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REVIEW

Human ribonuclease P: Subunits, function, and intranuclear localization

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ABSTRACT

Catalytic complexes of nuclear ribonuclease P (RNase P) ribonucleoproteins are composed of several protein subunits that appear to have specific roles in enzyme function in tRNA processing. This review describes recent progress made in the characterization of human RNase P, its relationship with the ribosomal RNA processing ribonucleoprotein RNase MRP, and the unexpected evolutionary conservation of its subunits. A new model for the biosynthesis of human RNase P is presented, in which this process is dynamic, transcription-dependent, and implicates functionally distinct nuclear compartments in tRNA biogenesis.

Keywords: Cajal bodies; catalytic ribonucleoprotein; nucleolus; RNase MRP; RNase P; tRNA

RIBONUCLEOPROTEIN COMPLEXES OF RNase P

Extensive purification analysis of RNase P from HeLa cells has revealed that the nuclear form of this tRNA processing holoenzyme is composed of at least 10 protein subunits associated with a single RNA species, H1 RNA (Table 1; Eder et al., 1997; Jarrous & Altman, 2001). These protein subunits are designated Rpp14, Rpp20, Rpp21, Rpp25, Rpp29, Rpp30, Rpp38, Rpp40, hPop5, and hPop1 (Lygerou et al., 1996b; Eder et al., 1997; Jarrous et al., 1998, 1999a, 2001; van Eenennaam et al., 1999, 2001). The tight association of these proteins with highly purified nuclear RNase P obtained by different purification schemes implies that they constitute the core structure of the holoenzyme (Jarrous & Altman, 2001).

A recent study has shown that the mitochondrial form of HeLa RNase P possesses an RNA that is identical to the H1 RNA (Puranam & Attardi, 2001). This enzyme has a sedimentation coefficient of ~17S in glycerol gradients, compared to ~15S of the nuclear counterpart, and exhibits properties typical of a ribonucleoprotein enzyme (Puranam & Attardi, 2001). This finding contradicts earlier biochemical analyses that support the concept that human mitochondrial RNase P is not a ribonucleoprotein complex (Rossmanith et al., 1995; Rossmanith & Karwan, 1998). These opposing findings provoke further debate on the biochemical nature of mitochondrial and other organellar RNase P enzymes (Frank & Pace, 1998; Schon, 1999; Altman et al., 2000; Gegenheimer, 2000; Salavati et al., 2001), and therefore more biochemical and genetic means should be applied to resolve this issue.

Nuclear RNase P purified from *Saccharomyces cerevisiae* has nine distinct protein subunits and genetic studies established that these subunits are essential for yeast viability and enzyme activity in tRNA processing (see Xiao et al., 2001). A multi-subunit ribonucleoprotein has also been described for nuclear RNase P purified from *Aspergillus nidulans* (Han et al., 1998).

In addition to the protein subunits described above (Table 1), several other proteins transiently interact with RNase P in yeast and human cells. As judged by two-hybrid genetic screens in yeast, the subunit Rpp20 interacts with the heat shock protein Hsp27 and the subunit Rpp14 contacts several proteins, including the LIM domain protein 1 (LIMD1) and HSPC232 (Jiang & Altman, 2001); the latter is an SR-rich protein that exhibits partial similarity to splicing factors SC-35 and SRp46. The interaction of Rpp20 with Hsp27 was verified by biochemical analysis (Jiang & Altman, 2001).

In *S. cerevisiae*, a complex of seven Sm-like proteins (Lsm2–8) is associated with the precursor RNA subunit, Rpr1, of nuclear RNase P and with U6 snRNA (Salgado-Garrido et al., 1999; Pannone et al., 2001).

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TABLE 1. Subunits of human RNase P, evolutionary conservation and possible functions.

