Tumor-immunotherapeutic Efficacy of Serratia marcescens Polyribosomes

Richard W. Urban, Bruce S. Edwards, and William Segal

ABSTRACT

The ability of polyribosomes, obtained from several bacterial species, to suppress the development of cutaneous SaD2 fibrosarcomas in DBA/2 mice was evaluated. Suppression of tumor appearance depended upon the tumor load at the time of treatment, dose of polyribosomes, and species source of polyribosomes, with Serratia marcescens being superior to Escherichia coli, Streptococcus pneumoniae, Mycobacterium bovis (Pasteur), Mycobacterium smegmatis, and Propionibacterium acnes (formerly Corynebacterium parvum). A single injection of 5 or 50 μg of Serratia polyribosomes at the tumor site 72 hr after the intradermal administration of 1.5 × 10² SaD2 cells resulted in 66 to 95% survival. All untreated animals expired within 50 days. Tumor suppression occurred at both flank and footpad sites. Presensitization with polyribosomes and incorporation of polyribosomes into adjuvant were not required for the tumor-suppressive effect. Treatment of Serratia polyribosomes with RNase or pronase reduced the number of survivors. Endotoxin was not detectable with the Limulus amebocyte lysate assay.

INTRODUCTION

Several bacterial species belonging to the CMN³ group have proven to be active immunopotentiators in the suppression of tumors in animals and humans. BCG, a live attenuated strain of Mycobacterium bovis, has been most intensively investigated and has been found to be therapeutic in many animal tumor systems, as well as in malignant melanoma and acute myelogenous leukemia in humans (5–7, 10, 25). However, there are several serious limitations to therapy using whole bacterial cells, especially the variability of the tumor response and the high incidence of clinical complications including deaths.

In several laboratories, investigators have managed to extract fractions from bacterial cells which are immunotherapeutically active and which reduce the harmful side effects seen with whole cells. The methanol-extracted residue of BCG (24), the mycobacterial RNA fraction of Millman et al. (16), and the P. acnes cytoplasmic fraction of Millman et al. (15) seem the most promising in this respect.

Youmans and Youmans (27–32) established several years ago that ribosomal vaccines prepared from Mycobacterium tuberculosis confer protection against homologous challenge. Since then, several investigators have demonstrated that ribosomal vaccines prepared from a great variety of organisms protect animals against homologous infection (2, 4, 8, 9, 13) or homologous and heterologous infections (1, 17, 23). The emphasis of this work has been directed toward the treatment of infectious disease, and little effort has been made to evaluate these fractions in the treatment of tumors. Millman et al. (14, 16) did, however, extend the use of mycobacterial RNA vaccines to the treatment of tumors.

The mechanism of the action of the ribosomal fraction differs according to the ribosome source. Although the majority of these vaccines require adjuvant for activity, ribosomal vaccines prepared from Staphylococcus aureus (26) and Neisseria meningitidis (22) do not. In addition, vaccines prepared from M. tuberculosis (11) and Salmonella typhimurium (20) appear to induce a cell-mediated response, whereas those prepared from Streptococcus pneumoniae and Streptococcus pyogenes mediate a humoral response (21). Ribosomal vaccines therefore deserve investigation as immunotherapeutic agents, since there is a potential for manipulating the immune response and since such vaccines are generally considered to be nontoxic.

This study represents an extension of the use of ribosomal vaccines to the treatment of tumors through the use of the as yet untried polyribosome fraction. Polyribosomes from selected CMN bacteria, as well as from unrelated organisms not commonly used as tumor immunotherapeutic agents, were examined to avoid the a priori assumption of CMN antitumor superiority.

MATERIALS AND METHODS

Mice. Five-week-old male DBA/2 mice (The Jackson Laboratory, Bar Harbor, Maine) were housed under standard conditions and maintained on a Purina mouse chow diet and water ad libitum.

Tumor. Male DBA/2 mice carrying nonmetastatic SaD2 fibrosarcomas (originating as a spontaneous tumor in DBA/2 mice) were obtained from The Jackson Laboratory. Tumors were aseptically excised and mechanically dissociated in balanced salt solution (0.49% NaCl, 0.75% KCl, 0.048% CaCl₂, 0.3% MgCl₂-6H₂O, and 0.17% sodium acetate in water) using sterile forceps. Cells were quantitated in a Neubauer hemocytometer, and viabilities were determined by the trypan blue exclusion method. Tumor stocks were maintained by passaging at biweekly intervals in nonimmunosuppressed mice. For passage, 2 × 10⁶ tumor cells in 0.2 ml balanced salt solution were injected at cutaneous flank sites.

