Minireview

PSF and p54^{nrb}/NonO – multi-functional nuclear proteins

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Abstract Proteins are often referred to in accordance with the activity with which they were first associated or the organelle in which they were initially identified. However, a variety of nuclear factors act in multiple molecular reactions occurring simultaneously within the nucleus. This review describes the functions of the nuclear factors PSF (polypyrimidine tract-binding protein-associated splicing factor) and p54^{nrb}/NonO. PSF was initially termed a splicing factor due to its association with the second step of pre-mRNA splicing while p54^{nrb}/NonO was thought to participate in transcriptional regulation. Recent evidence shows that the simplistic categorization of PSF and its homolog p54^{nrb}/NonO to any single nuclear activity is not possible and in fact these proteins exhibit multi-functional characteristics in a variety of nuclear processes.

Key words: Pre-mRNA splicing; Transcription; DNA pairing; RNA retention; Nucleus; TLS

1. Introduction

The nucleus is a complex organelle in which a wide range of processes occur. Specific nuclear factors are assigned to these activities. For example, being a 'splicing factor' will usually mean binding to RNA and participating in RNA splicing activities while the term 'transcription factor' will insinuate interactions with DNA and regulation of transcription. However, nuclear reactions occur simultaneously and in very close proximity [1]. In fact, there is cross-talk between nuclear processes and certain proteins can take part in multiple nuclear events. In this review we discuss the data regarding two such multi-functional proteins, PSF and p54^{nrb}/NonO.

PSF (polypyrimidine tract-binding protein (PTB)-associated splicing factor), a 100 kDa polypeptide, was identified and characterized in a complex with PTB [2]. The polypyrimidine tract is a region found in most introns of higher eukaryotes to which several factors can bind and is important for the definition of the 3′-splice site. However, most of PSF is associated with the nuclear matrix and is not bound to PTB [3]. Immunofluorescent staining has shown nucleoplasmic distribution of PSF in both diffuse and punctate patterns [4,5] where localization in nucleoplasmic foci is determined by the presence of a RNA recognition motif (RRM) 2 (Fig. 1) [6]. The proline/glutamine-rich N-terminus of PSF might be involved in protein–protein interactions [2].

p54^{nrb} (human) and NonO (mouse) are highly homologous to the C-terminus of PSF (Fig. 1) [7,8]. Proteomics have identified PSF and p54^{nrb}/NonO in the nucleolus [9] and in association with the nuclear membrane [10]. p54^{nrb}/NonO was recently shown to be a component of a novel nuclear domain termed paraspeckles [11]. The *Drosophila* homolog of these proteins is the NONA/BJ6 protein encoded by the *no-on-transient* A gene required for normal visual and courtship song behavior [12]. Another homolog, hrp65, is identified in *Chironomus tentans* as a component of nuclear fibers functioning in nuclear export [13]. This family of proteins is highly homologous in the two C-terminal RRMs, implying a role in RNA processing. Yet, prior to their cloning, PSF and p54^{nrb}/NonO were characterized as a p100/p52 DNA-binding heterodimer [14] and indeed these proteins bind to dsDNA, ssDNA and RNA [2,8,15,16]. Several groups have identified PSF and p54^{nrb}/NonO in a variety of systems and complexes. In this review we try to present a coherent picture of the known nuclear activities of these multi-functional proteins.

2. PSF and p54^{nrb}/NonO in nuclear RNA processing

The first function attributed to PSF is participation in constitutive pre-mRNA splicing [2]. Initially, PSF and its 68 kDa proteolytic form were identified as spliceosome-associated proteins SAP102 and SAP68 of the B complex representing the complete spliceosome [17]. PSF binds to polypyrimidine tracts and is shown to be an essential factor required for in vitro splicing [2] acting during the second catalytic step of splicing (Fig. 2A) and a component of the spliceosome C complex [18]. Additional findings connect PSF to splicing activities: it co-purified in 25S particles containing U4, U5 and U6 snRNPs [19] and physically interacted with U1A in a complex which contains a form of U1A that is not associated with U1–snRNP. This complex is thought to function both in splicing and in polyadenylation [20]. PSF can bind to U5–snRNA (J.G. Patton, personal communication) and can interact with CUG tracts found in the 3′-UTR of the *DMPK* gene which causes myotonic dystrophy [21]. p54^{nrb}/NonO has high affinity for RNA via its N-terminus [8] and can bind to β-globin pre-mRNA and RNA [15] and the intronic pyrimidine-rich sequence in β-tropomyosin pre-mRNA [22]. However, direct involvement of p54^{nrb}/NonO in pre-mRNA splicing has not been shown.

