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Protein Synthesis in Eukaryotic Cells in the Translational Initiation Phase

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Abstract

A crucial factor in controlling protein synthesis in eukaryotic cells is the eukaryotic Initiation Factor 2, which is associated with the translational initiation phase. As ocean urchin eggs are fertilised, protein synthesis activity quickly increases, which is crucial for the formation of embryonic mobileular cycles. Here, we show that fertilisation causes eIF2 to dephosphorylate, which is accompanied by an increase in protein synthesis, and that eIF2 phosphorylation is specifically linked to an inhibition of protein synthesis and the arrest of the cell cycle. We verified that dephosphorylation of eIF2 is necessary for protein synthesis hobby and mobileular department development after fertilisation by microinjecting a phospho-mimetic protein into sea urchin eggs.

Keywords: Protein synthesis; embryonic mobileular cycles; Dephosphorylate; Fertilisation

Introduction

For further information, see the website. A ternary complex is created when the three subunits of eIF2 bind both GTP and the initiator methionyl-tRNA. At the initiation phase of translation, eIF2 mediates the binding of initiator methionyl-tRNA to the ribosomes [1, 2]. Many different organisms use the phosphorylation of the eIF2 alpha subunit at a conserved serine as a method of controlling translation. The enhanced affinity of phosphorylated eIF2 for its alternative guanine nucleotide component, eIF2B, results in the sequestration of eIF2B as an inactive complex with eIF2 and GDP. The reduced normal rate of guanine nucleotide alternate at the final phosphorylated eIF2 then inhibits the production of all proteins, which paradoxically leads to the interpretation of a subset of mRNAs with upstream short open reading frames. Four well-known serine/threonine protein kinases have been identified that phosphorylate eIF2 and share a common kinase area but respond to different stimuli through distinct regulatory domains. These kinases include the general control non-derepressible 2 that is activated by uncharged tRNA, the PKR-like endoplasmic reticulum kinase that is activated by misfolded proteins in endoplasmic [3, 4]. All eukaryotes have GCN2, metazoans have PERK, vertebrates have HRI as well as a few species of yeast, bugs, and invertebrates, and vertebrates alone have PKR. It is now accepted that translational control via eIF2 phosphorylation is a conserved paradigm to the mobileular strain that predated the emergence of eukaryotes.

The ability to deal with translational law in a physiological condition and beyond the state of strain is provided by fertilisation of the ocean urchin egg. Protein synthesis occurs in unfertilized eggs at a relatively modest rate. Independent of mRNA transcription and ribosome biogenesis, protein synthesis begins minutes after fertilisation [5, 6]. Additionally, the development of the first mobileular department depends on protein synthesis. Increased rates of translation initiation and elongation, as well as mRNA recruitment into polysomes, are some of the multifactorial mechanisms that impose translational up-law. During fertilisation of sea urchin eggs, the cap-installed translation inhibitor 4E-BP is unexpectedly phosphorylated and destroyed, which is most important for the release of eIF4E and its association with the scaffolding protein eIF4G. As a result, eIF4E is now recognised as a key player in the beginning of the primary mitotic division after fertilisation, indicating that cap-installed translation is specifically controlled with regard to the course of this process. Yet this one actor won't be able to apply translational rule in the direction of fertilisation alone, as the inclusion of other factors like eIF2 and eIF2B in sea urchin egg extracts stimulated protein synthesis rate [7, 8]. This statement implies that recycling of eIF2 during fertilisation is also an important regulatory step in the production of proteins. In the past, we established a correlation between the phosphorylation of the eIF2 subunit and the suppression of protein synthesis in response to the treatment of embryos with the DNA-poor chemical MMS. In this study, we investigate where eIF2 is phosphorylated during translational activation and the first mitosis that occurs after fertilisation.

Results

In the sea urchin genome, which was released in 2006, there is one gene that codes for eIF2. In order to stabilise the interaction of the OB area (oligonucleotide-binding region, such as a five-stranded anti parallel -barrel) and the -helical region inside the human eIF2 protein, two cysteine residues at positions 69 and 97 are involved. Because the Cys residue in position 69 is not conserved in drosophila or yeast, it has been suggested that this residue serves a function unique to vertebrate eIF2. The residue at position 69 is also a cysteine, according to the ocean urchin eIF2 collection [9, 10]. A comparable search of genome databases from yeast to human confirmed the presence of this cysteine residue in deuterostomes from sea urchin to human, in three of the four species of nematodes, and in cnidarians, but it was undoubtedly absent in bugs and yeasts. Our findings rule out the hypothesis that the Cys residue at position 69 is unique to vertebrates and suggest that this residue is conserved in metazoans and has been lost in some phyla.

Discussion

A long-standing and crucial question in biology is the method by which the rate of protein synthesis will increase following fertilisation. Two years ago, it was noted that the eIF2 gene should participate in the protein synthesis regulation occurring during sea urchin fertilisation. On the basis of this documentation, we were able to demonstrate

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that the eIF2 subunit was phosphorylated at some point during the fertilisation of the ocean urchin egg [11]. When eIF2 is phosphorylated through the use of a phosphatase inhibitor or by activating a kinase signalling pathway, protein synthesis is inhibited, which leads to the arrest of the cell cycle. We proved that dephosphorylation of eIF2 is necessary for protein synthesis expansion and for the mobileular cycle department that monitors sea urchin eggs being fertilised by using a phosphomimetic mutant of eIF2. Our findings thus indicate that eIF2 in sea urchins contributes to the law of protein synthesis, which is necessary for the initiation of the primary mobileular department.

Our discovery that eIF2 law is concerned in mobileular cycle development during fertilisation in sea urchins is intriguing because eIF2 phosphorylation has been particularly identified as a pressure-triggered event. The physiological role of the eIF2 law has recently been investigated in a number of developmental processes, including the maturation of mouse meiosis, Caenorhabditis elegans epidermal morphogenesis, and aggregation and proliferation of Dyctiostelium [12]. Degeneration and growth arrest in mouse embryos result from impaired controlled eIF2 dephosphorylation, which is consistent with the known role of excessive eIF2 phosphorylation in promoting mobileular death.

Many studies show that a subset of mRNAs with upstream short open reading frames are preferentially translated in response to eIF2 phosphorylation, as demonstrated by the use of GCN4 in yeast during amino acid deprivation or ATF4 during pressure in humans [13]. Similar to this, during Dictyostelium development, chalones mRNA translation is enhanced in response to eIF2 phosphorylation. From conception until organogenesis, the correct developmental process depends on selective mRNA translation. The intricate web of processes that coordinate the recruitment of mRNA is still being thoroughly researched. Our findings point to novel gene expression regulation mechanisms that may involve selective translation via upstream open reading frames in early development.

Conclusion

The law that we tested allows for the possibility of selective translation inside the post-fertilization manager of gene expression, which may be examined using the sea urchin model. Insights into the role of eIF2 phosphorylation on global and selective translation in sea urchin embryos, and more specifically at the translational controls at the fertilisation and early cleavage tiers of embryo development will come from an analysis of the mRNAs that can be recruited into polysomes before and after fertilisation.

Conflict of Interest

None

Acknowledgement

None

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