Tumor Suppression. Mice were examined 3 times/week for the development of tumors. Those mice that did not develop tumors were maintained for a minimum of 100 days following treatment.

Tumor Kinetics. A generation time for the SaD2 cells was approximated by the method of Attia and Weiss (3).

Tumor Immunity. Mice successfully rejecting a primary tumor transplant were challenged 30 days later at a contralateral site with 1.5 × 10² SaD2 cells. Absence of tumor development...
at the challenge site indicated the development of systemic tumor immunity. A challenge control group received the same number of tumor cells at the same site.

**RNase Treatment.** RNase (Sigma Chemical Co., St. Louis, Mo.; 0.5 mg/100 mg RNA dissolved in 10 mm Tris/HCl, pH 7.6) was added to a fresh polysome preparation and incubated at 4°C for 30 min prior to injection.

**Pronase Treatment.** Crystalline pronase (Sigma; 0.05 mg/ml polysome suspension) was added, and the mixture was incubated at 4°C for 30 min prior to injection.

**Endotoxin Assay.** The Limulus Amebocyte Lysate Pyrogen standard assay kit was from Mallinckrodt Chemical Works, St. Louis, Mo.

**Cultures.** *Escherichia coli B*, *S. pneumoniae*, *Serratia marcescens*, and *Mycobacterium smegmatis* were obtained from departmental stocks. BCG (Pasteur) and *Propionibacterium acnes* were provided by the National Jewish Hospital (Denver). Stock cultures were maintained in appropriate media and transferred at regular intervals.

Bacterial cultures for polyribosome extraction were raised in liquid media shaker cultures at 37°C and harvested during mid-log phase. *E. coli*, *S. marcescens*, and *S. pneumoniae* were grown as spheroplasts or protoplasts in hypertonic nutrient broth (Difco Laboratories, Inc., Detroit, Mich.) containing penicillin G potassium (E. R. Squibb and Sons, Princeton, N.J.; 200 units/ml). *P. acnes* was grown as a stationary culture in thioglycollate broth (Difco). Mycobacteria were grown in 7H11 medium containing 4.97 g of Middlebrook 7H9 broth, 5.0 ml of glycerol, 1.0 g of casein hydrolysate, and 5.0 ml of a 10% solution of Tween 80 (Sigma) per liter.

**Cell Lysis.** Prior to harvesting, all cultures were rapidly chilled to 0°C in acetone-dry ice. From this point on, all procedures were carried out at 0–4°C.

**E. coli.** Pneumococcal and *Serratia* cultures were osmotically lysed by suspension in 8 to 10 ml ribosome buffer (10 mM MgSO4·50 mM NH4Cl·10 mM Tris-HCl, pH 7.6) containing 0.15% sodium deoxycholate, DNase (Sigma), 10 mg/ml, and 1.0 mg lysozyme (Sigma). *P. acnes* and the mycobacterial species were suspended in 8 to 10 ml ribosome buffer and mechanically disrupted by passage through a prechilled pressure cell (American Instrument Co., Silver Spring, Md.) at 10,000 psi (*P. acnes*) or 15,000 psi (mycobacteria).

**Polysomes.** Cell lysates were allowed to clear for 15 to 20 min after which cellular debris was removed by centrifugation at 30,000 x g for 15 min in a Sorval RC-2B centrifuge fitted with a SS-34 head. The resulting supernatant was immediately layered on discontinuous gradients consisting of 3 ml of 15% sucrose and 5 ml of 30% sucrose for pelleting. Sucrose gradients were made with ribosome buffer as diluent. Discontinuous gradients were run at 108,000 x g for 66 min at 0–4°C with a Beckman 50 rotor in a Beckman Model L ultracentrifuge. No protease or RNase inhibitors were utilized in this study.

Polysome dosages were based on RNA content determined by the Warburg nomograph (Calbiochem, Los Angeles, Calif.) following absorbance determinations at 260 and 280 nm.

**Treatment.** Tumor cells (1.5 x 10⁶) in balanced salt solution were injected intradermally at shaved left flank (0.05 to 0.1 ml) or left footpad sites (0.02 to 0.04 ml). A given polysome dosage was administered in 0.05 to 0.1 ml ribosome buffer at 24, 48, or 72 hr after the injection of tumor cells. Both injections were administered at the same site.

**Statistics.** Survival data were arranged in a 2 x 2 contingency table, and χ² analysis was carried out using the Yates correction factor for small sample size. Where indicated, polysome-induced tumor suppression was analyzed through the use of a functional, negative, exponential transformation (θ = 0.01; t = 100 days). A detailed discussion of the method and criteria for the application of transformations is given by Liddell (12).