Recently, p54^{nrb}/NonO and PSF were found to act in the binding and nuclear retention of defective RNAs [23]. RNAs

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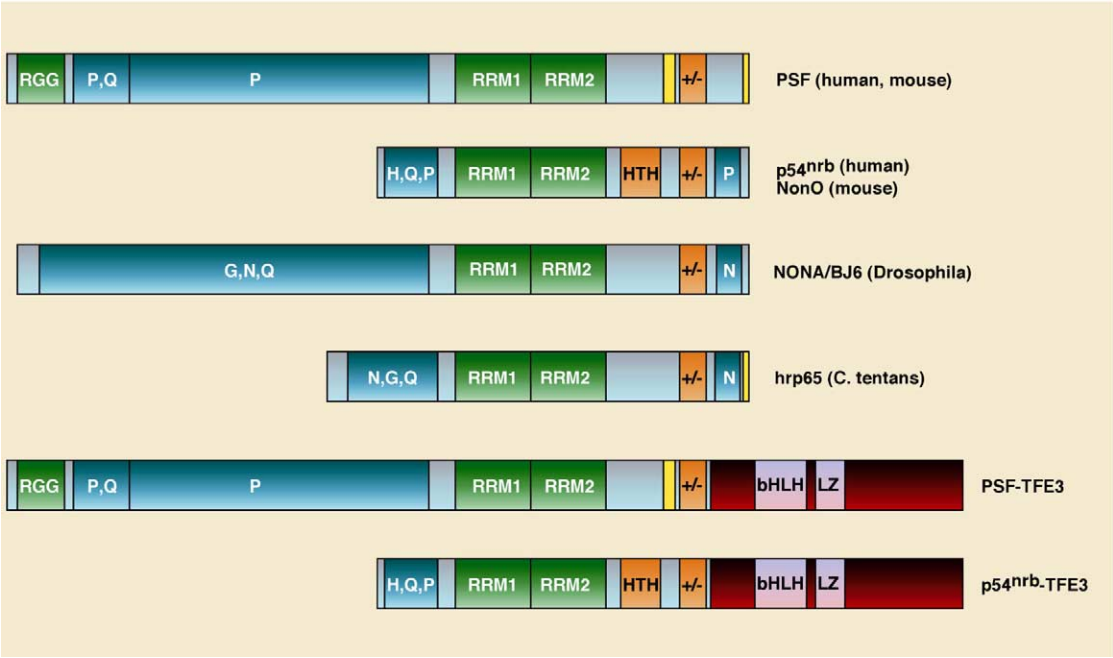

Fig. 1. Structural elements in PSF, p54^{nrb}/NonO, NONA/BJ6 and hrp65 proteins. The C-terminus harbors the RRMs, the homologous element in these proteins. In addition, N- and C-termini contain regions rich in proline (P), glutamine (Q), histidine (H), glycine (G) and asparagine (N). PSF has an RNA-binding RGG element that is probably methylated and therefore cannot bind RNA. Yellow boxes show identified nuclear localization sequences. p54^{nrb}/NonO has a region predicted to form a HTH structure followed by a basic/acidic (±) stretch of amino acids which together might form a DBD. When translocated, most of PSF and p54^{nrb}/NonO fuse with the C-terminus of the TFE3 transcription factor (red) that contains basic helix–loop–helix (bHLH) and leucine zipper (LZ) domains.

in the nucleus can be edited either in a selective manner thus leading to the production of protein, or can be promiscuously hyperedited, theoretically causing the translation of mutated proteins. The latter RNAs must be retained within the nucleus. In the editing reaction, adenosines (A) of dsRNA undergo hydrolytic deamination to inosines (I). It was shown that indeed many such A-to-I edited RNAs were confined to the nucleus by a protein complex consisting of p54^{nrb}/NonO, PSF and matrin3. The interaction between p54^{nrb}/NonO and I–RNA was shown both in vitro and in vivo [23]. Since matrin3 is a component of the nuclear matrix [24] and in itself does not bind I–RNA, and matrin4 is known to be PSF [23], it is speculated that this p54^{nrb}/PSF/matrin3 complex serves as a 'nuclear arm' which anchors promiscuously edited RNAs as part of a mechanism of nuclear retention (Fig. 2B).

