—Mini Review—

Mechanism of Translation in the Period of Oocyte to Zygote Transition in Mammals

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Abstract: *In the mouse, maturing oocytes and zygotes until the late 1-cell stage are transcriptionally inert. The development of early preimplantation embryos, including reprogramming of differentiated germ cells into totipotent embryos, is regulated by the translation of mRNAs in oocytes preliminarily stored during oocytogenesis (maternal mRNAs). In the period of oocyte to zygote transition in mammals, the translational promotion or repression of maternal mRNAs does not start in unison. For example, a set of maternal mRNAs that are translationally quiescent in the growing stage become translated after the start of maturation and/or fertilization, but another group of maternal mRNAs that are actively translated in the growing stage become inactivated during maturation. This selective and temporal translational profile of maternal mRNAs seems to be regulated by RNA-binding proteins that bind to maternal mRNAs and decide the timing of their entry into the ribosome and by special short sequences in maternal mRNAs that recognize specific RNA-binding proteins. In this review, we focus on the mechanisms that modulate the profile of post-transcriptional regulation in the period of oocyte to zygote transition in mammals.*

Key words: *Mammalian, post-transcriptional regulation, Maternal mRNAs, Oocyte to zygote transition*

Introduction

Metazoan maturing oocytes and zygotes in their early developmental stage are transcriptionally inert [1–3]. In invertebrates, the oocyte to zygote transition, represented by phenomena such as completion of meiosis, initiation of the first mitosis and activation of transcription from zygotic genes, progresses under the control of mRNAs synthesized and stored during oocyte growth (maternal mRNAs), and it occurs after visible differentiation [2, 3]. In mammals, *de novo* synthesis of transcripts in oocytes ceases as they enter meiosis, and new transcription from the embryonic genome is activated at the 2-cell up to the 8- to 16-cell stage depending on the species [4]. In the mouse, the embryonic genome is activated at the late 1-cell stage and this transcriptionally quiescent period lasts almost 26–32 h [5]. This period is important for embryogenesis because the differentiated oocyte and sperm nuclei are reprogrammed to become the new totipotent embryo. Since the inhibition of protein synthesis of mouse 1-cell embryos by cycloheximide treatment suppresses the transcription of 80% of zygotic genes that are known to be activated in non-treated zygotes [6], the post-transcriptional regulation of maternal mRNAs stored in zygotes seems to be essential for oocyte to zygote transition and for induction of the reprogramming of the zygotic nucleus.

A characteristic aspect of post-transcriptional regulation in oocytes and zygotes is the selective translation or repression of maternal mRNAs; that is, a subset of maternal mRNAs translationally quiescent in growing oocytes are activated after the start of maturation and/or fertilization, while others that are translationally active during oocyte growth lose their activity after the start of oocyte maturation [6–9]. The mechanism underlying this selective translation of maternal mRNAs during oocyte to zygote transition has been reported to be as follows. In oocyte growth, maternal mRNAs are coupled with various RNA-binding proteins to protect the mRNAs from inappropriate translational activation or repression [10–12]. During maturation, some maternal mRNAs that are bound to

Received: September 5, 2005
Accepted: September 19, 2005
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some RNA-binding proteins are released possibly due to the remodeling of the structure of RNA-binding proteins induced by phosphorylation [12–14]. In addition, some maternal mRNAs have several types of special short sequences in their 3' untranslated region (3'UTR) which interact with their corresponding RNA-binding proteins [9, 12]. Since each combination of the short sequence and the RNA-binding protein has its own translational regulation, these special short sequences seem to contribute to the subtle control of timing and extent of their translation [9, 12, 15–17]. To discuss the mechanisms by which the translation pattern is orchestrated in the period of oocyte to zygote transition, we review the post-transctiptional regulation of maternal mRNAs in the period of oocyte to zygote transition, mainly in the mouse, together with information on the machanisms of post-transcriptional regulation in other cells.