**RESULTS**

Tumor kinetic studies (data not presented) demonstrated that the time interval required to develop a palpable 1.0-mm mass (10⁶ cells) was directly related to the number of tumor cells injected in the range of 10² to 5 x 10⁶ cells. All animals receiving injections of tumor cells within this range, at flank sites, developed tumors and expired within 50 days. Tumor metastasis did not occur.

Tumor volumes increased exponentially and doubled every 1.1 days. Following the injection of 1.5 x 10⁶ SaD2 cells at flank sites, 61% (36 of 59 animals examined) developed a 1.0-mm mass in 9 to 12 days. This corresponded to a doubling time of approximately 1.3 days. The mean tumor appearance time for all animals was 12 days (range, 9 to 21 days). The slight difference in tumor appearance in the remaining animals was probably due to an extended lag phase prior to the onset of tumor growth.

Equivalent doses (in terms of nucleic acid content) of polyribosomes from different bacteria were administered intradermally at the sites of syngeneic SaD2 fibrosarcoma transplants in age-matched (7- to 12-week-old) male DBA/2J mice, and the immunotherapeutic effectiveness was evaluated in terms of the time at which a palpable (approximately 1 mm diameter) tumor appeared and in terms of long-term survival (100 days). The polyribosomes from *S. marcescens* were significantly (p < 0.01 to p < 0.001) superior to all the others tested (Table 1). BCG, *E. coli*, *S. pneumoniae*, *P. acnes*, and *M. smegmatis* were consecutively less effective in delaying tumor appearance (Chart 1) and in promoting long-term survival, given the limitations of the specific conditions of culture, the specific strains, and the specific doses of each of these species.

When polyribosomes from *S. marcescens* were tested in graded doses against 3-day-old fibrosarcoma transplants, a bimodal dose-response relationship was observed. Significant numbers of survivors were obtained only after the administration of 5 or 50 µg *Serratia* polysomes at the tumor site. Although the 50-µg dose was superior to the 5-µg dose in delaying tumor appearance, equivalent numbers of long-term survivors were observed in both groups in individual experiments. A 100-µg dose of *Serratia* polysomes did not delay tumor appearance significantly; however, it did suppress the rate of tumor growth (controls, 31.8 mm diameter, versus treated, 16.6 mm diameter, at 32 days posttreatment). Other doses tested (1.25, 2.5, 10, and 20 µg) were ineffective in delaying tumor appearance and in producing significant numbers of tumor-free animals. Polyribosomes prepared from the other organisms examined were ineffective at these doses.

Successful prevention of tumor appearance depended on the tumor load (Table 2). All mice receiving greater than 2 x 10⁵ SaD2 cells or treatment later than 72 hr after the receipt of 1.5 x 10⁵ tumor cells developed and succumbed to their...
Tumor Immunotherapy by *S. marcescens* Polysomes

Prior to the treatment of 72-hr flank tumor transplants resulted in insignificant numbers of survivors, 40% (4 of 10) and 20% (2 of 10), respectively (Table 3).

Endotoxin was not detectable in 5- and 15-μg samples of *Serratia* polysomes in repetitive trials. *E. coli* endotoxin (5 ng) in sterile pyrogen-free water and ribosome buffer were used as positive controls. Sterile pyrogen-free water and ribosome buffer served as negative controls.

Preliminary studies also demonstrate that 50% (5 of 10 animals; p < 0.01) of those animals suppressing a primary tumor transplant also reject a secondary transplant of 1.5 × 10³ SaD2 cells at a contralateral site with all challenge controls developing pathology in 14.6 ± 2.7 days.

**DISCUSSION**

The results reported here demonstrate that polyribosomes can be effective in the immunotherapeutic treatment of at least one tumor type at both flank and footpad sites. The effectiveness of this modality thus far appears to be dependent upon the source of polyribosomes, with those fractions obtained from *Serratia* being superior to all other sources examined, given the limitations of the specific conditions of culture, strain, and dose for each of the species used. The dose-response relationship appears to be bimodal with both the 5- and 50-μg *Serratia* polysome doses being equally effective. At these low dosages, no significant differences were noted between any polysome source or control groups before or after the treatment of 72-hr flank tumor transplants.