3. Regulation of transcription by PSF and p54^{nrb}/NonO

Splicing and transcription are coupled nuclear processes [25]. Besides RNA-binding properties, PSF binds DNA [14] and p54^{nrb}/NonO binds ssDNA (and RNA) through its N-terminus and dsDNA through its C-terminus [8]. PSF binds the insulin-like growth factor response element in the porcine *P450scc* gene which produces a steroidogenic enzyme. This binding causes inhibition of the transcriptional activity of this element. The inhibition originates from the N-terminus of PSF [26,27]. Other work shows that PSF can bind to the DNA-binding domain (DBD) of thyroid hormone receptors (TR) and retinoid X receptors (RXR) [28]. p54^{nrb}/NonO is bound to PSF in this complex. Interactions of full length PSF with the DBD of TR in the absence of the hormone ligand has a repressive effect on transcription, also mediated by the N-terminus of PSF. Moreover, PSF in this complex interacts directly with the repressor Sin3A which in turn recruits a class I histone deacetylase (HDAC), a known partner of Sin3A in the mediation of transcriptional repression. Similarly, PSF and p54^{nrb}/NonO are shown to repress basal transcription of the human *CYP17* gene involved in steroidogenesis and are found in complex with Sin3A, HDAC and SF-1 (steroidogenic factor). This repression is alleviated by cAMP stimulation, phosphatase activity and increased binding of SF-1/PSF/p54^{nrb} to the promoter, together with the release of Sin3A–HDAC from the complex (Fig. 3A) [29,30].

p54^{nrb}/NonO has low affinity for octamer motifs found in the IgH promoter in B cell leukemia cells [8]. In addition to its own DNA-binding abilities, it can induce the binding of several transcription factors to their response elements [31] and binds directly to the Spi-1/PU.1 transcription factor [22]. A direct implication in transcriptional control comes from work showing that p54^{nrb}/NonO binds to an enhancer element in the long terminal repeats of murine intracisternal A particles and activates transcription [15].

4. PSF and p54^{nrb}/NonO activities in DNA unwinding and DNA pairing

During DNA replication, DNA topoisomerase I cleaves one of the DNA strands in the duplexes formed and allows the uncleaved strand to pass through the break, in this way reducing the tension in the DNA supercoils. PSF and p54^{nrb}/NonO co-purified with DNA topoisomerase I at a 1:1:1 ratio in nickel affinity chromatography [32]. However, PSF and topoisomerase I can independently bind to nickel and therefore it is still unclear whether this is a natural complex [23].

