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RNP, Sm and SS-B Antigens from Calf Thymus: Molecular Stability upon Enzymatic Digestion

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RNP, Sm and SS-B nuclear antigens from calf thymus were studied with respect to the size distribution on sucrose gradients as well as to the molecular integrity and related structural changes when they were subjected to enzymatic digestions under different conditions. Making a difference with RNP particles, the Sm size distribution is concentration dependent, a property in accordance with the complexity of the Sm particles in comparison with the RNPs. The use of combined effects of temperature, endogenous proteases and RNase A, allowed us to gain insight into the limits of stability of the three antigenic particles. Following treatments in the absence of RNAse A, the degradation products (32-38 Kd molecular weight) of the 70 Kd RNP polypeptide remain stable and associated with other molecules within the RNP particle. It was also found that the phosphate groups of the SS-B protein moiety are only accessible to alkaline phosphatase if the RNA of the SS-B particle is degraded by the action of RNAse A.

Key words: Autoantibodies, Sm, SS-B, RNP, U1snRNP, USnRNPs, Anti-Sm, Anti-RNP.

The discovery that sera from rheumatic patients recognize a set of small ribonucleoproteins has facilitated the study of the structure and function of such particles. RNP, Sm and SS-B nuclear antigens are classes of ribonucleoproteins composed by different small RNAs associated with one or more polypeptides (15).

Evidence indicates that the antigenic determinants of RNP and Sm antigens reside in the protein moieties (12). It has been suggested that both ribonucleoproteins are involved in the pre-mRNA splicing mechanism (3-5, 10). The RNA moiety of SS-B (La) antigen is associated to a single phosphorylated polypeptide (7, 18) that is recognized by anti-SS-B sera. A possible implication in the transport mechanism of small RNAs has been stated for the SS-B ribonucleoprotein (8, 20).

Previous results (6, 16), using calf thy-

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mus as a source of nuclear antigens, demonstrated that the antigenic protein moieties of RNP, Sm and SS-B can keep their molecular integrity in extracts prepared under conditions of minimal degradation, whereas they can undergo degradable processes during the preparation of nuclear extracts or by the action of exogenous proteases. The susceptibility of these three antigens to particular enzymatic treatments, mainly to ribonuclease and protease digestions, has also been reported by other authors (1). In general, the effect of such enzymes is deduced from changes observed in the immunoprecipitation lines using the technique of counterimmunoelectrophoresis. This technique yields valuable but limited information, mainly because difficulties exist in the interpretation of results different from an all-none effect.

In this paper, we present a study on the size distribution of the above mentioned antigenic particles, as well as on their molecular stability when they are treated with degradative enzymes under different conditions. Our findings, based on the comparison of the three antigens, are a contribution to the knowledge of these antigens that appear so important to our understanding of several autoimmune diseases, and so important for several functional mechanisms within the cell.

Materials and Methods

Inhibitors. — Unless stated, all buffers contained the following proteolytic inhibitors: $PhMeSO_2F$* 1 mM; leupeptin 4 µg/ml and aprotinin 340 kallikrein inhibitor units/ml (2).

* *Abbreviations:* ASS, ammonium sulphate saturation; HSS, high sped supernatant; Pi/NaCl, 10 mM sodium phosphate, 0.15 M NaCl, pH 7.5; $PhMeSO_2F$, phenylmethylsulphonyl fluoride; SDS/PAGE, sodium dodecylsulphate/polyacrylamide gel electrophoresis; Smax, sedimentation coefficient at the maximum antigenic activity.

Sera. — Three specific human sera from rheumatic patients, coded as SO, GG and EM, were used as a source of anti-Sm, anti-RNP and anti-SS-B-/Sm, respectively. The serum specificity was demonstrated by an immunoblotting procedure described elsewhere (12). The SO serum reacts with Sm polypeptides (the 29, 30 Kd doublet and the 15 Kd and 11 Kd, single components); the GG serum recognizes the 70 Kd RNP polypeptide as well as the RNP degradation products ranging 25-38 Kd; finally, the EM serum reacts with the 52 SS-B polypeptide, as well as with the 29, 30 Kd Sm doublet and the 11 Kd Sm polypeptide.

