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Lentinan, a New Immuno-accelerator of Cell-mediated Responses

BCG is almost the only agent now used as the immuno-accelerator of cell-mediated responses[1–3], but it has various biological side effects and a complicated chemical structure, so that it is not necessarily the most suitable agent. We reported that lentinan[4,5] and pachymaran[6] strongly inhibited the growth of transplanted tumours in mice, and these two polysaccharides are worth considering as excellent immuno-accelerators.

The antitumour effect of lentinan is lost in neonatal thymectomized mice, and decreased considerably by administration of antilymphocyte serum (ALS). SWM/MS mice were thymectomized by the method of Sjodin *et al.*[7] within 48 h of birth. After 6 weeks, 0.05 ml. (about 6×10^6 cells) of 7 day old sarcoma 180 ascites tumour was transplanted subcutaneously into the right groin of the TX mice (body weight 21–23 g), and from the following day 1 mg/kg of lentinan was injected intraperitoneally daily for 10 days. Five weeks after transplantation, the tumours were removed and their weights were compared with those of untreated control thymectomized mice to give the inhibition ratio. Table 1 shows the results and the antitumour activity of lentinan on normal mice. In normal mice, the tumour inhibition ratio of lentinan was 99.6% and regressed tumours completely in nine out of ten cases, but in TX mice the inhibition ratio was 6.4% and no tumours regressed.

Antilymphocyte serum (ALS) was prepared in Japanese white rabbits using mesenteric lymph node of SWM/MS mice as antigen[8]. As in the previous experiment, sarcoma 180 cells were transplanted subcutaneously in the SWM/MS mice and, from 24 h onwards, 1 mg/kg of lentinan and 0.1 ml. of ALS were injected intraperitoneally once a day for 10 days. Comparison of the tumour weight 5 weeks after trahsplantation with that of untreated control mice showed that the strong antitumour effect of lentinan was markedly reduced by ALS (Table 2).

ALS has a selective immunosuppressive effect[9–13] and is said to suppress especially cell-mediated immune responses, having little influence on humoral immune responses. According to Miller[14] and Waksman *et al.*[15–17], selective depletion of thymus-derived circulating small lymphocytes and loss of cell-mediated responses have been recognized in neonatal thymectomized mice. The fact that lentinan does not cause the regression of a tumour graft in thymectomized mice and is compensated by the administration of ALS indicates that the mode of action of lentinan is part of the thymus-derived immune mechanism, in which small lymphocytes, play an important part. This is a reasonable explanation of the suggestion that regression of a tumour caused by lentinan is the result of stimulation of cell-mediated responses, so that lentinan will provide an effective reagent for cellular immunology. Further studies on the influences of lentinan in other cell-mediated responses, such as homograft rejection and delayed type hypersensitivity, are in progress. We have no evidence that lentinan enhances the production of humoral antibody.

Table 1 Effect of Neonatal Thymectomy (TX) on Antitumour Activity of Lentinan

Mice	Sample	Dose	Body weight change	Average weight of tumour	Inhibition ratio	Complete regression
Normal mice	Lentinan	1 mg/kg × 10	+2.3 g	0.1 g	99.6%	9/10
	Control		+2.4 g	10.3 g		0/10
TX mice	Lentinan	1 mg/kg × 10	+1.6 g	7.3 g	6.4%	0/5
	Control		+2.8 g	7.8 g		0/5

Table 2 Effect of Antilymphocyte Serum (ALS) on Antitumour Activity of Lentinan

Sample	Dose	Body weight change	Average weight of tumour	D/A	Inhibition ratio	Complete regression
Lentinan	1 mg/kg × 10	+8.1 g	0.2 g	1/7	98.6%	5/7
ALS+ lentinan	1 mg/kg × 10 0.1 ml. × 10	+1.6 g	5.8 g	1/8	43.4%	0/8
ALS	0.1 ml. × 10	+1.0 g	8.5 g	1/7	16.7%	0/7
NRS+ lentinan	0.1 ml. × 10 1 mg/kg × 10	+4.8 g	2.4 g	3/5	76.7%	2/6
Control		+4.3 g	10.2 g	0/8		0/8

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