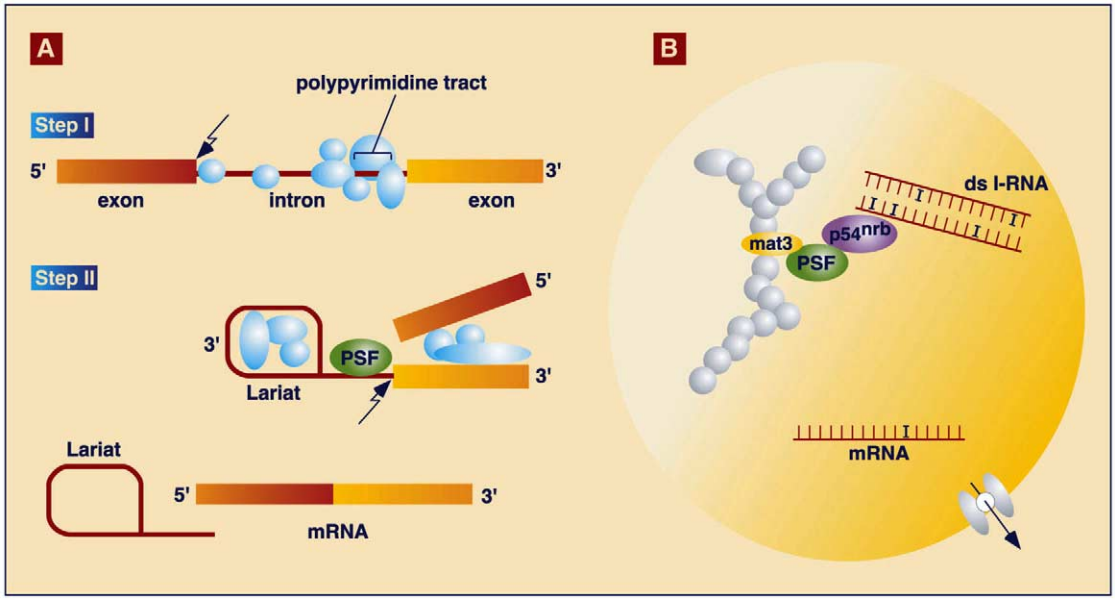

Fig. 2. PSF and p54^{nrb}/NonO interactions with RNA. A: Pre-mRNA splicing proceeds in two steps. During the first step, splicing factors assemble on intronic and exonic *cis*-elements, including the polypyrimidine tract found in the 3′ of the intron. A nucleophilic attack (arrow) detaches the 5′-exon from the intron, and the intron forms a lariat. During the second step of splicing there is some interchanging of proteins. PSF interacts with the polypyrimidine tract. A second nucleophilic attack occurs and the mature spliced mRNA is formed while the intronic lariat is discarded. B: Promiscuously edited I–A dsRNA is retained in the nucleus by a p54^{nrb}/PSF/matrin3 'arm' connected to the nuclear matrix, while selectively edited mRNA can be exported through nuclear pores to the cytoplasm.

Yet, functional evidence for such interactions does exist. When recombinant PSF or PSF/p54^{nrb} complexes are incubated in vitro with recombinant or purified topoisomerase I, the specific activity of the enzyme is greatly enhanced, especially with the PSF/p54^{nrb} heterodimer. The latter alone does not cause DNA relaxation [32]. Furthermore, the PSF/p54^{nrb} complex stimulates dissociation of topoisomerase I from the DNA after cleavage and enhances its 'jumping' between two separate DNA helices (Fig. 3B) [33]. PSF and topoisomerase I are found to partially co-localize in nucleoplasmic areas of interphase cells. During mitosis topoisomerase I remains with the chromatin compartment while PSF disperses in the cytosol [32].

PSF does not only affect the unwinding of DNA but functions also in the annealing of DNA. Homologous DNA pairing is a step required in several nuclear functions such as DNA recombination, repair, replication and more. RecA in *Escherichia coli* and its homologs in eukaryotes are well known ATP-dependent homology promoting factors. In the search for additional proteins that promote homologous DNA pairing, two proteins were identified and termed hPOMp75 and hPOMp100 [34], later identified as TLS/FUS and PSF, respectively [35,36]. TLS is encoded by a pro-oncogene translocated in several cancers. p54^{nrb}/NonO does not possess DNA pairing activity (B.S. Lopez, personal communication). PSF and TLS require ssDNA and dsDNA with sequence homology between them for their in vitro pairing activity, as well as divalent cations. In contrast to the RecA protein family, no ATP is required and PSF and TLS do not contain any associated exonuclease activity [34]. Mechanistically, PSF exhibits DNA reannealing activity, i.e. the formation of duplex DNA from two homologous DNA strands. In addition, PSF can promote the invasion of a ssDNA between a DNA duplex and produce a D-loop formation required for homologous recombination (Fig. 3C). This property is enhanced when PSF is phosphorylated by protein kinase C (PKC). Other splicing factors such as SF2/ASF and U2AF^{65} were also able to cause DNA reannealing but could not form D-loops [36].

5. PSF and p54^{nrb}/NonO in tumorigenesis

The pairing activities of PSF and TLS are demonstrated in non-immortalized cells and are elevated in transformed cells [35,37] indicating a connection with proliferation. Indeed, proliferating cells exhibit a two-fold higher activity than quiescent cells. Furthermore, induction of differentiation causes a pronounced decrease in their pairing activities [35]. Although direct physical interactions between PSF and TLS or p54^{nrb}/NonO and TLS have not been found [28,35] (B.S. Lopez, F. Moreau-Gachelin, D. Storm, personal communications and our unpublished results), it appears that some interactions are occurring in larger protein complexes. These proteins co-purify with EWS (a TLS homolog also involved in translocations) in large RNA–protein complexes [38]. They all re-localize to similar types of nucleolar caps during actinomycin D induced transcriptional inhibition (Shav-Tal et al., submitted). PSF and TLS can bind to TR and RXR [28] and, as will be described below, p54^{nrb}/NonO and TLS interact with Spi-1/PU.1 and affect its activity [22,39]. We speculate that these proteins are in close proximity in large RNA–protein complexes.