Nuclear extract. — The preparation of the nuclear extract, referred to as HSS, was previously described (6, 21). The protein concentration in this extract, as well as in the extracts described in the two next paragraphs, was determined by the method of Lowry *et al.* (14).

Whole protein extract. — Whole calf thymus tissue was prepared as previously described (2).

Extract containing an undegraded SS-B enriched fraction. — An enriched SS-B extract called fast 90 % ASS fraction, with no RNP or Sm activity, was obtained from whole calf thymus tissue by ammonium sulphate saturation (70-90 %) as previously described (2).

Enzymatic treatments. — Extracts containing RNP, Sm and SS-B antigens were treated with RNAse A (80 U/mg, Sigma) in Pi/NaCl under conditions stated in each experiment (see figs. 2-7). In the case of SS-B digestions prepared for analysis on non-denaturing gels, a 0.4 M Tris-HCl, 0.1 mM EDTA (pH 8.9) incubation buffer was used (fig. 8).

The above mentioned SS-B 90 % AAS fraction was digested for 30 min at 37 °C with alkaline phosphatase (2000 U/mg,

Boehringer) in 0.4 M Tris-HCl, 0.1 mM EDTA (pH 8.9) incubation buffer with 8.3 U enzyme/mg protein (fig. 8).

Incubations of samples to be analyzed by ultracentrifugation (figs. 2, 6, 7) in a sucrose gradient were stopped by cooling to 0 °C, and the samples were immediately applied to the sucrose cushion. Incubations of samples to be analyzed by SDS/PAGE (figs 3, 4) were stopped by addition of the corresponding sample buffer; the samples were cooled to 0 °C, and immediately loaded into the electrophoretic tracks. In the case of non-denaturing electrophoresis (fig. 8), before loading into the tracks, incubations were stopped by cooling to 0 °C, and the samples made dense with 4 % ficoll and coloured with 0.001 % bromophenol blue.

Density gradient centrifugation assays. — Samples (200 µl) were loaded on a linear 5-30 % sucrose gradient in Pi/NaCl and centrifuged for 13 h at 256,000 *g* at 4 °C. *E. coli* 23 S, 16 S and 5 S rRNA (Boehringer) were used as markers. Fractions of 0.5 ml were collected and the protein concentration was determined. The maximal protein content was located around 4-5 S. The fractions were also assayed for antigenic activity by the dot immunodetection method and immunoblotting as described below. Since both methods yielded a very similar distribution of antigenic activities along the gradient, only the immunodot pattern is presented in the figures. Duplicate experiments were performed, and the same results were obtained each time.

Low speed centrifugation assays. — A sample (150-200 µl) of the suspension of the above described whole protein extract was digested at 37 °C for 30 min with RNAse A. An aliquot (50 µl) of the product of the digestion was centrifuged at 10,000 *g* for 10 min at 4 °C. The pellet was suspended in 50 µl of Pi/NaCl. Supernatant and pellet should complement one another in terms of the antigenic RNP bands corresponding to the digest products. Laemmli's sample buffer (150 µl) was added to each 50 µl of the supernatant and the resuspended pellet. Further treatments of the samples were performed as in the case of RNase A digests. The final samples were analyzed by SDS/PAGE and immunoblot using an anti-RNP serum as a probe. Duplicate experiments yielded the same results.

Electrophoresis, immunoblotting and dot immunodetection. — 15 % SDS/PAGE was performed according to the LAEMLI procedure (11). Bovine serum albumin (66 Kd, Biochemicals), ovalbumin (45 Kd, Sigma), carbonic anhydrase (29 Kd, Sigma), soybean trypsin inhibitor (21 Kd, Sigma) and lysozyme (14.3 Kd, Sigma) were used as markers.

Polyacrylamide gel electrophoresis (4-18 %) in non-denaturing conditions was carried out according to the method described by the PAGE Pharmacia manual (1980), but without stacking gel. Bovine serum albumin was used as a control of protein mobility. Gels were stained with Coomassie brilliant blue R250, and immunoblotted as described below.

The electroblotting procedure was carried out by transferring polyacrylamide gels to nitrocellulose sheets (BA85, Schleider and Schüll) at 210 mA for 6 h in a Bio-Rad Transblot device (19) in the presence of 0.1 % SDS. Immunodetections were performed as described elsewhere (6).

