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Minireview

The nuclear pore complex

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Over the past years, significant progress has been made both in the analysis of the structural and molecular organization of the nuclear pore complex (NPC) and the mechanism of nuclear transport. In this minireview, I will focus on some of the recent developments in this field. Structural studies employing high resolution EM have revealed a detailed view of the three-dimensional organization of the NPC. In addition, an isolation procedure which yields highly enriched NPCs from yeast has given insight into the molecular complexity of the NPC organization. By biochemical, immunological and genetic approaches, a series of novel pore proteins were identified. Exploiting yeast as a genetic system, several mutants defective in nuclear import of proteins and export of RNA were selected. By in vitro nuclear transport assays, soluble cytoplasmic factors including NLS (nuclear localization sequence) binding proteins and heat shock proteins required for nuclear accumulation were found. The aim of the future research must be to put these various components of the NPC and nuclear transport machinery in a topological and functional context.

Nuclear pore; Nuclear pore complex; Nuclear transport; Nuclear envelope; Nuclear localization sequence; Nucleoporin

1. GENERAL OVERVIEW

The nucleus is surrounded by a double membrane which compartmentalizes nuclear and cytoplasmic reactions. Besides its key role in regulating nucleocytoplasmic transport, the nuclear membrane provides a structural support for the attachment of other macromolecular structures such as the nuclear lamina, nucleoskeleton, cytoskeleton and chromatin. Furthermore, the outer nuclear membrane, which is covered with ribosomes and continuous with the ER, is a site for protein synthesis and protein translocation.

The transport of molecules and macromolecules across the nuclear membrane occurs through the nuclear pore complexes (NPCs). Several aspects of both the structural organization of the NPC and its role in nuclear transport reactions have been reviewed extensively [1–10]. It has been estimated that up to one hundred proteins constitute the NPC. How these proteins are involved in the biogenesis and structural organization of the nuclear pore complex and in nucleocytoplasmic trafficking remains a challenging question for the next decade of research.

For molecules to enter the cell nucleus, two mechanisms exist: passive diffusion of small molecules, and active transport of large macromolecules. The exclusion limit for diffusion is approximately 40–60 kDa [11]. If large molecules have to enter the nucleus, they require active transport which is ATP and temperature dependent [12]. However, even small and diffusable nuclear proteins such as histone H1 are actively imported into the nucleus [13,14].

Targeting sequences on nuclear proteins are responsible for specific organelle sorting. One of the first nuclear targeting signals (**NLS** = **n**uclear **l**ocalization **s**equence) to be identified was the short, 7 amino acid long sequence Pro-Lys-Lys-Lys-Arg-Lys-Val (PKKKRKV) of SV40 large T antigen which was considered to be the prototype of a NLS [15]. The model was extended when a bipartite NLS was found within nucleoplasmin. A typical feature of the bipartite NLS is two clusters of basic regions separated by a 10 residue long spacer sequence [15], although more complex NLS exist [16,17]. In general, nuclear proteins constitutively enter the nucleus after synthesis in the cytoplasm; in a few cases nuclear transport is regulated, i.e. the nuclear protein is retained in the cytoplasm and only upon a stimulus is transported into the nucleus (for review, see [18,19]). Modification of NLS (e.g. by phosphorylation/dephosphorylation [20,21] or masking/demasking [22,23]) are important mechanisms to regulate nucleocytoplasmic transport. The NLS is not proteolytically removed from the nuclear protein after its import. Since many nuclear proteins are released into the cytoplasm during mitotic nuclear envelope breakdown, they require the permanent presence of the NLS to be re-imported into the newly formed nucleus at the end of mitosis.

Export of rRNA, mRNA, snRNA and tRNA from the nucleus or import of snRNP into the nucleus, occurs through the nuclear pore complexes; RNA transport

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resembles protein transport in many respects being receptor-mediated, ATP-consuming and inhibited by wheat germ agglutinin [24,25]. Although RNA transport requires signals on the RNA moiety (e.g. a monomethyl cap on the snRNA for export [26] or trimethyl cap on the snRNP for import [27,28], proteinaceous components bound to RNA are also required. In the case of mRNA export, carrier proteins which shuttle between the nucleus and the cytoplasm have been implicated to play a crucial role [29].