Chromosomal translocations of the TLS gene occur in two types of cancer. Similarly, both *PSF* and *p54^{nrb}/NonO* translocate to the *TFE3* gene in cases of papillary renal cell carcinoma [40]. The TFE3 transcription factor contains a DNA-binding helix–turn–helix (HTH) and an adjacent leucine zipper (LZ) required for dimerization. In addition, there are two

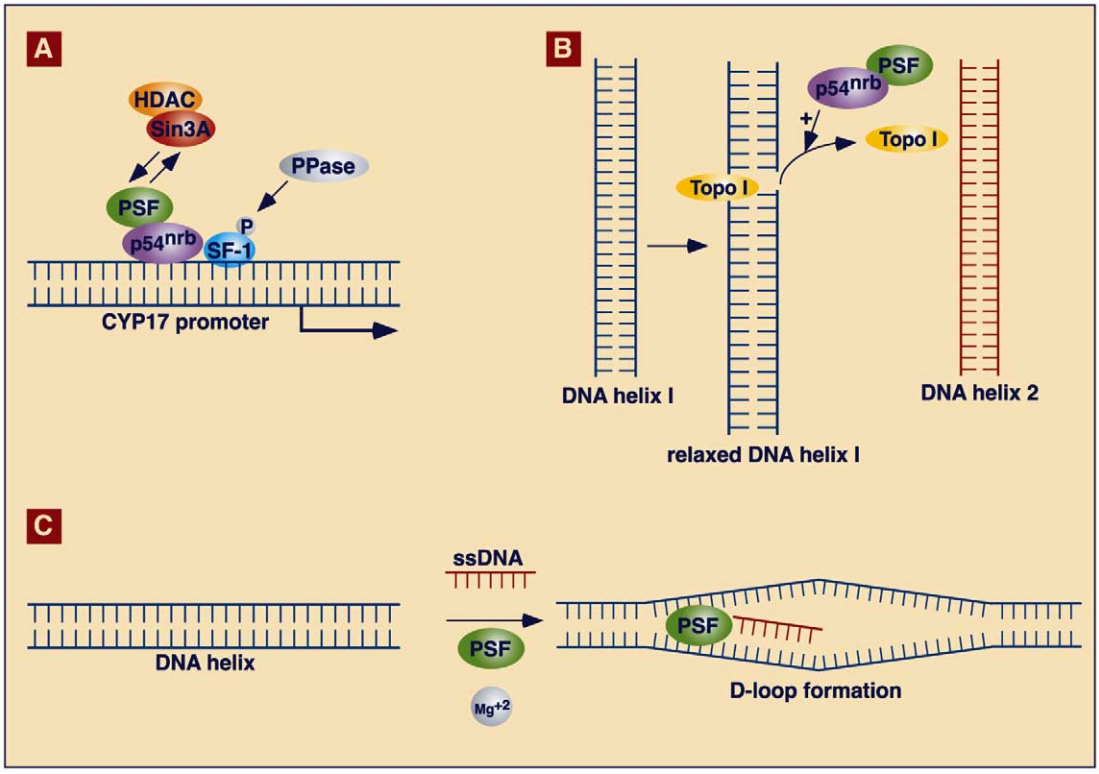

Fig. 3. PSF and p54^{nrb}/NonO interactions with DNA. A: PSF and p54^{nrb}/NonO can form a complex with SF-1 and together bind the *CYP17* promoter. Repression of transcription is achieved by the binding of the Sin3A repressor to PSF along with HDAC. Removal of repression occurs by cAMP stimulation, the removal of Sin3A/HDAC and the dephosphorylation of SF-1. B: Topoisomerase I relaxes tension in DNA helices. PSF/p54^{nrb} complex enhances topoisomerase I activity and induces its 'jumping' to other DNA helices after cleavage. C: PSF can bind to both dsDNA and ssDNA. It has DNA pairing activity and also can form D-loop structures as depicted. In this case it allows the insertion of a homologous ssDNA between a DNA duplex.

transcriptional activation domains. The fusion protein contains PSF or p54^{nrb}/NonO sequences fused to the C-terminus of TFE3, harboring the HTH, LZ and one activation domain (Fig. 1). Since most of the protein encoding sequences of the *PSF* and *p54^{nrb}/NonO* genes are translocated to *TFE3*, it is possible that their functions as proteins are preserved. However, GFP–NonO–TFE3 does not enhance transcription and its localization is altered in comparison to GFP–NonO which co-localizes with splicing factor-rich speckles [41]. The functional significance of these translocations remains to be elucidated.