Subunit	Chromosomal localization of gene	M_r/*pI*	Function/interaction	Homolog[a]
Rpp14[b]	3p23-cen	14/7.6	Substrate binding[c]	
Rpp20[d]	7q22	20/8.6	ATPase/helicase[e]; Hsp27[f]	Pop7/Rpp2
Rpp21[c]	6p21	21/9.6	Substrate binding[c]	Rpr2
Rpp25[g]	15[g]	25/9.7	H1 RNA binding[g]	
Rpp29[b]	19p13	29/10.2	Substrate binding[c]/NS29[h]	Pop4
Rpp30[i]	10	30/9.2	H1 RNA binding[g]	Rpp1
Rpp38[i]	10p	38/9.6	Localization[h]/H1 RNA binding	—
Rpp40[d]	6pter-6p21.1	40/5.2		
hPop1[j]	8q22	115/9.6	Localization	Pop1
hPop5[k]	10	19/7.9		Pop5
H1 RNA[l]	14q11.2	105/	Catalysis	Rpr1

[a] See Chamberlain et al., 1998.
[b] Jarrous et al., 1999a.
[c] Jarrous et al., 2001.
[d] Jarrous et al., 1998.
[e] Li and Altman, 2001.
[f] Jiang and Altman, 2001.
[g] C. Guerrier-Takada and S. Altman, unpubl. data; Jiang et al., 2001.
[h] Jarrous et al., 1999b.
[i] Eder et al., 1997.
[j] Lygerou et al., 1996b.
[k] van Eenennaam et al., 2001.
[l] Amé et al., 2001.

Abbreviations: ptRNA: precursor tRNA; NS29 and NS38: nucleolar localization domain of Rpp29 and Rpp38.

Notes: Pop7 is identical to Rpp2 (Stolc et al., 1998) and Rpp29 is known as hPop4 (van Eenennaam et al., 1999). Recombinant Rpp14, Rpp21, and Rpp29 bind to precursor tRNA, as judged by gel shift mobility analysis (Jarrous et al., 2001; H. Mann & N. Jarrous, unpubl. data). The genetic positions of *RPP* gene candidates on chromosomes have been identified by LocusLink search in the National Center for Biotechnology Information and by Blast searches of databases. *RPP21* resides in the MHC class I gene cluster near the HLA-E gene (Jarrous et al., 2001). Hsp27 stimulates RNase P activity (Jiang & Altman, 2001). NS29 and NS38 are nucleolar localization domains. Rpp29, Rpp38, and Pop1 may function in nucleolar localization of H1 RNA mediated by the P3 domain (Jacobson et al., 1997; van Eenennaam et al., 2000). Rpp38 has a conserved domain (107–190) found in the ribosomal protein L7Ae/L30e/S12e/Gadd45 family and is predicated to bind an RNA secondary structure motif, K-turn, in the RNase MRP RNA (Klein et al., 2001). As judged by immunoprecipitation experiments, RNase P and RNase MRP share several protein subunits, including Rpp20, Rpp29, Rpp30, Rpp38, hPop1, and hPop5 (van Eenennaam et al., 2001). Rpp21, Rpp29, Rpp30, and Pop5 have homologs in archaea (Jim Brown, pers. comm.; and CD-domain Search, NCBI).

This complex is not part of the mature Rpr1 RNA, and therefore it may function in the assembly process or recycling of RNase P (Salgado-Garrido et al., 1999; Pannone et al., 2001). Of note, these Lsm proteins are not associated with the RNA subunit of RNase MRP (Salgado-Garrido et al., 1999), a mitochondrial and ribosomal RNA processing ribonucleoprotein (Lygerou et al., 1996a; Lee & Clayton, 1997) that shares eight of its protein subunits with nuclear RNase P (see Chamberlain et al., 1998). Furthermore, two archaeal Sm proteins, AF-Sm1 and AF-Sm2, physically interact with the RNase P RNA (Toro et al., 2001). Thus, a set of Sm and Lsm proteins required for mRNA processing are implicated in tRNA biogenesis in archaea and eucarya (Toro et al., 2001).

Taken together, many proteins interact transiently or loosely with RNase P or its subunits, thus forming complexes and subcomplexes of different subunit compositions.

CONSERVATION OF PROTEIN SUBUNITS OF NUCLEAR RNase P

Six of the protein subunits of human RNase P have been shown to exhibit a moderate similarity at the primary amino acid sequence with their corresponding *S. cerevisiae* counterparts (Table 1), whereas the remaining subunits may exhibit some common biochemical and structural features. Moreover, several Rpp subunits, including Rpp21, Rpp29, Rpp30, and hPop5, are conserved in archaea (Hall & Brown, 1999; Koonin et al., 2001; Jim Brown, pers. comm.). This unexpected conservation may indicate that these proteins have essential roles in RNase P function in tRNA processing (Table 1). Although some RNA subunits of archaeal RNase P are catalytic entities in vitro (Pannucci et al., 1999), these conserved proteins may be essential for enzyme activity in vivo, as is the case with their homologs in yeast (see Xiao et al., 2001). The conservation

of protein subunits of nuclear RNase P in archaea is consistent with the idea that the nuclear RNA processing machinery in eukaryotic cells has an archaeal-related origin (Altman et al., 2000; Horiike et al., 2001). The eubacterial RNase P with its single protein component, C5, may then represent one specialized form derived from a more complex, ancient RNase P. Alternatively, eubacterial RNase P may have additional subunits, other than the C5 protein, which are loosely associated with the holoenzyme (Stark et al., 1978).