A dot immunodetection assay under non-denaturing conditions was employed to detect the antigenic activity in all fractions recovered from the ultracentrifugation in sucrose gradients. Aliquots (150 µl) of each fraction were blotted onto nitrocellulose paper according to the method described previously (2). Autoradiograms were scanned in a Joyce-Loebl microdensitometer. For each set of experiments, the antigenic activity (measured in arbitrary units) was normalized with respect to the

maximum value and plotted against the sedimentation coefficient of the corresponding fraction.

When electrophoresis, immunoblotting and dot immunodetection duplicated experiments were performed, identical results were obtained.

Results and Discussion

RNP antigen. — Previous results showed that the calf thymus 70 Kd RNP protein is mostly degraded during the preparation of HSS extracts giving rise to two shorter polypeptides of apparent molecular weights in the range of 32-38 Kd. These polypeptides can be considered as stable structural domains of the 70 Kd antigenic moiety (6), in the sense that they are very resistant to a further endogenous proteolytic degradation. It would be interesting to know the effect of molecular degradations on the properties of the RNP particle. In the present paper we describe the behaviour and structural alterations of the undissociated RNP complex subjected to combined partial digestions of both the protein and nucleic acid moieties under different experimental conditions.

First, we studied by density gradient centrifugation the sedimentation behaviour of the RNP particles, containing the 32-38 Kd polypeptides concentrations (4 and 14 mg protein/ml), representative of series of experiments performed at different protein concentrations. As fig. 1 shows for both protein concentrations, the significant antigenic distribution is between 9 S and 20 S with a Smax at about 10.5-11.85 (showing variations not higher than ± 1.5 S, in different experiments). As a control, the presence of the 32-38 Kd polypeptides was detected by immunoblotting in all the antigenic fractions of the gradient (results not shown). The size of the particles, as well as the lack of antigenicity in fractions of low S values, indicate that proteolysis of the 70Kd protein takes place within the particle, with no previous dissociation. It also indicates that the 32-38 Kd polypeptides remain firmly

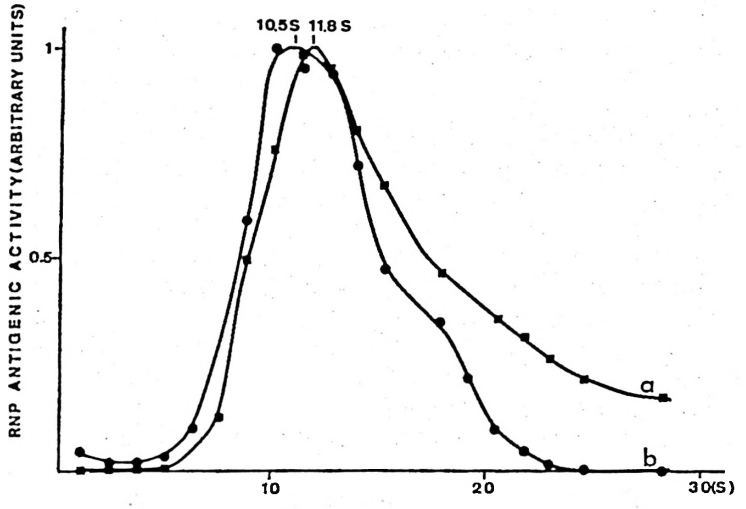

Fig. 1. *Concentration effect on size distribution of the RNP antigen through sucrose gradient detected by the immunodetection method.*
Freshly prepared HSS extracts were loaded onto sucrose cushions at two protein concentrations: a) 14 mg protein/ml, and b) 4 mg protein/ml. The GGanti-RNP serum was used for detecting the RNP activity.