p54^{nrb}/NonO is a binding partner of the Spi-1/PU.1 transcription factor which is overexpressed in Friend erythroleukemia [22]. Since the interaction occurs between the DBD of Spi-1/PU.1 and the RNA-binding domain of p54^{nrb}/NonO, it is assumed that this might have functional effects. Indeed, Spi-1/PU.1 binds RNA sequences preferred by p54^{nrb}/NonO, inhibits the binding of p54^{nrb}/NonO to the polypyrimidine tract of β-tropomyosin pre-mRNA, interferes with in vitro splicing reactions [22] and can interact with TLS [39]. Thus, interference with RNA-binding proteins might be an important step in the leukemic process.

6. p54^{nrb}/NonO has carbonic anhydrase (CA) enzymatic activity

The maintenance of pH homeostasis in the body is mediated by the family of CAs comprising 11 active forms of varying specific activities (5–3000 U/mg). A new 66 kDa protein, which turned out to be the p54^{nrb}/NonO protein, was identified in Leydig cells using anti-CAII antibodies. Recombinant p54^{nrb}/NonO was then shown to bind to a CA inhibitor affinity chromatography matrix that normally binds the different types of CAs. However, homology of p54^{nrb}/NonO with CAs is low and the classical CA zinc-binding domain is not found. The specific enzymatic activity of recombinant p54^{nrb}/NonO is 25 U/mg [42]. No such activity is known for PSF.

7. Perspectives

Most nuclear proteins interacting with nucleic acids contain either DBD or RNA-binding domain. Uniquely, PSF and p54^{nrb}/NonO possess both domains. For p54^{nrb}/NonO it is shown that these properties are located in two different parts of the protein. Indeed, these proteins are found, as a heterodimer or alone, in several nuclear complexes involved in the binding and processing of nucleic acids. How are these multifunctional proteins operating in the simultaneous processes occurring in the nucleus? We propose that PSF and p54^{nrb}/NonO mediate different functions depending on the nuclear compartment (nuclear matrix, nucleoplasm, nuclear foci, nucleolus) in which they are located, and that localization might be regulated by phosphorylation [5,43,44]. PSF was recently found to be associated with a retained nuclear fraction of activated PKCα which is usually cytoplasmically localized,

and also serves as a substrate for this kinase [45]. Due to their dual RNA/DNA-binding properties and the ability to interact with several protein counterparts, these proteins might be regarded as 'sticky' proteins that can link multiple nuclear processes. The ability to either heterodimerize or to remain as monomers, and to bind RNA/DNA or interact with other nuclear factors or both, allows the production of a variety of nuclear complexes active in different nuclear reactions.

One option to consider is that PSF and p54^{nrb}/NonO serve structural functions through their multiple interfaces. The nuclear matrix fraction of these proteins might connect the nuclear scaffold to other parts of the nucleus. The work showing PSF and p54^{nrb}/NonO as part of a nuclear matrix anchor for the retention of I-RNAs or in association with the nuclear envelope may exemplify this concept. Similarly, these heterodimers, once in the soluble fraction of the nucleus, might serve as docking sites for other factors in the formation of transcription complexes and spliceosomes. In these cases, their binding to RNA/DNA will allow the recruitment of additional factors and the formation of complexes. The DNA-bound transcription complexes containing PSF/p54^{nrb}/SF-1, together with interchanging components Sin3A/HDAC and the RNA processing complexes harboring PSF, imply such structural interactions.

On the other hand, PSF and p54^{nrb}/NonO do not serve simply as bridging proteins. These proteins are shown to directly affect DNA pairing, stimulation of topoisomerase I activity, transcriptional activation or repression, CA activity and promotion of pre-mRNA splicing. In these cases they are usually identified in monomeric form and this might indicate nucleoplasmic localization. Indeed, translocated forms of these proteins localize aberrantly and it is speculated that perturbations of function and the natural binding to nuclear partners occur. Moreover, modified expression of p54^{nrb}/NonO and PSF is observed in cancer cells and in differentiating cells [4,46–51]. Therefore, the abundance of monomeric and heterodimeric forms in different cells probably varies, subsequently determining which complexes will assemble in each type of cell. Still, the fine details of understanding the simultaneous involvement of PSF or p54^{nrb}/NonO in this diversity of nuclear reactions remains to be determined.

8. Note added in proof

Recently, proteomic analysis of the human spliceosome has verified the presence of PSF in this large complex [52].