FUNCTIONS OF PROTEIN SUBUNITS OF HUMAN RNase P

Using model tRNA substrates, it has been shown that the acceptor stem, T stem and loop, and a base bulge between these two subdomains in precursor tRNAs are required for cleavage by purified HeLa RNase P (see Altman & Kirsebom, 1999). In addition, nuclear RNase P of *S. cerevisiae* seems to recognize both single-stranded RNA and tRNA structural features (Ziehler et al., 2000). Therefore, processing of precursor tRNAs by nuclear RNase P may be preceded by multiple steps of substrate binding and verification mediated by distinct protein subunits. Recombinant Rpp14, Rpp21, and Rpp29 have been shown to selectively bind precursor tRNAs, as determined by gel shift mobility analysis, whereas other Rpp polypeptides have failed to do so (Jarrous et al., 2001; H. Mann & N. Jarrous, unpubl. data). This suggests that several proteins of RNase P can physically interact with precursor tRNA (True & Celander, 1998). Whether these proteins recognize a specific sequence or structure in tRNA or that they coordinate multiple binding modes of substrates by the holoenzyme remains to be determined. Because RNase MRP shares Rpp29 (van Eenennaam et al., 1999) and apparently Rpp14 (N. Jarrous, unpubl. data), these two polypeptides may recognize general features in RNA substrates for both holoenzymes. The *S. cerevisiae* homolog of Rpp21, designated Rpr2, is not shared by RNase MRP (Chamberlain et al., 1998), and thus it may facilitate the recognition of specific determinants in tRNA by RNase P.

Protein subunits of human RNase P may have their own intrinsic activities. Thus, a recent study has shown that the subunit Rpp20 is an ATPase (Li & Altman, 2001). The role of this ATPase activity in RNase P function is not clear. Rpp20 does not bind directly to H1 RNA (Jiang et al., 2001) or precursor tRNA (Jarrous et al., 2001) and RNase P itself does not require ATP or GTP for processing of precursor tRNA in vitro. However, the possibility exists that RNase P may utilize ATP or GTP in cells. RNase MRP also possesses Rpp20 (see van Eenennaam et al., 2001) and therefore this protein may function in rRNA processing in which several ATP-dependent RNA helicases have been implicated (Colley et al., 2000). Moreover, Rpp20 hydrolyzes ATP as a free polypeptide, and hence it may function independently of these two enzymes (Li & Altman, 2001).

REGULATION OF RNase P ACTIVITY

The biosynthesis of human RNase P should involve the coordination of expression of the genes coding for its RNA and protein subunits. In addition, the biogenesis of RNase P should be tightly coupled to the translation machinery (Pederson & Politz, 2000). Nonetheless, control of expression of a single Rpp subunit may regulate the entire holoenzyme and its activity in tRNA processing. Examples of regulation mechanisms that modulate RNase P activity or the expression of its proteins in human and yeast cells are described below.

The enzymatic activity of human RNase P is regulated by the La antigen that directly interacts with precursor tRNAs (Fan et al., 1998; Intine et al., 2000; Maraia, 2001). In *S. cerevisiae*, processing of precursor tRNA by RNase P is also controlled by a La homolog (Yoo & Wolin, 1997). An RNA recognition motif and a G/ATP-binding site in the carboxy terminal domain of the human La phosphoprotein prevent precursor tRNA from being processed by RNase P through blocking the site of cleavage. Phosphorylation and dephosphorylation events of the La protein regulate the recycling and initiation of RNA polymerase III transcription units as well as modulate the activity of RNase P (Maraia & Intine, 2001). Thus, phosphorylation of the La protein on serine 366 facilitates the cleavage of precursor tRNA by RNase P (Intine et al., 2000), whereas it inhibits gene transcription by RNA polymerase III (Fan et al., 1997). The bipartite binding mode of the La antigen to 5′ (5′-pppG/A) and 3′ (UUU-OH) termini of nascent precursor tRNAs and its dissociation from the 5′ end upon phosphorylation suggests that RNase P acts after termination of tRNA gene transcription and the nascent transcript being assembled with the La antigen into a small ribonucleoprotein (Maraia & Intine, 2001; Maraia, 2001). An RNA helicase activity may then be required for the active disruption of the La antigen-tRNA complex for RNase P-mediated cleavage.