2. THE NUCLEAR PORE COMPLEX (NPC)

2.1. *Structural analysis of the NPC*

Our current knowledge of the 3D pore structure stems from studies using a variety of electron microscopical techniques [30–33]. The pore complex has a diameter of 80–100 nm and a molecular mass of 125 MDa [32]. The nuclear pore complex consists of an outer and an inner coaxial ring with eight subunits arranged in octagonal symmetry and a central ring whose eight spokes protrude into the pore channel. In the center of the pore, a central plug (called the transporter) is frequently seen, and is proposed to control the active, NLS-mediated nucleocytoplasmic transport [31]. Recently, in addition to the large central pore, eight smaller peripheral channels have been noticed in the NPC which could be the main routes for passive diffusion of ions and small molecules through the pore complex [33]. By high resolution scanning electron microscopy, both surfaces of the nuclear envelope have been visualized in greater detail revealing structures adherent to the nuclear pore complex. At the nucleoplasmic face, a basket-like structure (called 'fishtraps') attached to the nucleoplasmic ring [34–36] and a novel, highly regular fibrous network of filaments, termed the nuclear envelope lattice (NEL) attached to the distal ring of the inner basket structure became visible [36]. The functional role of the baskets and NEL is unknown, but could be involved in RNP export.

2.2. *Isolation of nuclear pores and pore components*

Recently, a method was pioneered which allows the purification of mg quantities of highly enriched NPCs from yeast both on the basis of negative stain electron microscopy and coenrichment of characterized pore protein antigens [37]. Yeast might be the organism of choice to get purer pore complex preparations, because it might lack a nuclear lamina or, if existing, the nuclear lamina could be less tightly associated with the pore complexes. The purified nuclear pore complexes exhibit a disc-shaped structure with the central transporter surrounded by an annulus of octagonal symmetry. It is estimated that the purified pore preparation contains between 50 and 100 individual pore proteins.

Pore components were first identified by raising antibodies against (partially) purified nuclear pore proteins and screening for antibodies which react with pore proteins by indirect immunofluorescence. By this approach, a protein spanning the nuclear membrane at the NPC, called gp210 [38], and cytoplasmatically located pore proteins termed nucleoporins were found [39,40]. Vertebrate nucleoporins are characterized by *N*-acetyl glucosamin sugar modification (GlcNAc) and therefore bind the lectin wheat germ agglutinin. Interestingly, wheat germ agglutinin and monoclonal antibodies against nucleoporins inhibit nuclear transport [41–43]. Nucleoporins carrying GlcNAc residues therefore are essential components of the nuclear import machinery.

One prominent nucleoporin p62 [39] has been cloned from a variety of organisms including rat, human, mouse and *Xenopus* [44–46]. P62 can be divided into three parts consisting of a N-terminal domain with 12 repeats similar to those found in the yeast pore proteins NSP1 [47] and NUP1 [48], an adjacent Ser/Thr rich sequence followed by a unique carboxy-terminal domain which is organized into amphiphilic heptad repeats with the potential to form coiled-coil interaction.

A cDNA for a nuclear pore complex protein NUP153 from rat liver cells has recently been cloned and sequenced that shares degenerate pentapeptide repeats as found in p62 and yeast nucleoporins (see also later) [49]. NUP153 is exclusively localized on the nucleoplasmic side of the pore complex. Interestingly, it contains four zinc finger motifs which mediate binding to rat genomic DNA in a zinc-dependent fashion. It is therefore possible that this nucleoporin could be a DNA-binding subunit of the NPC that may link nuclear pores to specific DNA chromosomal sequences. It has been speculated that NUP153 is involved in the 3-dimensional organization of the genome allowing gene gating of transcribable genes to distinct nuclear pore complexes [50].

Yeast nuclear envelope proteins were identified which react with the monoclonal antibodies against mammalian nucleoporins [51]. Among these were the pore proteins NUP1 [48], NUP2 [52], NUP49, NUP100 and NUP116 [53]. Besides, the nuclear pore protein NSP1 [47] was identified in yeast by raising antibodies against the insoluble nuclear fraction [54]. NSP1 seems to be the homologue of vertebrate nucleoporin p62 [45]. Nucleoporins NUP49 and NUP116 are identical to NSP49 and NSP116 which had been found independently in a genetic screen [55]. This genetic approach provided in vivo evidence that distinct members of the nucleoporin family physically interact or share overlapping function in nuclear pore complexes.