**Table 1**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Dosage (μg)</th>
<th>S/N a</th>
<th>% of survivors b</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Serratia</em></td>
<td>1.25</td>
<td>0/10</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2.5</td>
<td>0/10</td>
<td>0</td>
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</tr>
<tr>
<td></td>
<td>5.0</td>
<td>20/30</td>
<td>66.7&lt;sup&gt;d&lt;/sup&gt;</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>4/10</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>3/10</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td></td>
<td>50</td>
<td>8/10</td>
<td>80</td>
<td>&lt;0.01</td>
</tr>
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<td></td>
<td>100</td>
<td>0/10</td>
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<td><em>E. coli</em></td>
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<td></td>
</tr>
<tr>
<td></td>
<td>2.5</td>
<td>0/10</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>5.0</td>
<td>4/20</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>1/20</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>0/20</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td><em>BCG</em></td>
<td>5.0</td>
<td>1/20</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td><em>P. acnes</em></td>
<td>5.0</td>
<td>0/20</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td><em>M. smegmatis</em></td>
<td>5.0</td>
<td>0/10</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Ribosome buffer only</td>
<td>5.0</td>
<td>1/10</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>No treatment</td>
<td>0/100</td>
<td>0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup> All mice received 1.5 × 10³ SaD2 cells i.d. at Time 0 and were given no treatment, ribosome buffer, or a single injection of polyribosomes at the same site 72 hr later.

<sup>b</sup> S/N, tumor-free animals 100 days posttreatment per total number treated.

<sup>c</sup> Number of tumor-free animals at 100 days per total number of treated animals.

<sup>d</sup> Represents 3 trials. Individual results were: 6 of 10, 6 of 10, 8 of 10.

<sup>e</sup> Dosages listed under *Serratia* were negative for this organism.

<sup>f</sup> Pooled controls.

**Table 2**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>72 (hr)</th>
<th>S/N a</th>
<th>% of survivors b</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>No treatment</td>
<td>20/30</td>
<td>66.7&lt;sup&gt;d&lt;/sup&gt;</td>
<td>&lt;0.01</td>
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<tr>
<td>24</td>
<td>66&lt;sup&gt;d&lt;/sup&gt;</td>
<td>&lt;0.01</td>
<td></td>
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<tr>
<td>48</td>
<td>95&lt;sup&gt;d&lt;/sup&gt;</td>
<td>&lt;0.01</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup> All mice received 1.5 × 10³ SaD2 cells i.d. at Time 0 and were subsequently given no treatment, ribosome buffer, or a single injection of 5 μg of *Serratia* polyribosomes at the same site 24, 48 or 72 hr later.

<sup>b</sup> S/N, tumor-free animals 100 days posttreatment per total number treated.

<sup>c</sup> Number of tumor-free animals at 100 days per total number of treated animals.

<sup>d</sup> Represents 3 trials. Individual results were: 6 of 10, 6 of 10, 8 of 10.

<sup>e</sup> Represents 2 trials. Individual results were: 6 of 10, 6 of 10, 7 of 10.

<sup>f</sup> Pooled controls.

**Table 3**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>S/N a</th>
<th>% of survivors b</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 μg polysomes</td>
<td>6/10</td>
<td>60</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>5 μg RNase-treated polysomes</td>
<td>4/10</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td>5 μ pronase-treated polysomes</td>
<td>2/10</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>RNase only</td>
<td>0/10</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Pronase only</td>
<td>0/10</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Buffer only</td>
<td>0/10</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>No treatment</td>
<td>0/10</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup> All animals received 1.5 × 10³ SaD2 cells i.d. at Time 0 and were given no treatment, ribosome buffer, RNase in ribosome buffer, pronase in ribosome buffer, 5 μg polysomes, 5 μg RNase-treated polysomes, or 5 μg pronase-treated polysomes in equivalent doses and volumes.

<sup>b</sup> S/N, tumor-free animals 100 days posttreatment per total number treated.

<sup>c</sup> Number of tumor-free animals at 100 days per total number of treated animals.

---

*Source of Polyribosomes* | T<sub>A</sub> | SE | ΔT<sub>A</sub> (DAYS) | 10 | 20 | 30
<table>
<thead>
<tr>
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<th></th>
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<tbody>
<tr>
<td><em>S. Marcescens</em></td>
<td>0.8820</td>
<td>0.043</td>
<td></td>
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<td></td>
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<tr>
<td><em>M. Bovis</em> (BCG)</td>
<td>0.5718</td>
<td>0.058</td>
<td></td>
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<tr>
<td><em>E. Coli</em></td>
<td>0.5404</td>
<td>0.048</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td><em>S. Pneumoniae</em></td>
<td>0.5004</td>
<td>0.063</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><em>C. Parvum</em></td>
<td>0.4703</td>
<td>0.028</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>M. Smegmatis</em></td>
<td>0.4323</td>
<td>0.024</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>UNTREATED</td>
<td>0.4179</td>
<td>0.041</td>
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</tr>
</tbody>
</table>