Another protein that is related to tRNA biosynthesis and modulates RNase P activity is the tRNA pseudouridine 55 synthase, which is encoded by *PUS4* in yeast (Qiu et al., 2000). Overexpression of PUS4 selectively interferes with the 5′ processing of precursor $tRNA_i^{Met}$. Overexpression of the RNase P RNA subunit, RPR1, relieves this *PUS4*-mediated interference (Qiu et al., 2000). PUS4 may compete with RNase P for binding to a set of precursor tRNAs or for a tRNA chaperone protein required for 5′ processing of the initiator tRNA (Qiu et al., 2000).

Splicing variation of mRNA determines the association of the subunit Rpp21 to human RNase P and thereby may control enzyme activity in the nucleus (Jarrous et al., 2001). Thus, processing of *RPP21* pre-

cursor mRNA, which is transcribed from a gene that has five exons and four introns, is regulated by a mechanism that involves intron retention and splice site variation (Jarrous et al., 2001). Intron 1 is retained in-frame in ~20% of Rpp21 mRNA and seems to be coupled to the selection of an alternative 5′ donor site for exon 4. This alternative splicing generates a new protein product, Rpp21i. Rpp21i is not associated with the majority of RNase P and it is mainly localized in the nucleolus (see below). High expression of an exogenous Rpp21i in transfected HeLa cells causes alterations in the nucleolar structure and expels endogenous Rpp29 from its normal nucleolar location to the nucleoplasm (Jarrous et al., 2001). Work is in progress to determine how splicing of the Rpp21 mRNA regulates RNase P activity in tRNA processing.

INTRANUCLEAR LOCALIZATION OF HUMAN RNase P SUBUNITS

In situ RNA hybridization analysis and microinjection of labeled H1 RNA into human cell lines demonstrate that this RNA transiently enters the nucleolus before it diffuses in the nucleoplasm (Jacobson et al., 1997; Table 2). The endogenous H1 RNA was also detected in the cytoplasm, the nucleoli, and the perinucleolar compartment (see Wolin & Matera, 1999). Because H1 RNA is essential for enzyme activity and exists in the nucleoplasm, in contrast to the *S. cerevisiae* RNase P RNA that is predominantly found in the nucleolus (Bertrand et al., 1998; Kendall et al., 2000; Lewis & Tollervey, 2000), human RNase P may function in this compartment. The nucleolus of human cells seems to serve as an assembly site for RNase P (Pederson & Politz, 2000).

TABLE 2. Intracellular localization of some subunits of human RNase P.

Subunit[a]	Cytoplasm	Nucleoplasm	Cajal bodies	Nucleolus	PNC[b]	Other[c]
H1 RNA	+	+++		+	+	
Rpp14		+		+++		+
Rpp21		+++		+		
Rpp29		+	+++	+++		+
Rpp30		+		+++		
Rpp38		+	+++	+++		+
Rpp40				+++		
hPop5		+		+++		
hPop1		+		+++		

[a] The intracellular localization of H1 RNA was determined by RNA cytochemistry approaches (see Wolin & Matera, 1999). The localization of the protein subunits indicated was determined by immunofluorescence analysis using specific antibodies and/or fusion with GFP (Lygerou et al., 1996b; Jarrous et al., 1999b, 2001; van Eenennaam et al., 1999, 2001; N. Jarrous, unpubl. data). One plus indicates that the fluorescence signal was visible in the specified compartment and three pluses designate a stronger fluorescence signal.

[b] Anti-Th sera do not cross-react in the perinucleolar compartment (PNC) with their corresponding Th antigen, which is associated with RNase P and RNase MRP (van Eenennaam et al., 2000). Rpp30, Rpp38, and hPop1 serve as Th antigens (Lygerou et al., 1996b; Eder et al., 1997).

[c] Some of the Rpp subunits show nuclear punctate staining that does not correspond to nucleoli and Cajal bodies (Jarrous et al., 1999b). The identity of these nuclear bodies is not yet known.

