Mini Review

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Electron microscopy of nuclear nanoribonucleoproteins (nanoRNPs)

Abstract

In the cell nucleus several ribonucleoproteins related to gene expression are present. The nucleolus, coiled bodies and other nuclear particles are among these structures. Particles of nanometer size include perichromatin fibrils, perichromatin and Balbiani ring granules, interchromatin granules and Lacandonia granules. All of them are involved in pre-messenger RNA intranuclear metabolism. Previous and recent research suggests that these particles are involved in transcription and processing of pre-messenger RNA within the cell nucleus.

Keywords: Balbiani ring, cell nucleus, *Lacandonia*, microscopy, nucleolus, RNPs

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Abbreviations: BRG, Balbiani ring granules; IGCs, interchromatin granules; LGs, lacandonia granules; nanoRNPs, nanoribonucleoproteins; PCGs, perichromatin granules; PFs, perichromatin fibrils

Introduction

The cell nucleus is a highly dynamic and compartmentalized cell organelle.[1] In addition to harbor the majority of the genome of a species, most early gene expression is carried out in it. Eukaryotic early gene expression includes the synthesis and processing of transcripts. The transcripts are coupled to several factors constituting ribonucleoproteins (RNPs). On the one hand, the nucleolus is the largest RNP;[2] on the other hand other structures called nuclear particles are also present which measure nanometers in diameter. We use the term nanoRNPs as to refer to them.

Interchromatin granules (IGCs) were first described in 1959 by Swift[3] in Ehrlich ascites tumor cells of mammalians. They are 20-25nm in diameter nuclear RNPs present as clumps in the interchromatin space.[4–6] Monneron & Bernhard[7] characterized them as ribonucleoprotein particles. They contain abundant splicing factors and may play a role in the metabolism of pre-mRNA as storage sites for splicing molecules.[4–7] More recently, atomic force microscopy,[8] proteomic analysis[9] after isolation procedures[10] have been achieved.

Perichromatin granules (PCGs) were described by Watson[11] in 1962 in animal cells. PCGs are 30-50 nm in diameter nuclear particles present at the periphery of clumps of compact chromatin, and are surrounded by a clear halo of 25 nm width. They are composed of about 1.5nm width fibrils. Sometimes, the PCGs are connected to tiny fibrils of 2-3nm diameter.[7] Research on these granules includes efforts in the isolation and biochemical characterization work.[12] PCGs are ultrastructurally equivalent structures to Balbiani ring granules.[13] Several lines of evidence point to a role in transport and/or storage of some types of mRNA within the cell nucleus.

Perichromatin fibrils (PFs) were described for the first time by Monneron & Bernhard[7] in a number of mammalian cells. In addition, they have been found in a large variety of eukaryote cells.[14,15] PFs are composed of tiny fibrils of about 3-5nm width and are present at the periphery of clumps of compact chromatin. They label rapidly after short pulses of tritiated uridine[16,17] and contain transcription and processing factors as evaluated by immunoelectron microscopy.[15,18] PFs are considered a conserved morphological *in situ* form of early pre-mRNA transcription and splicing.

Balbiani ring granules (BRGs) were described in 1954 by Beerman & Bahr[19] in the Balbiani rings of polytene chromosomes present in larvae of some insects as *Drosophila* and *Chironomus*. They are ribonucleoprotein particles of 30-50nm diameter.[13] Ultrastructural studies including quantitative measurement of phosphorus have pointed out that BRGs are morphologically equivalent to perichromatin granules.[20] Therefore, they are proposed as storage and/or transport of mRNAs.

Lacandonia granules were described in 1992 by Jiménez-García et al.[21] in the nucleus of the plant *Lacandonia schismatica*. They are nuclear particles about 32nm in diameter nuclear particles present as large clumps in the perichromatin and interchromatin space, are present in several plant of cells as *Lacandonia schismatica*, *Triuris brevistylis*,[21] *Ginkgo biloba*,[22] bryophytes (*Marchantia polymorpha*, a liverwort; *Polytrichum juniperinum*, a moss; *Anthoceros punctatus*, a hornwort),[23] and *Welwitschia mirabilis*.[24] Using several ultrastructural cytochemical techniques it has been observed that they contain RNA, are associated to splicing factors and vary in number during the development of the flower.[25] Their ultrastructural features suggest that they are equivalent to Balbiani ring granules found in salivary gland cells larvae of some dipters as *Drosophila* and *Chironomus*[19] and also to perichromatin granules. More recently, LGs have been visualized by the atomic force microscope.[26–28]