The yeast nucleoporins reveal a diagnostic modular domain structure with many conserved repeat sequences. Comparison of the known members suggests to group them into two subfamilies: nucleoporins NSP1, NUP1 and NUP2 share in their central domain repeated 'GFSFG' motifs whereas NUP49/NSP49, NUP116/NSP116 and NUP100 have as a common re-

peat sequence the 'GLFG' motif [53,55]. Whether this distinction also signifies a common functional role remains to be shown.

2.3. *Targeting of components to the nuclear pore complex*

As shown for the pore protein NSP1, the carboxy-terminal domain carries all the information to target attached passenger proteins, such as cytosolic DHFR, to the nuclear pores [56]. For this process, not a short targeting signal, rather than the entire 220 amino acid long carboxy-terminal domain is required. This domain is organized into amphiphilic heptad repeats suggesting that coiled-coil interaction with another protein at the pore could mediate targeting to and assembly into the pore complex. For vertebrate p62, a similar targeting mechanism to the pore can be expected.

The glycoprotein gp210 is located in the 'pore membrane', i.e. at the nuclear pore complex where outer and inner nuclear membrane are joining. It has a large cisternal domain facing the perinuclear space, followed by a single transmembrane sequence and a 58-residue long cytoplasmic tail [57,58]. The large, luminal domain of gp210 does not contain sorting signals, whereas the transmembrane domain and, albeit weaker, the cytoplasmic carboxy-terminal segment are sufficient for targeting to the pore membrane [59]. It was suggested that the transmembrane helix forms a homo- or heterodimer thereby constituting the mechanism of pore targeting. The cytoplasmic gp210 tail may assist in nuclear pore targeting by binding to other peripheral pore proteins [59]. Interestingly, the mitotic gp210 which is dispersed throughout the mitotic cytoplasm remains associated with nucleoporins.

3. MECHANISM OF NUCLEAR TRANSPORT

3.1. *A role of nuclear pore proteins in nuclear transport and pore biogenesis*

Forbes and co-workers used polyclonal antibodies against p62 to immunodeplete it from *Xenopus* nuclear reconstitution extracts [60]. P62 depleted nuclei still contained nuclear pores, but were found to be defective in nuclear transport. A strict linear correlation between the amount of immuno-depleted p62 and the efficiency of transport of proteins into nuclei was observed. In independent studies, not only nuclear transport, but also the formation of nuclear pores was inhibited upon immunodepletion of p62 from *Xenopus* nuclear reconstitution extracts [61].

Expression of the *NSP1* gene, which encodes the yeast homologue of p62, was stopped in living cells using a regulatable promoter. NSP1 depleted cells showed mislocalization of nuclear reporter proteins in the cytoplasm [62]. Furthermore, the nuclear pore density decreased within the nuclear membrane during early NSP1 gene repression. However, if the *NSP1* gene was switched on again after NSP1 depletion, NSP1 was targeted to the nuclear pores, the nuclear pore density increased and nuclear reporter proteins re-accumulated inside the nucleus. The decrease in pore density could result either from the fact that NSP1 is a structural component of the nuclear pores and its depletion causes a stop in pore biogenesis, or NSP1 could be required for nuclear transport of crucial structural components of the nuclear pore complex.

The role of gp210 in pore structure and function was analyzed by expressing a monoclonal antibody directed against the luminal domain of gp210 in cultured rat cells [63]. This antibody was targeted after translocation into the ER lumen to the nuclear pore complex where it bound to the luminal domain of gp210. Strikingly, the antibody bound to gp210 perturbs pore function since it inhibited NLS-mediated nuclear transport and passive diffusion through the pore. Gp210 is directly or indirectly connected to these pore complex components which mediate nucleocytoplasmic transport.

