). *Biochemistry*, **5** : 236–244, 1966.

*Address reprint request to : M.P. Lee, P.O. Box 394, Austin, Texas 78767, U.S.A.