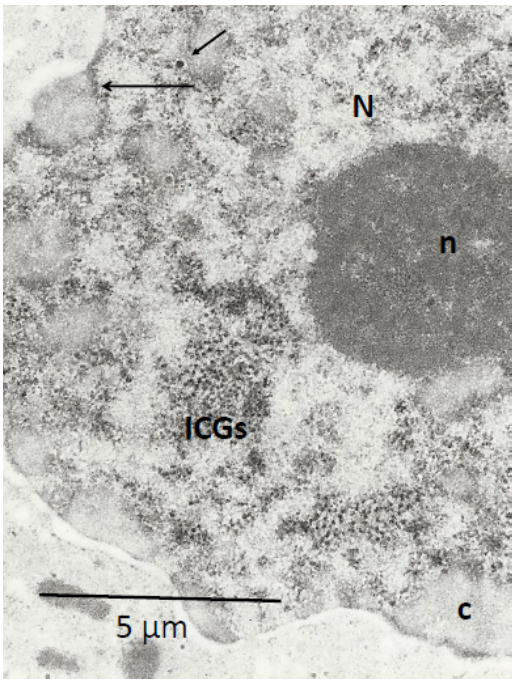

Figure 1 Transmission electron microscopy of nuclear nanoribonucleoprotein particles in the cell nucleus of a rat suprarenal mammalian cell (Courtesy of Profs. G.H. Vázquez-Nin and O. M. Echeverría, UNAM, México).

Abbreviations: N, nucleus; n, nucleolus; IGCs, interchromatin granule clusters; small arrow, perichromatin granule; PFs, large arrow, perichromatin fibrils. EDTA-regressive staining

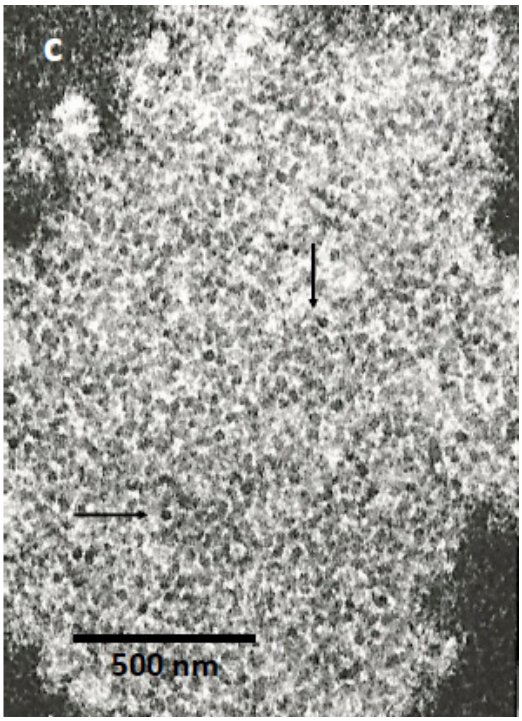

Figure 2 Transmission electron microscopy of Lacandonia granules in a tegument cell of the plant *Lacandonia schismatica*. Lacandonia granules (arrows) are present among large strands of compact chromatin (c). Uranyl acetate-lead citrate staining.

Figure 3 Schematic representation of the different nuclear nanoRNPs.

Discussion

There are several nuclear ribonucleoprotein particles measuring some nanometers in diameter within the cell nucleus. Here we use the term nanoRNPs to refer to them. Nuclear particles have been described since more than 60 years ago. Research in this field was first mainly devoted to ultrastructural analysis, but soon after the use of ultrastructural approaches combining cytochemical and high resolution autoradiography, as well as ultrastructural immunocytochemical techniques produced significant advances as to know the *in situ* composition at high resolution. The use of antibodies and molecular probes as nucleic acids for *in situ* hybridization suggested that gene expression was associated to these particles, particularly transcription and RNA processing. In fact, there is an area of some 200nm far from chromatin called perichromatin region that surrounds clumps of compact chromatin, where perichromatin fibrils and granules are present.[29] Therefore, most transcription and processing of pre-mRNA as splicing, capping and polyadenylation take place there. Many disease as cancer and dystrophy are related to these basic molecular functions and nuclear particles may be involved. Novel techniques using also light microscopy at high resolution, the green fluorescent protein , and molecular approaches as genomic and proteomics, support the current view of the cell nucleus as a very compartmentalized and dynamic organelle, that at the same time contains the majority of the genome of a species.

Finally, while interchomatin granules and perichromatin fibrils display counterparts by staining patters by light microscopy in a cellular pattern known as speckled pattern,[5,6] no staining patters by fluorescence are available for perichromatin and Lacandonia granules. Future work may be devoted to isolate both proteins and nucleic acids

from these several particles and perform high resolution microscopy to know more about their precise function.

Conclusion

Within the cell nucleus, several nuclear nanoribonucleoproteins are present, they are related to different stages of gene expression as transcription, processing, transport and storage of mRNA. They are detected by transmission electron microscopy and are widely distributed among cells of animal and plant species.

Acknowledgments

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Conflicts of interest

The authors declare there are no conflicts of interest.

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