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References

[1] Cramer, P., Srebrow, A., Kadener, S., Werbajh, S., de la Mata, M., Melen, G., Nogues, G. and Kornblihtt, A.R. (2001) FEBS Lett. 498, 179–182.
[2] Patton, J.G., Porro, E.B., Galceran, J., Tempst, P. and Nadal-Ginard, B. (1993) Genes Dev. 7, 393–406.
[3] Meissner, M., Dechat, T., Gerner, C., Grimm, R., Foisner, R. and Sauermann, G. (2000) J. Cell. Biochem. 76, 559–566.
[4] Shav-Tal, Y., Lee, B.C., Bar-Haim, S., Schori, H. and Zipori, D. (2001) J. Cell Biochem. 81, 379–392.
[5] Shav-Tal, Y., Cohen, M., Lapter, S., Dye, B., Patton, J.G., Vandekerckhove, J. and Zipori, D. (2001) Mol. Biol. Cell 12, 2328–2340.
[6] Dye, B.T. and Patton, J.G. (2001) Exp. Cell Res. 263, 131–144.
[7] Dong, B., Horowitz, D.S., Kobayashi, R. and Krainer, A.R. (1993) Nucleic Acids Res. 21, 4085–4092.
[8] Yang, Y.S., Hanke, J.H., Carayannopoulos, L., Craft, C.M., Capra, J.D. and Tucker, P.W. (1993) Mol. Cell Biol. 13, 5593–5603.
[9] Andersen, J.S., Lyon, C.E., Fox, A.H., Leung, A.K., Lam, Y.W., Steen, H., Mann, M. and Lamond, A.I. (2002) Curr. Biol. 12, 1–11.
[10] Dreger, M., Bengtsson, L., Schoneberg, T., Otto, H. and Hucho, F. (2001) Proc. Natl. Acad. Sci. USA 98, 11943–11948.
[11] Fox, A.H., Lam, Y.W., Leung, A.K., Lyon, C.E., Andersen, J., Mann, M. and Lamond, A.I. (2002) Curr. Biol. 12, 13–25.
[12] Kulkarni, S.J., Steinlauf, A.F. and Hall, J.C. (1988) Genetics 118, 267–285.
[13] Miralles, F., Ofverstedt, L.G., Sabri, N., Aissouni, Y., Hellman, U., Skoglund, U. and Visa, N. (2000) J. Cell Biol. 148, 271–282.
[14] Zhang, W.W., Zhang, L.X., Busch, R.K., Farres, J. and Busch, H. (1993) Biochem. J. 290, 267–272.
[15] Basu, A., Dong, B., Krainer, A.R. and Howe, C.C. (1997) Mol. Cell. Biol. 17, 677–686.
[16] Guillonneau, F., Labas, V., Auvin, C. and Praseuth, D. (2001) Electrophoresis 22, 4391–4403.
[17] Bennett, M., Michaud, S., Kingston, J. and Reed, R. (1992) Genes Dev. 6, 1986–2000.
[18] Gozani, O., Patton, J.G. and Reed, R. (1994) EMBO J. 13, 3356–3367.
[19] Teigelkamp, S., Mundt, C., Achsel, T., Will, C.L. and Luhrmann, R. (1997) RNA 3, 1313–1326.
[20] Lutz, C.S., Cooke, C., O'Connor, J.P., Kobayashi, R. and Alwine, J.C. (1998) RNA 4, 1493–1499.
[21] Tiscornia, G. and Mahadevan, M.S. (2000) Mol. Cell 5, 959–967.
[22] Hallier, M., Tavitian, A. and Moreau-Gachelin, F. (1996) J. Biol. Chem. 271, 11177–11181.
[23] Zhang, Z. and Carmichael, G.G. (2001) Cell 106, 465–475.
[24] Nakayasu, H. and Berezney, R. (1991) Proc. Natl. Acad. Sci. USA 88, 10312–10316.
[25] Proudfoot, N. (2000) Trends Biochem. Sci. 25, 290–293.
[26] Urban, R.J., Bodenburg, Y., Kurosky, A., Wood, T.G. and Gasic, S. (2000) Mol. Endocrinol. 14, 774–782.
[27] Urban, R.J., Bodenburg, Y.H. and Wood, T.G. (2002) Am. J. Physiol. Endocrinol. Metabol. 283, E423–E427.
[28] Mathur, M., Tucker, P.W. and Samuels, H.H. (2001) Mol. Cell. Biol. 21, 2298–2311.
[29] Sewer, M.B., Nguyen, V.Q., Huang, C.J., Tucker, P.W., Kagawa, N. and Waterman, M.R. (2002) Endocrinology 143, 1280–1290.
[30] Sewer, M.B. and Waterman, M.R. (2002) Endocrinology 143, 1769–1777.
[31] Yang, Y.S., Yang, M.C., Tucker, P.W. and Capra, J.D. (1997) Nucleic Acids Res. 25, 2284–2292.
[32] Straub, T., Grue, P., Uhse, A., Lisby, M., Knudsen, B.R., Tange, T.O., Westergaard, O. and Boege, F. (1998) J. Biol. Chem. 273, 26261–26264.
[33] Straub, T., Knudsen, B.R. and Boege, F. (2000) Biochemistry 39, 7552–7558.
[34] Akhmedov, A.T., Bertrand, P., Corteggiani, E. and Lopez, B.S. (1995) Proc. Natl. Acad. Sci. USA 92, 1729–1733.
[35] Bertrand, P., Akhmedov, A.T., Delacote, F., Durrbach, A. and Lopez, B.S. (1999) Oncogene 18, 4515–4521.
[36] Akhmedov, A.T. and Lopez, B.S. (2000) Nucleic Acids Res. 28, 3022–3030.
[37] Thyagarajan, B. and Campbell, C. (1997) J. Biol. Chem. 272, 23328–23333.
[38] Deloulme, J.C., Prichard, L., Delattre, O. and Storm, D.R. (1997) J. Biol. Chem. 272, 27369–27377.
[39] Hallier, M., Lerga, A., Barnache, S., Tavitian, A. and Moreau-Gachelin, F. (1998) J. Biol. Chem. 273, 4838–4842.
[40] Clark, J., Lu, Y.J., Sidhar, S.K., Parker, C., Gill, S., Smedley, D., Hamoudi, R., Linehan, W.M., Shipley, J. and Cooper, C.S. (1997) Oncogene 15, 2233–2239.
[41] Skalsky, Y.M., Ajuh, P.M., Parker, C., Lamond, A.I., Goodwin, G. and Cooper, C.S. (2001) Oncogene 19, 178–187.
[42] Karhumaa, P., Parkkila, S., Waheed, A., Parkkila, A.K., Kaunisto, K., Tucker, P.W., Huang, C.J., Sly, W.S. and Rajaniemi, H. (2000) J. Biol. Chem. 275, 16044–16049.

