INFORMOSOMES

In the 1950s and 1960s, Neifakh [1] studied the effect of radiation on embryo development in various animals (echinoderms, fish, and amphibians) and observed a periodicity in the morphogenetic function of nuclei. Spirin and colleagues studied the molecular basis of this phenomenon. It was found that the majority of mRNAs synthesized in early development are not translated in polysomes, but occur in the cytoplasm in the form of ribonucleoprotein (RNP) complexes in loach *Misgurnus fossilis* [2, 3] and urchin *Lytechinus pictus* [4]. A physico-chemical feature of these complexes is that their buoyant density in CsCl gradients is 1.40–1.45 g/cm$^3$, in contrast to a density of 1.51–1.52 g/cm$^3$ characteristic of polysomes. The complexes vary in size as a result of heterogeneity of their mRNAs. The RNA-containing RNPs were termed informosomes. Based on their buoyant density, the protein content in informosomes is 75–80%. It was assumed that the informosome proteins transfer mRNA from the nucleus into the cytoplasm, protect it from RNases, and regulate (modulate) protein synthesis at the translational level [5]. The functional regulation of translation was especially clear in the case of mRNAs that accumulate during oogenesis and start translation in embryo development. Such mRNAs are known as masked. The periodicity of the morphogenetic function of the nucleus during embryo development was explained by a periodic initiation of synthesis of certain proteins from masked templates. More recently, informosomes were found in cells of various eukaryotes, including both animals and plants [6, 7]. Informosomes containing viral mRNAs were described [8]. High-molecular-weight heterogeneous RNAs, which are mRNA precursors, were detected in the form of RNPs with properties similar to informosomes in animal cell nuclei [9, 10]. When polysomes were dissociated with EDTA, mRNAs were released from ribosomes in the form of mRNPs with a buoyant density of 1.45 g/cm$^3$ in a CsCl gradient [11].

It was of interest to compare the protein composition for different mRNPs, such as nuclear, free cytoplasmic, and polysome-associated mRNPs. Attempts were made to isolate pure informosomes for this purpose. However, it was objectively difficult to do this because mRNPs occur in minute amounts compared with the amounts of polysomes and ribosomes, informosomes are heterogeneous in size, and formaldehyde fixation is necessary for separating polysomes and ribosomes in a CsCl density gradient. Because of these factors, discrepant data on the sets of informosome proteins were reported even for the same subjects by different researchers [12]. Progress was made upon preparative isolation of globin mRNPs from rabbit reticulocytes, which intensely produce hemoglobin, while other proteins are synthesized in minor amounts, if at all. The globin mRNA occurs in so large an amount in reticulocytes that it is detectable by UV absorption. As a result, Blobel [13, 14] described a protein from polysome-associated mRNPs, which led to a discovery of the poly(A)-binding protein (PABP). Purification of free informosomes from reticulocytes made it possible to isolate YB1 (p50) as their major protein [15]. Informosomes were no longer studied in other subjects, and the term informosome went out of use. However, it is commonly accepted now that mRNA occurs in complexes with proteins in the cell. The complexes are termed free mRNPs in contrast to polysome-associated mRNPs. Numerous other mRNA-binding proteins involved in mRNPs were identified owing to the development of gene-engineering techniques, such as cDNA synthesis and sequencing and production of recombinant proteins. To date, several dozens of RNA-binding proteins have been described to regulate the function of various mRNAs [16–21]. The proteins...
are detectable in various mRNP granules with the use of immunohistochemical methods and fluorescent labels. The granules are differently termed according to the proteins and cells under study.

HEAVY INFORMOSOMES

It was noted in early studies on embryo cell informosomes that their major fraction sediments in sucrose gradient quicker than ribosome, as is the case with polysomes [4, 5, 22]. Since the mRNA size in heavy informosomes was the same as in light postribosomal informosomes, heavy informosomes were assumed to be aggregates of light ones [23]. This conclusion was supported by the fact that heavy informosomes dissociate into light informosomes upon RNP fixation with UV light and treatment with sodium dodecyl sulfate without changing their buoyant density, that is, without losing their proteins [24]. In addition, a certain amount of rRNA was found in the heavy informosome fraction [25]. It was assumed that light informosomes associate with each other and with ribosomes when they bind to the cytoskeleton to be transported to a targeted location. Jansen [26] analyzed the RNA–cytoskeleton association studies of the 1990s and arrived at the same conclusion, indicating that mRNA interacts with microtubules and microfilaments in the form of large mRNPs, which contain components of the translation apparatus, including ribosomes, in some cases. The studies considered below confirm again that mRNPs are capable of forming large complexes and interacting with the cytoskeleton.