Post-transcriptional Regulation in Growing Oocytes

Masking of maternal mRNAs by RNA-binding proteins

Mammalian oocytes accumulate large quantities of maternal mRNAs during their prolonged growth phase for supporting their subsequent development. In the mouse, this period lasts for approximately 20 days, and the fully grown mouse oocyte contains about 80 pg of total mRNAs [18]. These maternal mRNAs are very stable and transcriptionally quiescent in growing oocytes with a half-life of 8–12 days [19]. This stable state is achieved by the packaging of maternal mRNAs into discrete RNA-binding proteins and the formation of ribonucleo proteins (mRNPs) in many animals (ascidian 20, *Xenopus* 12, *Drosophila* 21, mouse 15). The RNA-binding proteins are separated into two groups by their binding ability to mRNA. One group has affinity for a variety of RNA sequences such as members of the Y-box protein and DEAD box RNA helicase families, and the other group interacts with particular short sequences in mRNAs such as cytoplasmic polyadenylation element-binding proteins (CPEB) [10–12].

Y-box proteins are known as highly conserved multifunctional proteins that regulate translation and transcription. Y-box proteins consist of a variable N-terminus, highly conserved cold-shock domain (CSD) and a C-terminal tail domain. The variable N-terminus seems to correlate with the differences in functional specificity of each member of the Y-box proteins. The CSD has two RNA-binding motifs (RNP-1 and RNP-2), which are responsible for the protein's specificity for the Y-box (or reverse CCAAT box) present in the promoter of many genes. The C-terminal domain contains four islands of basic/aromatic amino acids (B/A) surrounded by acidic regions, which contain potential sites for serine/threonine phosphorylation, and this domain is involved in non-specific nucleic acid binding [22, 25]. In Xenopus, a germ-line-specific Y-box protein, FRGY2, packages 80% of maternal mRNAs in oocytes [22–24]. MSY2 is the mouse ortholog of FRGY2 protein, and the transcript of *Msy2* is only detected in germ cells [10]. MSY2 and maternal mRNAs start coupling in the growing oocytes, and the coupling continues up to the 2-cell stage. MSY2 is specifically localized in the cytoplasm up to the 2-cell stage and becomes detected not only in the cytoplasm but also in nuclei after the 4-cell stage [13]. *Msy2* knockdown female mice were infertile and showed failure in maturation and activation caused by perturbations in oocyte growth [26]. In male germ cells in the mouse, transcription ceases during the later stages of spermatogenesis, a period in which the haploid round spermatids differentiate into elongated mature spermatozoa. The synthesis of proteins required for this morphogenetic change depends on the timely recruitment of paternal mRNAs from mRNP pariticles that contain about 75% of the poly(A) mRNAs within the round spermatid [27–29]. The level of MSY2 gradually increases with the progression of spermatogenesis and peaks in the round spermatid, which undergoes nuclear condensation and elongation [30–32]. These findings indicate that MSY2 also likely plays a role in regulation of the translation of paternal mRNAs. Moreover, a recent study has revealed that a member of the family of Y-box proteins, named rat brain Y-box protein 1 (rBYB1), exists as a form of mRNP expressed at a high level in the cytoplasm of pre- and early post-natal dendrites of primary hippocampal neurons in the brain and that its expression level decreases to the adult level with brain development [33]. This protein is thought to function in storage and translational regulation of mRNAs for rapid progress of development of the postnatal brain, and it may also participate in the control of protein synthesis in dendrites in mature neurons.

RCK/p54 protein is a member of the family of DEAD box RNA helicase proteins (D-E-A-D being the single letter code of Asp-Glu-Ala-Asp) and exhibits ATP-dependent RNA-unwinding activity [34]. Another function of this protein is thought to be masking of mRNAs in oocytogenesis because RCK/p54 protein has been detected in the fraction of the lysate that contains RNA-binding protein derived from clam oocytes [11].

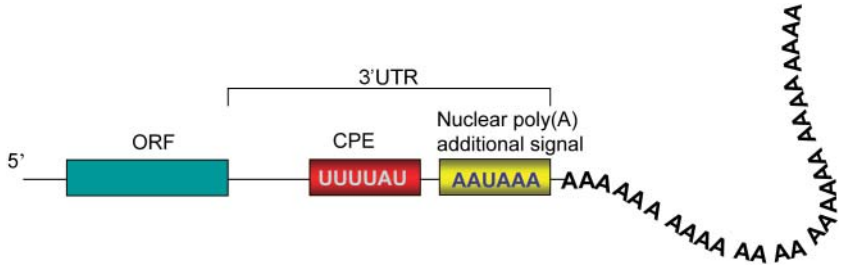

Fig. 1. Model of the sequence of maternal mRNAs. Short sequences in the 3' UTR regulate post-transcriptional translation during the oocyte to zygote transition.