3.2. *Identification of cytoplasmic components required for nuclear transport*

In vitro assays, used to measure nuclear transport were first the *Xenopus* nuclei reconstitution system [64,65] and, recently, the use of digitonin-permeabilized mammalian cells [66]. In vitro systems allowed enrichment for translocational intermediates and assessment of the need for soluble factors in the nuclear transport reaction [66,67]. By this approach, a 55 kDa NLS receptor was identified which specifically binds nuclear localization sequences in the cytoplasm thereby stimulating nuclear accumulation of proteins [68]. Another 70 kDa NLS-binding protein initially purified and characterized in yeast (called NBP) was found to be conserved throughout evolution [69]. Antibodies against the NBP inhibited nuclear transport in various in vitro assays including semi-permeabilized *Drosophila* tissue culture cells [69]. This indicates that the NBP phosphoprotein acts as a receptor for NLS and is required for nuclear accumulation of proteins. Anti-idiotype antibodies against the SV40 large T-antigen NLS allowed to identify several nuclear pore proteins conserved from yeast to man [70].

Moore and Blobel recently expanded the analysis of factors required for nuclear import and used the permeabilized system in combination with fractionated *Xenopus* cytosol [71]. Two fractions were obtained which mediated distinct steps in nuclear transport. One fraction reconstituted association of the substrate with the nuclear envelope, the other was promoting the translocation of the bound karyophile in an ATP-dependent fashion across the nuclear pore complex. Purification of the active component(s) of each of the cytosolic fractions should give insight into the molecular mechanism of nuclear transport.

Since nucleocytoplasmic transport requires ATP, it was suspected that heat shock proteins could be one of the ATP-consuming components [72]. In the permeabilized cell system, immunological depletion of hsc70 and hsp70 caused inhibition of nuclear transport [72]. Nuclear transport activity, however, was restored by addition of either purified hsc70 or hsp70. Furthermore, antibodies against hsc70 inhibited nuclear accumulation of karyophilic proteins [73]. Since heat shock proteins can shuttle between the nuclear and cytoplasmic compartment, they may indeed act as shuttling carriers for nuclear proteins during the translocation process. The molecular role of HSPs in nuclear transport is not clear, but they may help to keep the NLS exposed on the transported protein or in the correct conformation so that interaction of the NLS receptor(s) is facilitated [7]. In favour of this model is that bacterially expressed and purified hsc70 can bind to the intact, but less well to a mutant NLS of SV40 large T antigen [73].

NLS-mediated nuclear transport of proteins is blocked by wheat germ agglutinin and monoclonal antibodies which recognize O-linked glycoproteins [41–43]. To test whether cytosolic factors required for in vitro import of nuclear proteins directly bind to nucleoporins, O-linked glycoproteins released from the nuclear envelope were immobilized on Sepharose beads with bound wheat germ agglutinin or specific antibodies [74]. A cytosolic fraction depleted of components which bound to immobilized nuclear pore proteins was no longer active in supporting nuclear transport and it was suspected that a 180 kDa O-glycosylated protein is one of the factors which is involved in cytosol inactivation. The factor bound to the nucleoporins is not the 55 kDa NLS receptor.

Nopp140 is a nucleolar protein which upon phosphorlyation can bind NLS [75]. Nopp140 shuttles between the nucleolus and the cytoplasm and thus could be another mobile receptor transporting components between the nucleolus and the cytoplasm [76]. Interestingly, shuttling seems to occur on tracks inside the nucleus extending from the nucleolus, crossing the nucleoplasm and some of them being connected to the nuclear pore complexes. It was discussed that Nopp140 is a chaperone-like molecule for import into and/or export of preribosomal particles from the nucleolus following specific intranuclear tracks [76].