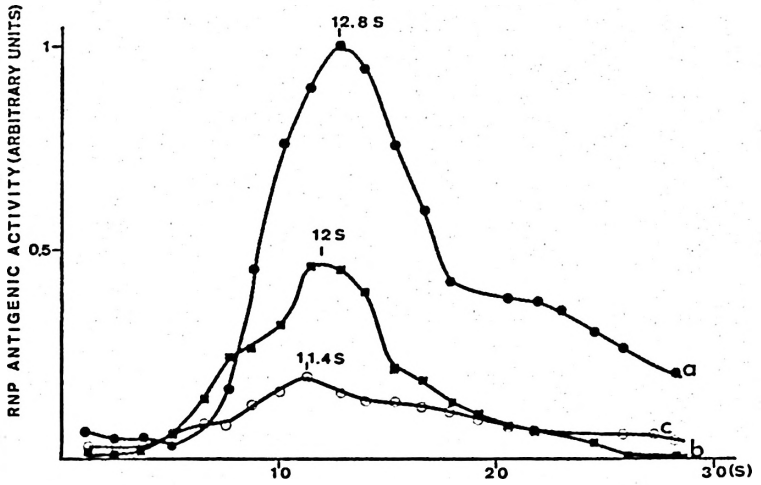

Fig. 2. *Effect of temperature and RNase A treatments on size distribution on the RNP antigen through sucrose gradients.*

The antigenic RNP activity was detected with the anti-RNP serum GG. Samples loaded onto each sucrose cushion were HSS extracts (14 mg protein/ml) treated at 37 °C during 1 h as following: a) in the presence of 1 mM $PhMeSO_2F$; b) with RNase A in the presence of protease inhibitor mixture (see Materials and Methods); c) with RNase A in the presence of $PhMeSO_2F$, 1 mM. In b) and c) the relation of concentrations was 1 mg RNase A/10 mg protein.

associated to snRNAs, since they still had the size of a particle (between 10.5-11.85).

In order to know whether the nucleic acid moiety stabilizes the integrity of the RNP particle, nuclear HSS extracts (14 mg of protein/ml) were digested with RNase A at 37 °C in the presence of protease inhibitors (either $PhMeSO_2F$ or the protease inhibitor mixture). This set of experiments allows to study the effect of protease inhibitors in stabilizing the protein moiety and preventing disruption of the whole antigenic particle by RNase A digestion. Curve a in the fig. 2 shows that, after 37 °C incubation of HSS in absence of RNase, the Smax (12.8 S) is still located in the range of untreated HSS extracts, a fact indicating that there is no relevant change in the overall size of the particles in the control experiment. Curve c in fig. 2 shows that the digestion with RNase A, performed in the presence of $PhMeSO_2F$, eliminates concomitantly the RNP antigenic activity, with the exception of a small peak around 11.4 S. As curve b of fig. 2 shows, the presence of the inhibitor mixture partially prevents the elimination of the RNP activity and the Smax is also located at 12 S.

From these experiments it can be concluded that there is a close relationship between RNA digestion and endogenous proteolysis (fig. 3). The 32-38 Kd polypeptides present in the HSS extract remain complexed to snRNAs, and the most effective proteolytic inhibitors stabilize, in part, the integrity of the RNP particles from RNase digestion, otherwise the Smax would shift to significant lower values.

Surprisingly, after an RNase A treatment, the 32-38 Kd RNP polypeptides cannot be detected in fractions with a sedimentation coefficient lower than 7 S, as revealed not only by the immunoblot technique used but also by immunoblotting (results not shown). This suggests that, either these polypeptides are un-

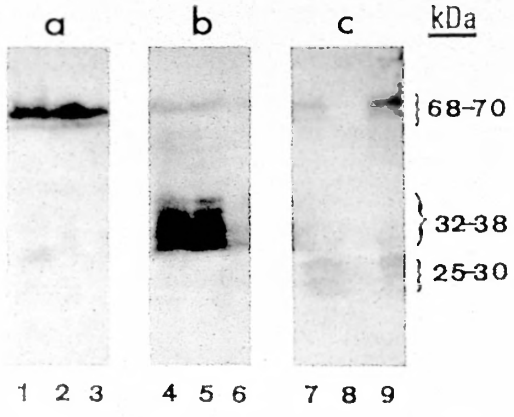

Fig. 3. *Effect of temperature and RNase A treatments on the stability of the antigenic RNP protein moiety.*
Treatments performed: a) the whole protein extract kept at 4 °C during 30 min; b) temperature treatment at 37 °C during 30 min; and c) with RNase (at a relation of 1 mg RNase A/10 mg protein) at 37 °C during 30 min. In all cases, the extracts were further centrifuged (10000 g, 10 min). Electroblots were incubated with protein extracts; lanes 2, 5, 8: supernatants; and lanes 3, 6, 9: pellets.

stable and are rapidly degraded, or that their tertiary structure is modified causing a loss of antigenicity. A third possibility is that, when release from RNA after RNase digestion, the polypeptides become insoluble, precipitate and are no longer detected. In order to gain insight into this question, we performed a set of experiments to follow the fate of the 70 Kd polypeptide corresponding to undegraded RNP and also of the 32-38 Kd RNP degradations after RNase A treatment.