Payton *et al.* [35] examined the expression profile of RCK/p54 mRNA in mouse oocytes and found that RCK/p54 mRNA was abundant in primary and secondary oocytes and that its degradation appeared to be complete by the mid-late 2-cell stage. However, a recent study using a real-time PCR technique has shown that the expression continues until the blastocyst stage even if the level is lower than that in the 1-cell embryo and that the same expression pattern of the protein was detected by western blot analysis [14]. Like MSY2, RCK/p54 protein is localized only in the cytoplasm at the 1-cell embryo stage, but it becomes localized not only in the cytoplasm but also in nuclei in the morula and blastocyst stages. The overexpression of *RCK/p54* caused slight delay in early embryogenesis and affected the birth rate [14]. DEAD box RNA helicases have been reported to be present in almost all organisms and to play an important role in RNA metabolism, but there has been no study on the function of RCK/p54 protein as an mRNP in cells other than male germ cells [14, 36]. Although the ability of RCK/p54 protein to bind RNA has not been examined, a large amount of RCK/p54 protein with forming granules has been detected in the cytoplasm of primary spermatocytes. The amount of RCK/p54 protein decreases with the progression of spermatogenesis, and RCK/p54 protein is not present in the spermatid [14]. Spermatogenesis of the male mouse that lacks Mvh or Grth/ddx25 protein, members of the family of DEAD box proteins, has been reported to be arrested at the premeiotic stage because the round spermatid has failed to elongate [14, 37, 38].

In general, translational regulation of mRNAs is correlated with changes in poly(A) length: mRNAs that receive poly(A) tails are subsequently translated, and mRNAs that lose their poly(A) tails are dissociated from the ribosome [39, 40]. This mechanism is also observed in the translation process of maternal mRNAs in many animal species, such as the clam, *Drosophila*, *Xenopus* and mouse [1, 3, 15, 41]. Maternal mRNAs that show a rapid increase in translation after maturation contain bipartite short signal sequences within their 3' UTR: one is AAUAAA, a highly conserved sequence that is required for nuclear polyadenylation and is present in every mRNA (nuclear poly(A) additional signal), and the other is a sequence that has been reported to be typically UUUUAU (Fig. 1) [39, 40, 42]. Because the presence or absence of UUUUAU distinguishes mRNAs that receive poly(A) from those that do not, it has been termed a cytoplasmic polyadenylation element (CPE) [42]. In *Xenopus* and other animals, including mice, a protein that specifically binds to CPE, cytoplasmic polyadenylation element-binding protein (CPEB), has been found [42]. In growing *Xenopus* oocytes, the transcriptionally quiescent state is ended by interaction of CPEB and eIF4E (eukaryotic initiation factor 4E) which binds to the 5' cap sequence (methylated GpppG) of maternal mRNAs through the maskin protein (Fig. 2) [43]. Since oocytes derived from CPEB knockout female mice stop growing at the pachytene stage before meiosis, CPEB is thought to play an important role not only in oocyte to zygote transition but also in oocyte growth possibly by protecting some maternal mRNAs from inappropriate translational ability [44].

Post-transcription Regulation in the Period of Oocyte to Zygote Transition

Unmasking of maternal mRNAs from RNA-binding proteins in oocyte maturation

Entry into meiotic resumption causes selective translation or repression of maternal mRNAs in the *Xenopus* and mouse [8, 40]. This change of translation activity appears to be regulated by unmasking of maternal mRNAs and changing of their adenylation