3.3. *Genetic screens for nuclear transport mutants*

Mutants defective in nuclear protein import were found in yeast using an elegant genetic selection approach [77]. To identify proteins that are involved in recognition of nuclear localization signals, conditional-lethal **npl** (for **n**uclear **p**rotein **l**ocalization) mutants were isolated that missorted a conjugate between a mitochondrial protein fitted with a NLS to the mitochondria. In a wild-type cell, the NLS-conjugate was targeted into the nucleus. The genes corresponding to three complementation groups were cloned. npl1 is allelic to sec63 [78], a known gene required for translocation across the ER membrane; npl1 mutants are defective in nuclear retention rather than nuclear transport. Mutants of npl3 [79] and npl6 [10] alter the uptake of proteins into the nucleus with no apparent defect in nuclear retention. *NPL3* encodes a nuclear protein with a glycine/arginine rich sequence typically found in several nucleolar proteins, and an RNA binding sequence [79]. It was suggested that the mutant NPL3 protein could bind to components of the nuclear transport machinery thereby interfering with the import of other karyophiles. *NPL3* is allelic to *NOP3*, a gene which encodes a yeast protein shown to be also required for rRNA processing and ribosome biogenesis [80].

In a genetic approach similar to that reported by Silver and colleagues exploiting mistargeting of a NLS-cytochrome *c* fusion protein into mitochondria, the *NIP1* gene was found to be required for nuclear transport in yeast [81]. In the *nip1* mutant, nuclear accumulation of a lacZ nuclear reporter protein was impaired; how cytoplasmic NIP1 is involved in nuclear transport mechanisms remains unclear.

Recently, an assay was developed which allows the detection of mRNA within yeast cells by in situ hybridization [82,83]. Applying this assay, a collection of temperature-sensitive mutants was screened for aberrant patterns of mRNA distribution, e.g. for nuclear accumulation of mRNA [82], or a 'suicide' selection procedure was developed to enrich for mutants which cannot export mRNA [83]. In fact, a known mutant which is defective in mRNA export, *rna1–1*, turned out to accumulate poly(A)$^+$ mRNA at the nuclear periphery in the cells if shifted to the non-permissive temperature [82]. By screening a bank of ts yeast strains for nuclear mRNA accumulation at the restrictive condition, the *rat1–1* mutant was found which exhibited mRNA accumulation inside the nucleus in discrete spots and at the nuclear periphery [82]. The cloned *RAT1* gene encodes a 116 kDa protein with homology to exoribonucleases. Thus, mRNA metabolism is somehow linked to mRNA export, but it seems less likely that RAT1 is directly involved in RNA trafficking.

REFERENCES

[1] Akey, C.W. (1992) Curr. Opin. Struct. Biol. 2, 258–263.
[2] Yamasaki, L. and Lanford, R.E. (1992) Trends Cell Biol. 2, 123–126.
[3] Stewart, M. (1992) Cell Biol. 3, 267–277.
[4] Stochaj, U. and Silver, P. (1992) Eur. J. Cell Biol. 59, 1–11.
[5] Forbes, D.J. (1992) Annu. Rev. Cell Biol. 8, 495–527.
[6] Dingwall, C. and Laskey, R. (1992) Science 258, 942–947.
[7] Goldfarb, D.S. (1992) Cell 70, 185–188.
[8] Carmo-Fonseca, M. and Hurt, E.C. (1991) Chromosoma 101, 199–205.
[9] Hurt, E.C., Mutvei, A. and Carmo-Fonseca, M. (1992) Int. Rev. Cytol. 136, 145–184.
[10] Osborne, M.A. and Silver, P.A. (1993) Annu. Rev. Biochem. 62, 219–254.