In contrast to H1 RNA, several protein subunits, including Rpp14, Rpp29, Rpp38, hPop1, and hPop5, are mainly localized in nucleoli of human cells (Lygerou et al., 1996b; Jarrous et al., 1999b; Savino et al., 1999; van Eenennaam et al., 2001). Rpp29 and Rpp38 are also found in Cajal bodies (Table 2; Jarrous et al., 1999b), nuclear structures in which transcription and processing machineries preassemble (Lamond & Earnshaw, 1998; Gall, 2000, 2001). Unexpectedly, endogenous Rpp21 is mainly found in the nucleoplasm and a small fraction of it exists in nucleoli (Table 2; Jarrous et al., 2001). In addition, Rpp21 is not concentrated in Cajal bodies, as are Rpp29 and Rpp38. These observations indicate that the nuclear localization patterns of Rpp21, as well as H1 RNA, are different from those of other Rpp subunits (Table 2).

Moreover, protein subunits of RNase P may move rapidly from one compartment to another in the nucleus of human cells. Thus, fluorescence recovery after photobleaching (FRAP) and fluorescence loss in photobleaching (FLIP) techniques reveal that Rpp29 exchanges quickly between the nucleolus and nucleoplasm of HeLa cells (Chen & Huang, 2001). The high mobility of Rpp29 suggests that the intranuclear pool of this protein is not in association with a stationary complex. A high mobility in the nucleus has also been demonstrated for RNA and nucleolar proteins required for mRNA processing (Politz et al., 1998; Phair & Misteli, 2000; Chen & Huang, 2001; Pederson, 2001). Moreover, nuclear organelles, such as Cajal bodies, are in continuous movement and contact each other in the nucleus (Platani et al., 2000). Therefore, the localization pattern of Rpp29 in the nucleus does not necessarily mirror the exact distribution of the fully assembled RNase P holoenzyme.

A NEW MODEL FOR THE ASSEMBLY OF HUMAN NUCLEAR RNase P

There is a controversy over the location of active nuclear RNase P and tRNA processing in human cells (see Wolin & Matera, 1999; Maraia, 2001). Some recent observations suggest that human RNase P is a nucleolar enzyme (Jacobson et al., 1997; Jarrous et al., 1999b; Lewis & Tollervey, 2000; Pederson & Politz, 2000). However, the dynamic and flexible organization of nuclear structures, including the nucleolus, and their building components (Wei et al., 1998; Wolffe & Hansen, 2001) may imply that nuclear RNase P is not a fixed entity. The elucidation of the composition, subunit interactions, and intracellular distribution patterns of human RNase P, as summarized above, sheds new light on

the localization and assembly process of this ribonucleoprotein, as will be described below.

In the cytoplasm, translated protein subunits of RNase P should be first transported to the nucleus and then mobilized to specific intranuclear sites for their assembly with H1 RNA. Although how these subunits are prearranged in the cytoplasm is not clear, they must possess a set of domains required for their nuclear entry, trafficking through distinct nuclear zones, and assembly with other protein subunits and H1 RNA. The subunits Rpp29 and Rpp38 have been shown to possess functional nuclear and nucleolar localization domains (Jarrous et al., 1999b), whereas other subunits, including Rpp14 and hPop5, seem to enter the nucleus through piggyback mechanisms (Jarrous et al., 1999b; van Eenennaam et al., 2001). The extensive protein–protein and H1 RNA–protein interactions in RNase P (Jiang & Altman, 2001; Jiang et al., 2001) suggest that these subunits attract each other as part of the assembly process. Additional interacting factors may help in this process. The presence of significant amounts of H1 RNA in the cytoplasm (Lee et al., 1996) implies that RNase P or subcomplexes of this ribonucleoprotein may be assembled in this compartment.