Previous results (6) demonstrated by electroblot that freshly prepared nuclei from calf thymus (containing only the undegraded 70 RNP polypeptide), yielded 32-38 Kd polypeptides in the supernatant after an extraction with Pi/NaCl and a further low speed centrifugation. In contrast, the 70 Kd polypeptide remained in the pellet. In order to study the effect of enzymatic inhibitors on the integrity of the 70 Kd polypeptide subjected to endogeneous proteolysis, we obtained whole protein extracts in the presence of the protease inhibitor mixture and centrifuged at low speed. Fig. 3a shows the distribution of the undegraded 70 Kd polypeptide, before (lane 1) and after centrifugation (lanes 2-3). Unlike previous results for calf thymus nuclei (6), this polypeptide is mainly detected in the supernatant as an undegraded form (lane 2), as it is the case for the non-centrifuged aliquot and for the pellet. The success in keeping the 70 Kd polypeptide preserved from degradation must be attributed to a combination of the rapid performance, temperature, and presence of the mixture of inhibitors. As shown in fig. 3b for the control at 37 °C (*i. e.* using protease inhibitors but no RNase A) the 32-38 Kd banding pattern is predominant in all cases (non-centrifuged aliquot, supernatant and pellet). From the antigenic amounts recovered (fig. 3b), it can be deduced that the material detected in the pellet corresponds to contamination and most of the antigenic activity is in the supernatant. RNase A treatment under the same conditions (fig. 3c) shows the disappearance of the 32-38 Kd banding pattern, although a new group of weak antigenic bands (in terms of immunoresponse) in the range of 25-30 Kd are observed in the non-centrifuged aliquot (lane 7) and in the pellet (lane 9). The 25-30 Kd banding pattern is also observed in HSS extracts (that contain only the 32-38 Kd polypeptides) after RNase A digestion under similar conditions as those described for the whole protein extract (results not shown).

In order to follow the fate of the 70 Kd protein while the RNA moiety is being degraded, we performed two digestions of the whole protein extract at 0 °C with RNase at the enzyme/protein ratio of 1/1 and 1/10 (w/w). Fig. 4a shows that there is no apparent degradation of the 70 Kd polypeptide during incubations at low

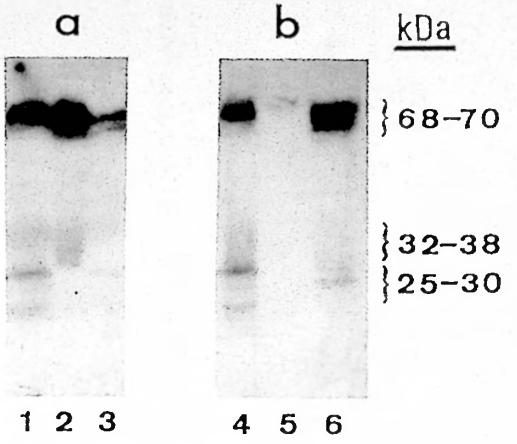

Fig. 4. *Effect of RNase A treatment at different enzymatic concentrations on the stability at low temperature of the RNP antigenic protein moiety.* Treatments performed: a) the whole protein extract treated with RNase A (at a relation of 1 mg RNase A/10 mg protein) at 0 °C during 30 min; and b) with RNase A (at relation 1 mg RNase/1 mg protein) at 0 °C during 30 min. In both cases, the extracts were further centrifuged (10000 *g*, 10 min. Electroblots were incubated with the GG anti-RNP serum. Lanes 1, 4: treated whole protein extracts; lanes 2, 5: supernatants; and lanes 3, 6: pellets.

RNase concentrations. However, in the presence of a higher concentration of the enzyme (fig. 4b), the undegraded 70 Kd polypeptide migrates with the pellet (lane 6) and is not detected within the supernatant (lane 5). The RNase A digestion of the RNP particle is effective at 37 °C but not at 4 °C. At this low temperature, it is necessary to increase the RNase concentration up to 10 times in order to reach complete digestion, a fact that causes insolubility of the remaining protein moiety. These findings on the RNA stability are in agreement with results reported by other authors (22, 23).