[43] Hirano, K., Erdodi, F., Patton, J.G. and Hartshorne, D.J. (1996) FEBS Lett. 389, 191–194.
[44] Otto, H., Dreger, M., Bengtsson, L. and Hucho, F. (2001) Eur. J. Biochem. 268, 420–428.
[45] Rosenberger, U., Lehmann, I., Weise, C., Franke, P., Hucho, F. and Buchner, K. (2002) J. Cell Biochem. 86, 394–402.
[46] Lee, B.C., Shav-Tal, Y., Peled, A., Gothelf, Y., Jiang, W., Toledo, J., Ploemacher, R.E., Haran-Ghera, N. and Zipori, D. (1996) Blood 87, 2283–2291.
[47] Chanas-Sacre, G., Mazy-Servais, C., Wattiez, R., Pirard, S., Rogister, B., Patton, J.G., Belachew, S., Malgrange, B., Moonen, G. and Leprince, P. (1999) J. Neurosci. Res. 57, 62–73.
[48] Traish, A.M., Huang, Y.H., Ashba, J., Pronovost, M., Pavao, M., McAneny, D.B. and Moreland, R.B. (1997) Diagn. Mol. Pathol. 6, 209–221.
[49] Shinozaki, A., Arahata, K. and Tsukahara, T. (1999) Int. J. Biochem. Cell. Biol. 31, 1279–1287.
[50] Shav-Tal, Y., Lee, B.C., Bar-Haim, S., Vandekerckhove, J. and Zipori, D. (2000) Exp. Hematol. 29, 1029–1038.
[51] Pavao, M., Huang, Y.H., Hafer, L.J., Moreland, R.B. and Traish, A.M. (2001) BMC Cancer 1, 15.
[52] Rappsilber, J., Ryder, U., Lamond, A.I. and Mann, M. (2002) Genome Res. 12, 1231–1245.