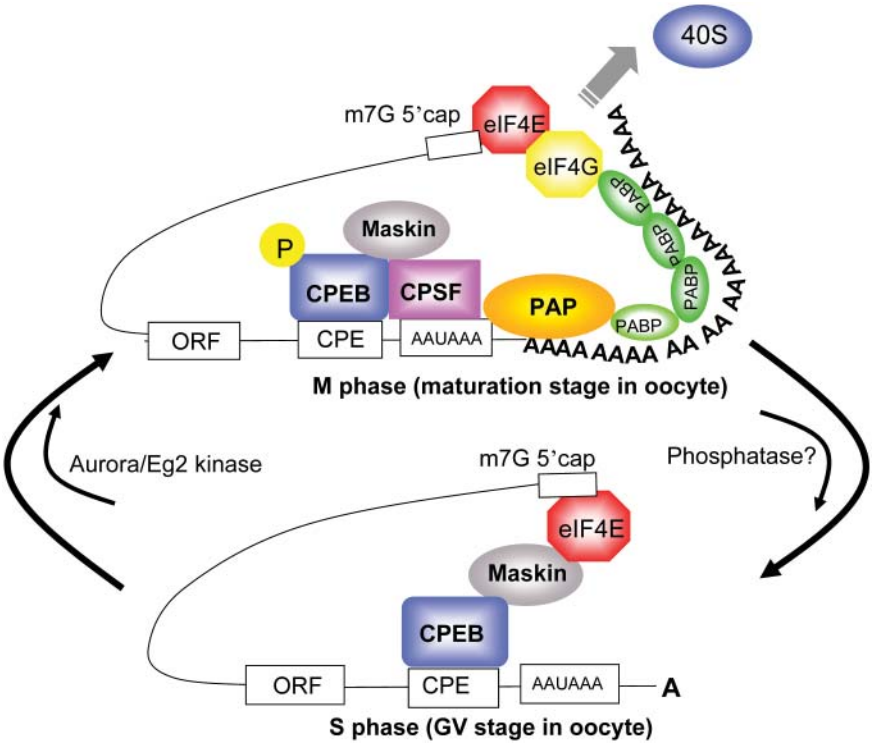

Fig. 2. Model for the translational control of maternal mRNAs. At the S phase, a complex of CPEB, maskin and eIF4E on the CPE prevents eIF4G from binding with eIF4E, and repression of translation is achieved. As cells enter the M phase, aurora/Eg2 kinase phosphorylates CPEB serine-174 and recruits CPSF, and in turn, poly(A) polymerase (PAP) attaches to mRNA adding a poly(A) tail. Poly(A) binding protein (PABP) then binds not only to the newly elongated poly(A) tail but also to eIF4G. This complex displaces maskin from eIF4E and allows eIF4G to position the 40S ribosomal subunit in the mRNA. These events stimulate the translation of maternal mRNAs that have CPE in their 3' UTR. When the cells begin to exit the M phase, an unknown phosphatase inactivates CPEB and induces deadenylation. The loss of PABP and the reassociation of maskin with eIF4E induce translational silencing.

states [15, 39].

MSY2 and RCK/p54 protein are formed and localized only in the cytoplasm in GV oocytes and 1-2-cell embryos but they are also observed in the nucleus after the 4-cell stage [13, 14]. This change in localization of MSY2 and RCK/p54 proteins seems to be associated with their ability to bind to maternal mRNAs. For example, the B/A island, one domain of the MSY2, has a functional nuclear localization signal sequence, and this sequence seems to be covered by binding of maternal mRNAs. This coverage seems to continue from GV oocytes to the 1-2-cell stage which retain MSY2 in the cytoplasm, and this retention is thought to be ended after the 4-cell stage by the remodeling of MSY2 [13]. Meric *et al*. [45] suggested that nucleoplasmin protein is required for releasing maternal mRNAs from the Y-box protein, because nucleoplasmin protein remodels the structure of FRGY2 and helps to release histone H4 mRNA, one of the maternal mRNAs in *Xenopus* oocytes, from FRGY2 in *Xenopus*.

In *Xenopus*, it has been revealed that the serine-174 residue of CPEB in full-grown oocytes in *Xenopus* was phosphorylated when it was primed with progesterone and induced maturation [46, 47]. This phosphorylation of CPEB was caused by the kinase, aurora/Eg2 kinase, which is one of the kinases known to be activated in *Xenopus* oocytes primed by progesterone [48]. The phosphorylated CPEB recruits a protein named, cleavage and polyadenylation specificity factor (CPSF). CPSF regulates the cleavage and polyadenylation of

mRNAs in the nucleus but regulates only polyadenylation of mRNAs in the cytoplasm and promotes the association of eIF4G with eIF4E [49]. This association promotes the release of maskin protein from eIF4E and recruits the 40S ribosomal unit (Fig. 2). In the mouse, although it has not been clarified whether this unmasking is caused by the phosphorylation state of CPEB, Stutz *et al.* [15] reported that CPEB appears to change its structure during meiotic resumption and release the target mRNA. Several studies have shown that neuron dendrites of the brain hippocampus appeared to require CPE-mediated repression and translation of mRNAs for robust changes in synaptic strength typified as long-term potentiation in mammals [50, 51]. These findings suggest that the mechanism of translational regulation that is mediated by CPE is also present in other somatic cells.