Sm antigen. — Studies on the size of the antigenic Sm particles were carried out by loading the nuclear HSS extracts in sucrose gradients. The experiments were simultaneously and similarly performed as described in the previous section.

At a protein concentration of 14 mg/ml, the distribution curve shows an Smax around 12.8 S (fig. 5, curve a), whereas at 4 mg/ml the Smax is clearly shifted to 8.8 S (fig. 5, curve b). It is interesting to note

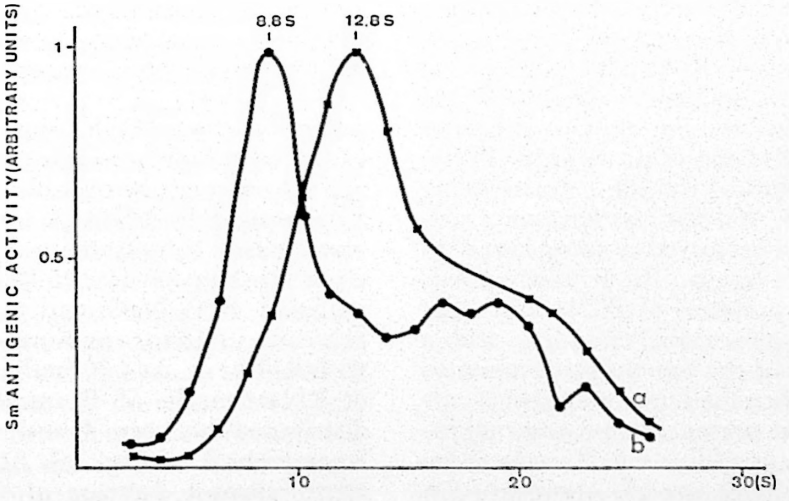

Fig. 5. *Concentration effect on size distribution of the Sm antigen through sucrose gradients.* Freshly prepared HSS extracts were loaded onto a sucrose cushion at two protein concentrations: a) 14 mg protein/ml, and b) 4 mg protein/ml. The anti-Sm serum (SO) was used for detecting the Sm activity.

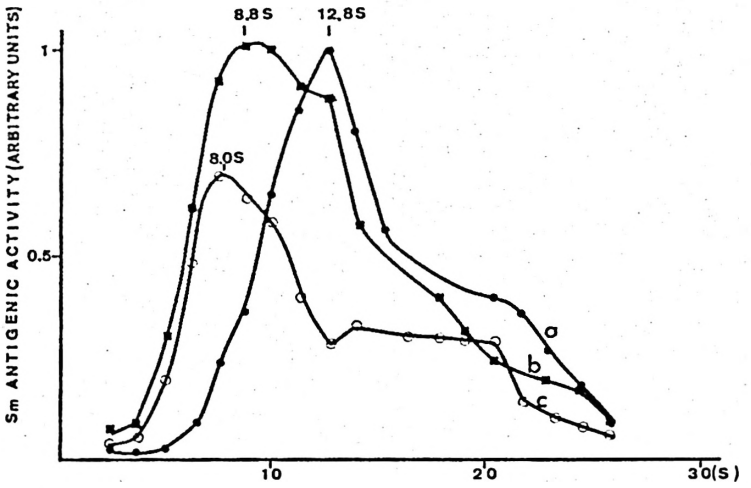

Fig. 6. *Effect of temperature and RNase A treatments on size distribution of the Sm antigen through sucrose gradients.*
The antigenic Sm activity was detected with the anti-Sm serum SO. Samples loaded onto each sucrose cushion were HSS extracts (14 mg protein/ml) treated at 37 °C during 7 h as following: a) in the presence of 1 mM $PhMeSO_2F$; b) with RNase A in the presence of the protease inhibitor mixture; c) with RNase A in the presence of 1 mM $PhMeSO_2F$. In b) and c) the relation of concentrations was 1 mg RNase A/10 mg protein.

that at high concentrations the maximum for the RNP and Sm activities are very close (around 12 S). However, an essential distinction is that the Sm size distribution is concentration-dependent.

