Stimulation of Humoral Immune Response by Pentosan Sulfate (SP 54)

Natural and synthetic polynuleotides and oligonucleotides[1] as well as polyanions such as polyacrylic acid[2], dextran sulfate[3], and alginic acid[4] among others[5] have been reported to stimulate the immune response to sheep red blood cells (SRBC) in mice. Antiviral activities of SP 54[6], inhibition of complement[7], and suppression of inflammatory processes by SP 54[8] have been reported recently.

It was of interest to test whether the therapeutic substance SP 54, a polyanion of low molecular weight (M $\sim$ 2000) composed of 6–12 sugar units and 2 sulfate groups per pentose, comparable in molecular weight to oligonucleotides, effects the humoral immune response as reported previously for other polyanions.

In this report we describe the effect of SP 54 on primary and secondary immune response in mice. 6–8 weeks old NMRI/Han mice were injected i.p. with SRBC suspended in 0.5 ml saline. Solutions of SP 54 (obtained from Bene-Chemie/München) containing 4.0 mg SP 54 were injected i.p. 4.0 mg SP 54 given i.p. 15 minutes prior to a suboptimal (2×10^6 SRBC) dose of antigen i.p. were found to give an optimal stimulation of immune response as compared to controls. However, no detectable effect on the immune response could be obtained in mice immunized with an optimal (2×10^8 SRBC) dose of antigen. Therefore assays to test the effects of SP 54 on the kinetics of primary and secondary immune response were performed under conditions mentioned above.

Direct (19 S) and indirect (7 S) plaque-forming cells (PFC) in the spleens of mice were assayed as described earlier[2]. Each group consisted of 7 mice. For statistical analyses the Wilcoxon test was used[9].

As shown in the Table, 4.0 mg SP 54 given at the time of priming and at the time of antigen challenge significantly enhanced the primary as well as the secondary immune response to SRBC. In contrast to poly A: poly U[1] SP 54 significantly enhanced the number of 19 S as well as 7 S PFC. Similar results (data not given here) can be obtained calculating PFC per 10^8 nucleated spleen cells.

The results demonstrate that a high molecular weight is not an inevitable requirement for the adjuvant activity of a polyanion[10].

PFC per spleen

Days after priming	19 S			7 S		
	A	B	p	A	B	p
2	128 (30–270)	281 (40–480)				
4	202 (60–420)	20,500 (4,700–64,000)	0.01			
5	601 (30–2,040)	14,350 (4,760–20,800)	0.01	366 (18–755)	8,490 (2,278–16,024)	0.01
7	266 (60–820)	4,214 (2,300–10,000)	0.01	186 (22–504)	2,750 (918–5,420)	0.01
31	182 (100–290)	374 (40–860)	N.S.	67 (5–175)	252 (6–520)	0.10
	C	D		C	D	
34	214 (80–620)	2,560 (440–9,660)	0.01	379 (99–722)	2,475 (696–62,60)	0.01
37	1,700 (700–5,960)	73,900 (21,500–132,000)	0.01	1,978 (411–7,639)	92,900 (5,784–161,460)	0.01
40	1,161 (200–4,100)	17,364 (850–41,550)	0.01	1,433 (86–4,113)	24,074 (1,250–56,637)	0.01

Mice were either B) injected with 4.0 mg SP 54 i.p. 15 min prior to the first antigen (2×10^6 SRBC) inoculation i.p. or A) injected i.p. with 2×10^6 SRBC alone. Mice of group C) were treated like group A) and challenged at the 32nd day with 2×10^6 SRBC i.p. Mice of group D were treated like group B) and injected with 4.0 mg SP 54 15 min prior to antigen challenge. N.S., not significant. The ranges are shown in brackets.

Zusammenfassung. Pentosan Sulfat (SP 54) erhöht sowohl die primäre als auch die sekundäre Immunantwort bei Mäusen, wenn diese mit einer suboptimalen Antigendosis geimpft werden.

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