In the nucleus, two issues should be stressed to understand the mechanism of the assembly of active RNase P. First, H1 RNA and its protein subunits are differentially distributed in several compartments, including nucleoli, Cajal bodies, the perinucleolar compartment and nucleoplasm (Table 2). These compartments are transcriptionally specialized sites and their structural integrity is dependent on continuous RNA synthesis (Lamond & Earnshaw, 1998; Pombo et al., 1999; Cook, 1999; Huang, 2000; Gall, 2001). Accordingly, RNase P is close to sites of active gene transcription. Second, the rapid mobility of protein subunits of RNase P, at least as shown for Rpp29 (Chen & Huang, 2001), supports the idea that these subunits associate with and dissociate from RNase P in a continuous manner (Lewis & Tollervey, 2000). Furthermore, the synthesis of new substrate RNAs, for example, tRNA transcripts, and their interaction with subunits of RNase P, such as Rpp14, Rpp21, Rpp29 (Jarrous et al., 2001), and the La antigen (Maraia, 2001), may play a role in the final formation and reorganization of the catalytic form of RNase P.

However, there is an additional factor that may play a role in the assembly of RNase P. At least six protein subunits of human RNase P, namely Rpp20, Rpp29, Rpp30, Rpp38, hPop1, and hPop5, have been shown to be associated with RNase MRP (Lygerou et al., 1996b; Pluk et al., 1999; van Eenennaam et al., 1999, 2001). This overlap in subunit composition raises the possibility that the assembly processes of these two ribonucleoproteins are related. The conservation of the P3 domains in H1 RNA and MRP RNA (Schmitt, 1999; Frank et al., 2000) and their common interacting proteins (Pluk et al., 1999; Jiang et al., 2001) support a functional relationship. This domain is required for the entry of the H1 and MRP RNAs to the nucleolus (Jacobson et al., 1995, 1997), a major assembly site for ribonucleoproteins (Pederson & Politz, 2000; Grosshans et al., 2001). Moreover, new ideas have been presented in which the assembly of RNase P in the nucleolus is coordinated with ribonucleoproteins of translation, for example, ribosome, SRP, and 5S RNP (Pederson & Politz, 2000).

Taken together, recent findings support the conclusion that human RNase P ribonucleoproteins are dynamically assembled and recruited to discrete sites of active gene transcription and RNA processing. Accordingly, RNase P is not restricted to a specific nuclear compartment.

NEW FUNCTIONS FOR RNase P AND RNase MRP

The nucleolus is a storage site for complexes required for cell mitosis (Bachant & Elledge, 1999) and Cajal bodies are implicated in gene transcription in a cell-cycle-dependent manner (Ma et al., 2000). These functions may also be relevant for some RNase P subunits concentrated in nucleoli and Cajal bodies. The fact that the nucleolus disassembles before the onset of mitosis, thus forming perichromosomal regions and nucleolus-derived foci (Dundr et al., 2000), and that hPop1 is associated with chromatids and the mitotic spindle region during anaphase (Dundr & Olson, 1998), raises the question if RNase P, RNase MRP, or their individual subunits have roles in the cell cycle. Such a functional connection is supported by the recent finding that mutations in the RNA subunit of human RNase MRP cause a pleiotropic genetic disorder, cartilage hair hypoplasia, which is manifested by abnormal body development, defective immunity, and predisposition to several types of cancer (Ridanpaa et al., 2001). In addition, genetic studies in *S. cerevisiae* reveal that Snm1, a protein subunit of RNase MRP, has a role in plasmid segregation and control of cell division (Cai et al., 1999; Clayton, 2001).

New functions are attributed to Rpm2, the protein subunit of the *S. cerevisiae* mitochondrial RNase P. Genetic studies relate Rpm2p to mitochondrial protein synthesis and protein degradation through the proteasome function (Lutz et al., 2000; Stribinskis et al., 2001).

CONCLUDING REMARKS

The ribonucleoprotein core of human nuclear RNase P has at least 10 distinct proteins associated with H1 RNA. The next major challenge will be the determination of the minimal subunits sufficient for reconstitution of RNase P activity in vitro and that will set the stage for future work on the structural biology of this ribo-

nucleoprotein. This can have general implications in understanding the function of other small nuclear and nucleolar ribonucleoproteins involved in RNA processing.

RNase P and its multiple subunits are spread in the nuclear space of mammalian cells. Coordination between distinct nuclear compartments and the cytoplasm should take place to ensure RNase P production and accurate processing of tRNA. The function of RNase P should not be disconnected from that of RNase MRP and thereby from rRNA processing. The findings that protein synthesis can be coupled to transcription within the nucleus (Iborro et al., 2001) and that RNase P biosynthesis is linked to that of ribonucleoprotein complexes of translation (Pederson & Politz, 2000) may reveal new roles of this holoenzyme and its subunits in gene transcription, RNA processing, and translation.

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