Experiments on RNase A treatment and further sucrose gradient analysis were also carried out for the Sm antigen at a concentration of 14 mg of protein/ml. In fig. 6, curve a shows, for the extracts being kept 1 h at 37 °C, that the Sm size distribution is well preserved as compared with that shown in fig. 5a. The RNase A treatment in the presence of $PhMeSO_2F$ (fig. 6c) rises complexes smaller in size, with a relevant loss of the Sm antigenic activity. However, when the same treatment is carried out in the presence of protease inhibitor mixture, in addition to the size shifting effect, a slight overall increase of Sm activity (about 20 %) is observed (fig. 6b). JUÁREZ *et al.* (9), using an ELISA method, have described an outstanding increase of the Sm activity upon RNase A digestion. The magnitude of the effect, as shown by these authors, is higher than in our case, but differences in the procedures followed and in the experimental conditions make difficult to evaluate the extent and meaning of both reported evidences.

SS-B antigen. Following a pattern of experiments similar to those used for RNP and Sm antigen, the overall stability of the SS-B antigen in RNase A treated extracts was studied by ultracentrifugation in sucrose gradients. A fast 90 % ASS fraction prepared in Pi/NaCl and containing the protease inhibitor mixture was treated with RNase A. At 4 °C and in the absence of RNase A the SS-B antigen is mostly distributed between 4 and 12 S with a Smax around 9 S (fig. 7a). At 37 °C treatment causes a decrease of SS-B activity with a broad maximum placed at 6-9 S (fig. 7b). The RNase A treatment at 37 °C during 30 min (fig. 7c) gives rise to a rather sharp antigenic distribution centered

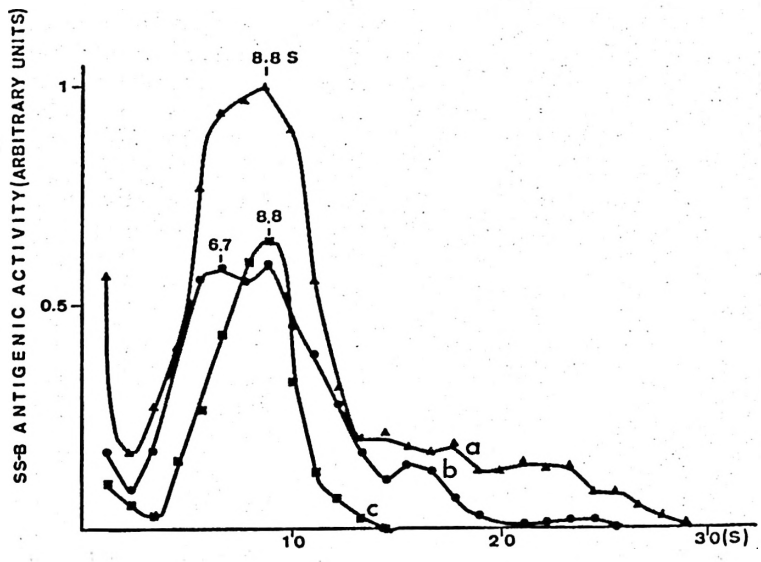

Fig. 7. *Effect of temperature and RNase A treatments on size distribution of the SS-B antigen through sucrose gradients.*
The antigenic activity in each fraction from the sucrose gradient was assayed by dot immunodetection and incubated with the anti SS-B/Sm serum (EM). The fast 90 % ASS fraction (exempt of Sm activity) was subjected to the following treatments: a) control at 4 °C during 30 min; b) temperature treatment at 37 °C during 30 min; and c) with RNase A (at a relation of 1 mg RNase A/10 mg protein) at 37 °C during 30 min. The three experiments were performed in the presence of the mixture of inhibitors.

around 9 S and an overall decreased activity in comparison with the two controls.