* Chart 1: Comparison of the immunotherapeutic effectiveness of polyribosomes from 6 species of bacteria. Mice bearing 72-hr-old transplanted fibrosarcomas (SaD2) were inoculated at the tumor site with 5 μg of the appropriate polyribosomal extract. *, mean tumor appearance time (statistical analysis performed after negative exponential transformation of data to eliminate censoring; see Ref. 12); 1, S.E.; †, transformed data reconverted to days; ΔT<sub>A</sub>, T<sub>A</sub> of polyribosome treated group − T<sub>A</sub> of controls.

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Tumors. When treatment was begun earlier (at 24 or 48 hr), the number of tumor-free mice increased, presumably due to a reduced tumor load at these times. Groups that received 5 μg *Serratia* polysomes at 24 or 48 hr following the injection of 1.5 × 10³ SaD2 cells at flank sites were, respectively, 95 and 65% tumor free at 100 days. Control animals (sham treated and untreated) all developed tumors at 14 ± 3.3 (S.E.) days and expired within 50 days.

Similar results were obtained at footpads sites. Intradermal injection of 1.5 × 10³ SaD2 cells in the left rear footpad, followed by 5 μg *Serratia* polysomes 72 hr later at the same site, resulted in 80% (8 of 10; p < 0.01) tumor-free mice at 100 days posttreatment.

Treatment of *Serratia* polysomes with RNase or pronase...
doses, the observed dose response could represent stimulation of 2 different effector cell populations. This possibility is currently being investigated in our laboratory. The results given here indicate that S. marcescens polyribosomes are effective against residual tumor loads; however, work in progress demonstrates consistent regression of established tumors (5 mm diameter) by Serratia polysomes, with the response being dose dependent.

The presence of endotoxin (a potent lipopolysaccharide found in the cell walls of gram-negative bacteria) in our preparation was not unequivocally ruled out. Treatment of Serratia polysomes with RNase or pronase reduced the number of survivors. Diarrhea, hair ruffling, ulceration of injection sites, and conjunctivitis have not been observed in non-tumor-bearing or tumor-bearing mice following single intradermal injections of Serratia polysomes in doses ranging from 1.25 μg to 1.0 mg. Single intradermal Serratia polysome injections (0.4 to 1.0 mg) in guinea pigs result in very mild localized inflammatory reactions with little or no erythema. The response is maximal at 24 hr and absent by 48 hr in non-tumor-bearing animals. Mice, guinea pigs, and rats respond to endotoxin with no temperature change or a hypothermic response. Thus far, all animals treated with Serratia polysomes have demonstrated a moderate hyperthermic response (2–3°C) which consistently begins in 30 min following treatment. The duration of hyperthermia appears to depend upon the presence or absence of tumor and the tumor load at the time of treatment. In addition, Limulus amebocyte lysate assays of Serratia polysome preparations are consistently negative; however, endotoxin could be present at concentrations of less than 5 ng/15 μg of polyribosomal RNA. Such a low concentration of endotoxin, if present, could not account for the observed tumor-suppressive effect. In addition, it is well established that endotoxin is not effective in the treatment of residual tumor loads.

The mechanism of the immune response could not be determined from the data presented here. Reduction in the number of survivors obtained, when polysomes were treated with pronase or RNase, suggested a requirement that these aggregates be intact in order to achieve an optimal response. Polysome profiles differed significantly among each of the organisms examined, and it is conceivable that the size of a particular aggregate or the degree of aggregation was an important parameter in determining the level of induction. The aggregate nature of polyribosomes was also probably responsible for the development of an effective response in the absence of complete or incomplete Freund’s adjuvant. Such adjuvants are usually required for effective use of most ribosomal vaccines.

By virtue of their RNA content and large molecular size, polyribosomes may stimulate the release and/or production of interferon which then could activate resident macrophages as nonspecific killers (18, 19). Interferon production is typically maximal within 24 hr of the inducing stimulators. The bimodal response could be explained if 2 different cell populations are stimulated. Polysome-based immunotherapy may then be more specific than other forms of immunopotentiation.

The predictable nature of the antitumor response, high levels of long-term survival, and absence of secondary complications suggest that polyribosomes may offer a new and more effective approach to the experimental study of tumor immunotherapy.

REFERENCES


28. Youmans, A. S., and Youmans, G. P. Immunogenic activity of a ribosomal...


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