[11] Peters, R. (1986) Biochim. Biophys. Acta 864, 305–359.
[12] Richardson, W.D. , Mills, A.D., Dilworth, S.M., Laskey, R.A. and Dingwall, C. (1988) Cell 52, 655–664.
[13] Breeuwer, M. and Goldfarb, M. (1990) Cell 60, 999–1008.
[14] Moreland, R.B., Langevin, G.L., Singer, R.H., Garcea, R.L. and Hereford, L.M. (1987) Mol. Cell. Biol. 7, 4048–4057.
[15] Kalderon, D., Roberts, B.L., Richardson, W.P. and Smith, A.E. (1984) Cell 39, 499–509.
[16] Silver, P.A., Keegan, L.P. and Ptashne, M. (1984) Proc. Natl. Acad. Sci. USA 81, 5951–5955.
[17] Kambach, C. and Mattaj, I.W. (1992) J. Cell Biol. 118, 11–21.
[18] Dingwall, C. (1991) BioEssays 13, 213–218.
[19] Nigg, E.A., Baeuerle, P.A. and Lührmann, R. (1991) Cell 66, 15–22.
[20] Rihs, H.-P., Jans, D.A., Fan, H. and Peters, R. (1991) EMBO J. 10, 633–639.
[21] Moll, T., Tebb, G., Surana, U., Robitsch, H. and Nasmyth, K. (1991) Cell 66, 743–758.
[22] Picard, D. and Yamamoto, K.R. (1987) EMBO J. 6, 3333–3340.
[23] Henkel, T., Zabel, U., Van Zee, K., Müller, J.M., Fanning, E. and Baeuerle, P.A. (1992) Cell 68, 1121–1133.
[24] Goldfarb, D.S. and Michaud, N. (1991) Trends Cell Biol. 1, 20–24.
[25] Izaurralde, E. and Mattaj, I.W. (1992) Sem. Cell Biol. 3, 279–288.
[26] Hamm, J. and Mattaj, I.W. (1990) Cell 63, 109–118.
[27] Fischer, U. and Lührmann, R. (1990) Science 249, 786–790.
[28] Hamm, J., Darzynkiewicz, E., Tahara, S.M. and Mattaj, I.W. (1990) Cell 62, 569–577.
[29] Piñol-Roma, S. and Dreyfuss, G. (1992) Nature 355, 730–732.
[30] Unwin, P.N. and Milligan, R.A. (1982) J. Cell Biol. 93, 63–75.
[31] Akey, C.W. (1989) J. Cell Biol. 109, 955–970.
[32] Reichelt, R., Holzenburg, E.L., Buhle, E.L., Jarnik, M., Engel, A. and Aebi, U. (1990) J. Cell Biol. 110, 883–894.
[33] Hinshaw, J.E., Carragher, B.O. and Milligan, R.A. (1992) Cell 69, 1133–1141.
[34] Ris, H. (1989) Inst. Phys. Conf. Ser. 98, 657–662.
[35] Jarnik, M. and Aebi, U. (1991) J. Struct. Biol. 107, 291–308.
[36] Goldberg, M.W. and Allen, T.D. (1992) J. Cell Biol. 119, 1429–1440.
[37] Rout, M.P. and Blobel, G. (1991) J. Cell Biol. 115, 458.
[38] Gerace, L., Ottaviano, Y. and Kondor-Koch, C. (1982) J. Cell Biol. 95, 826–837.
[39] Davis, L.I. and Blobel, G. (1986) Cell 45, 699–709.
[40] Snow, C.M., Senior, A. and Gerace, L. (1987) J. Cell Biol. 104, 1143–1156.
[41] Yoneda, Y., Imamoto-Sonobe, N., Yamaizumi, M. and Uchida, T. (1987) Exp. Cell Res. 173, 586–595.
[42] Finlay, D.R., Newmeyer, D.D., Price, T.M. and Forbes, D.J. (1987) J. Cell Biol. 104, 189–200.
[43] Featherstone, C., Darby, M.K. and Gerace, L. (1988) J. Cell Biol. 107, 1289–1297.
[44] Starr, C.M., D'Onofrio, M., Park, M.K. and Hanover, J.A. (1990) J. Cell Biol. 110, 1861–1871.
[45] Carmo-Fonseca, M., Kern, H. and Hurt, E.C. (1991) Eur. J. Cell Biol. 55, 17–30.
[46] Cordes, V., Waizenegger, I. and Krohne, G. (1991) Eur. J. Cell Biol. 55, 31–47.
[47] Nehrbass, U., Kern, H., Mutvei, A., Horstmann, H., Marshallsay, B. and Hurt, E.C. (1990) Cell 61, 979–989.