It has been reported that the SS-B protein contains phosphate (7, 18) and, therefore, the accessibility of these phosphorylated groups to phosphatases is a matter of interest. We studied the combined effects of RNase A and alkaline phosphatase on the migration of the SS-B complex in non-denaturing gels. Figure 8 (lane 1) shows the immunodetected pattern (one main band and a thinner one) of the SS-B complex present in the fast 90 % ASS fraction. A correspondence between the main band and the SS-B 52 Kd polypeptide was demonstrated (results not shown) either by electroblotting a second running in SDS/PAGE, or by immunoreaction with specific antibodies against the 52 Kd polypeptide eluted from nitrocellulose strips following a technique described previously (6). Samples containing fast 90 % ASS fraction were incubated at 37 °C and treated with RNase A and/or alkaline phosphatase in the presence of the protease inhibitor mixture. An immunoblot control from SDS/PAGE was made for each treatment in order to test that a unique 52 Kd polypeptide was present. The electrophoretic mobility of the SS-B particles as well as their antigenic activity are not affected by the incubation at 37 °C (fig. 8, lane 2). As shown in fig. 7, an RNase A treatment causes a partial decrease of the sedimentation coefficient, indicating that a fraction of the SS-B particles is partially degraded. This result correlates with the electrophoretic analysis under non-denaturing conditions of the same RNase A treated extract, since it

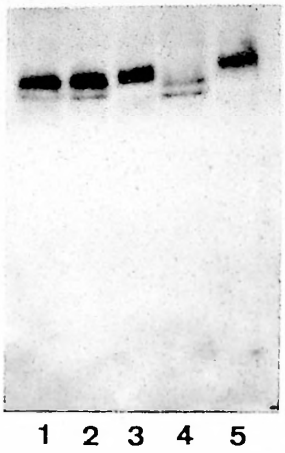

Fig. 8. *Combined effects of RNase A and alkaline phosphatase on the integrity of the antigenic SS-B protein moiety.*
The electroblot was performed from a non-denaturing gel incubated with the anti-SS-B/Sm serum (EM). Samples loaded were the fast 90 % ASS fraction subjected to the following treatments: lane 1, without treatment; lane 2, temperature control at 37 °C during 30 min; lane 3, with RNase A (at a relation of 1/10) at 37 °C during 30 min; lane 4, with alkaline phosphatase (at a relation of 8.3 U enzyme/mg protein) at 37 °C during 30 min; and lane 5, with RNase A (at a relation 1/10) and alkaline phosphatase (at a relation of 8.3 U enzyme/mg protein) at 37 °C during 30 min. All experiments were performed in the presence of the mixture of inhibitors.

shows (fig. 8, lane 3) that a partial RNase A treatment causes a change in the mobility of the SS-B complexes (fig. 8, lane 3), that might correspond to a partial degradation of the nucleic acid moiety giving rise to less acidic complexes. The alkaline phosphatase by itself does not cause any relevant change in the mobility of the complex (fig. 8, lane 4), but it rises a major shift when acting together with RNase A (fig. 8, lane 5). In some experiments we have observed a slight decrease of the antigenicity after alkaline phosphatase treatment (not shown). This observation agrees with PFEIFLE *et al.* (17) who reported that the binding of human autoantibodies against SS-B antigen increases 2-fold with increased SS-B phosphorylation. These experiments show that mobility of the SS particle is affected by alkaline phosphatase only if RNase is present, a fact indicating that the phosphate groups of the SS-B protein are only accessible if some of the RNA moiety is partially lost, allowing the action of the alkaline phosphatase. In addition, and combining the effects, the alkaline phosphatase could cleave terminal phosphate groups of residual ribonucleic acid present in the particle after a limited RNase A digestion.

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Resumen

Los antígenos nucleares RNP, Sm y SS-B de timo de ternera han sido estudiados con respecto a la distribución de tamaños en gradientes de sacarosa y a la integridad molecular y cambios estructurales relacionados cuando éstos están sujetos a digestiones enzimáticas bajo diferentes condiciones. A diferencia de las partículas RNP, la distribución de tamaños del antígeno Sm depende de la concentración, propiedad que está de acuerdo con la complejidad de las partículas Sm en comparación con las RNP. El uso de efectos combinados de temperatura, proteasas endógenas y RNasa A, permite profundizar en los límites de la estabilidad de las tres partículas antigénicas. Después de tratamientos en ausencia de RNasa A, los productos de degradación (32-38 Kd de peso molecular) del polipéptido RNP de 70 Kd permanecen estables y asociados con otras moléculas de la partícula RNP. Los grupos fosfato de la porción proteica SS-B son solamente accesibles a la fosfatasa alcalina si el RNA de la partícula SS-B es degradado por la acción de la RNasa A.

Palabras clave: Autoanticuerpos, Sm, SS-B, RNP, U1snRNP, UsnRNPs, Anti-Sm, Anti-RNP.

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