GW, P, AND EGP BODIES

These particles were initially described as cell compartments, or foci, that are found in the mammalian cell cytoplasm and contain 5'–3' exonuclease XRN1 [27]. The particles were larger than 300 nm in dimension. In 2002, human cells were observed to harbor particles containing the RNA-binding protein GW, which is enriched in glycine (G) and tryptophan (W) residues. The particles did not overlap the Golgi system, endosomes, lysosomes, and peroxysomes. They were termed GW bodies and were considered to be RNP involved in the posttranscriptional control of gene expression [28]. The term “processing (P) bodies” was initially applied to the yeast cell granules that accumulate mRNA-decapping enzymes [29] and were detected immunohistochemically. We think the term ill chosen because, in molecular biology, processing means the RNA transformation processes that occur in the nucleus and are not immediately related to cytoplasmic mRNPs. We will hereafter use the abbreviation PB. The presence of mRNA in PBs is demonstrated by the fact that PBs disappear when transcription or translation are suppressed at the elongation step or cells are treated with RNase [30, 31].

The cap is a crossing point of two competitive pathways in the mRNA fate. The cap appearing at the 5' end is essential for translation initiation on the majority of templates. This requires cap binding with the initiation factor eIF4E. The binding is stabilized by the binding of eIF4G and the poly(A)-binding protein, which is anchored at the 3' end of the poly(A) tail. The events provide a signal for starting translation and prevent the cap from interacting with decapping machinery, which involves DCP2, DCP1, and several other proteins. When eIF4E is detached from mRNA, the decapping enzymes bind to the cap, degrade it, and allow further exonucleolytic degradation of the mRNA [18, 21]. Decapping and its competition with translation have been reviewed in detail [32]. Since decapping precedes 5'-3' exonucleolytic mRNA degradation, it was assumed that PBs are a site where mRNA arrives from polysomes for subsequent degradation. Inactivation of the DCP2 decapping enzyme or XRN1 5'-3' exonuclease accelerates the formation of PBs [29, 33]. Manipulations that release mRNA from polysomes and increase the free mRNP pool in the cell similarly increase the PB amount [30, 31, 34]. There is evidence that deadenylation, which precedes decapping, also occurs in PBs [35, 36]. PBs lack enzymes involved in 3'-5' mRNA degradation, which are concentrated in exosomes, suggesting a difference in compartmentalization of the mRNA degradation pathways [18]. PBs were found to additionally accumulate other proteins, which are involved in degradation of mRNAs with premature nonsense codons (NMD) [37–39], microRNA-dependent mRNA silencing [40–43], polyadenylation (cytoplasmic polyadenylation element-binding protein, CPEP) [44], and translation initiation [35, 45]. For instance, the DED1p translation factor (DEAD-box RNA helicase) causes PB accumulation in yeast cells [46]. Even viral RNAs and host antiviral proteins were detected in PBs [47]. Therefore, 5'-3' exonucleolytic RNA cleavage is not the only function of PBs. It should be noted that direct evidence of mRNA degradation in PBs is lacking.

Basal translation is inhibited at the level of its initiation, and part of mRNA accumulates in large PBs in yeast cells exposed to stress, for instance, glucose starvation [30]. The same effect was observed for overexpression of DED1p and PAT1 (decapping activator and translational repressor) [48]. These proteins occur in PBs and, possibly, are the main components that hold mRNA in PBs [32]. A special role of PAT1 and DCP2p in PB assembly is evident from a deletion analysis [49]. In addition, two other yeast proteins, EDC3 (enhancer of decapping 3) and LSM4 (like U6 small nuclear RNA associated) are necessary for physical interactions between mRNAs included in PBs [50–52]. Deletions from certain domains of these proteins cause a complete disappearance of PBs but exert no effect on mRNA translation and degradation. When stress ceases, a substantial part of yeast transcripts leaves PBs for polysomes [34]. Other yeast