[48] Davis, L.I. and Fink, G.R. (1990) Cell 61, 965–978.
[49] Sukegawa, J. and Blobel, G. (1993) Cell 72, 29–38.
[50] Blobel, G. (1985) Proc. Natl. Acad. Sci. USA 82, 8527–8529.
[51] Aris, J.P. and Blobel, G. (1989) J. Cell Biol. 108, 2059–2067.
[52] Loeb, J.D.J., Davis, L.I. and Fink, G.R. (1991) J. Cell Biol. 115, 318.
[53] Wente, S.R., Rout, M.P. and Blobel, G. (1992) J. Cell Biol. 119, 705–723.
[54] Hurt, E.C. (1988) EMBO J. 7, 4323–4334.
[55] Wimmer, C., Doye, V., Grandi, P., Nehrbass, U. and Hurt, E. (1992) EMBO J. 11, 5051–5061.
[56] Hurt, E.C. (1990) J. Cell Biol. 111, 2829–2837.
[57] Greber, U.F., Senior, A. and Gerace, L. (1990) EMBO J. 9, 1495–1502.
[58] Wozniak, R.K., Bartnik, E. and Blobel, G. (1989) J. Cell Biol. 108, 2083–2092.
[59] Wozniak, R.W. and Blobel, G. (1992) J. Cell Biol. 119, 1441–1449.
[60] Finlay, D.R., Meier, E., Bradley, P., Horecka, J. and Forbes, D.J. (1991) J. Cell Biol. 114, 169–183.
[61] Dabauvalle, M.-C., Loos, K. and Scheer, U. (1990) Chromosoma 100, 56–66.
[62] Mutvei, A., Dihlmann, S., Herth, W. and Hurt, E.C. (1992) Eur. J. Cell Biol. 59, 280–295.
[63] Greber, U.F. and Gerace, L. (1992) J. Cell Biol. 116, 15–30.
[64] Newmeyer, D.D., Lucocq, J.M., Bürglin, T.R. and De Robertis, E.M. (1986) EMBO J. 5, 501–510.
[65] Newmeyer, D.D., Finlay, D.R. and Forbes, D.J. (1986) J. Cell Biol. 103, 2091–2102.
[66] Adam, S.A., Marr, R.S. and Gerace, L. (1990) J. Cell Biol. 111, 807–816.
[67] Newmeyer, D.D. and Forbes, D.J. (1990) J. Cell Biol. 110, 547–557.
[68] Adam, S.A. and Gerace, L. (1991) Cell 66, 837–847.
[69] Stochaj, U. and Silver, P.A. (1992) J. Cell Biol. 117, 473–482.
[70] Stochaj, U., Bossie, M.A., Van Zee, K., Whalen, A.M. and Silver, P.A. (1993) J. Cell Sci. 104, 89–95.
[71] Moore, M.S. and Blobel, G. (1992) Cell 69, 939–950.
[72] Shi, Y. and Thomas, J.O. (1992) Mol. Cell. Biol. 12, 2186–2192.
[73] Imamoto, N., Matsuoka, Y., Kurihara, T., Kohno, K., Miyagi, M., Sakiyama, F., Okada, Y., Tsunasawa, S. and Yoneda, Y. (1992) J. Cell Biol. 119, 1047–1061.
[74] Sterne-Marr, R., Blevitt, J.M. and Gerace, L. (1992) J. Cell Biol. 116, 271–280.
[75] Meier, U.T. and Blobel, G. (1990) J. Cell Biol. 111, 2235–2245.
[76] Meier, U.T. and Blobel, G. (1992) Cell 70, 127–138.
[77] Sadler, I., Chiang, A., Kurihara, T., Rothblatt, J., Way, J. and Silver, P. (1989) J. Cell Biol. 109, 2665–2675.
[78] Rothblatt, J.A., Deshaies, S.L., Sanders, S.L., Daum, G. and Schekman, R. (1989) J. Cell Biol. 109, 2641–2652.
[79] Bossie, M.A., DeHoratius, C., Barcelo, G. and Silver, P. (1992) Mol. Biol. Cell 3, 875–893.
[80] Russell, I.D. and Tollervey, D. (1992) J. Cell Biol. 119, 737–747.
[81] Gu, Z., Moerschell, R.P., Sherman, F. and Goldfarb, D. S. (1992) Proc. Natl. Acad. Sci. USA 89, 10355–10359.
[82] Amberg, D.C., Goldstein, A.L. and Cole, C.N. (1992) Genes Dev. 6, 1173–1189.
[83] Kadowaki, T., Zhao, Y. and Tartakoff, A.M. (1992) Proc. Natl. Acad. Sci. USA 89, 2312–2316.