The recruitment of poly(A)-binding protein (PABP) is essential for removal of eIF4E from maskin protein and for lengthening of the poly(A) tail (Fig. 2). PABP1 has been reported to be present in the cytoplasm of all cells in metazoans with the exception of oocytes and early embryonic cells [52]; however, another form of PABP1 that is present only in oocytes and early embryos was discovered in *Xenopus* and named embryonic specific PABP (ePAB) [53]. ePAB is a protein that has 72% analogy with *Xenopus* PABP1 and is thought to be more important for oocyte and early embryonic development, because ePAB preferentially binds to eIF3, which is essential for interaction of maternal mRNAs and polysome [54]. Seli *et al.* [55] reported that a homolog of *Xenopus* ePAB was also detected only in mouse oocytes and 1-2-cell embryos and that a high level of expression of PABP1 was observed after the 8-cell stage.

Mechanism by which the poly(A) tail length of maternal mRNAs is adjusted in maturing oocytes

Post-transcriptional regulation of maternal mRNAs during oocyte to zygote transition is achieved by an increase or decrease in the translational activity caused by the balance of the activities of polyadenylation and deadenylation in the cytoplasm [39, 40]. In maternal mRNAs, constant activity of deadenylation has been reported to exist in this period as a 'default state' [40]. For example, constant expression of a mammalian poly(A)-specific ribonuclease, PARN, has been detected in oocytes of *Xenopus* and mouse [40, 56, 57]. On the other hand, the adenylation of maternal mRNAs seems to depend on their own sequence; that is, a group of maternal mRNAs that possesses CPE sequence in their 3' UTR becomes polyadenylated during maturation, and other maternal mRNAs that do not possess CPE in their 3' UTR become deadenylated during the period of maturation (Fig. 3). For example, maternal mRNAs of *Xenopus Mos* and mouse cyclin B1, tissue-type plasminogen activator (tPA) and hypoxanthin phosphoribosyltransferase (HPRT) have CPE in their 3' UTR and are adenylated and actively translated during oocyte maturation, but mouse housekeeping genes such as β-and γ-actins and α-tubulin mRNAs that do not have CPE are deadenylated and become translationally quiescent when oocytes enter into meiosis [8, 12, 15, 58, 59]. These studies suggest that mRNAs that possess CPE in their 3' UTR are actively translated in the period of maturation, because they can bind to CPEB and associate with the ribosomes (Fig. 2). However, mRNAs that do not have CPE cease translation in the period of maturation, because they cannot gain poly(A) as efficiently as maternal mRNAs that possess CPE in their 3' UTR, and are deadenylated by constant deadenylation activity in the cytoplasm such as that of PARN [40, 56, 57].

Mendez *et al.* [60] reported that maternal mRNAs possessing one CPE were polyadenylated at the start of meiosis but that maternal mRNAs possessing more than two CPEs started polyadenylation from metaphase I stage in *Xenopus* oocytes (Fig. 3). This is because when multiple CPEBs interact with mRNAs, they form a multimer and inhibit the recruitment of CPSF, and these redundant CPEBs are removed at metaphase I by the increased activity of Cdc2.

In somatic cells at the mitosis phase (M phase), poly(A) polymerase (PAP) is inactivated by multiphosphorylation caused by MPF and the translation activity level is not high in general [61]. However, the CPE-mediated transcription mechanism preferentially promotes adenylation in meiosis, which corresponds to the M phase in somatic cells. This higher level of translation ability in meiosis may be partially explained by the existence of mRNA encoding a PAP that lacks the major MPF phosphorylation sites found in *Xenopus* oocytes. This PAP, named GLD2, has been reported to be able to associate with CPEB and promote adenylation of maternal mRNAs of *Xenopus* oocytes [62]. These findings suggest that the CPE-mediated translation mechanism in oocytes is one of the mechanisms for overcoming translational repression during the M phase. This mechanism resembles the IRES (internal ribosome entry sites)-mediated translation system, which has been shown to be another mechanism by which translation in the M phase is promoted [63]. Recently, GLD2 has been

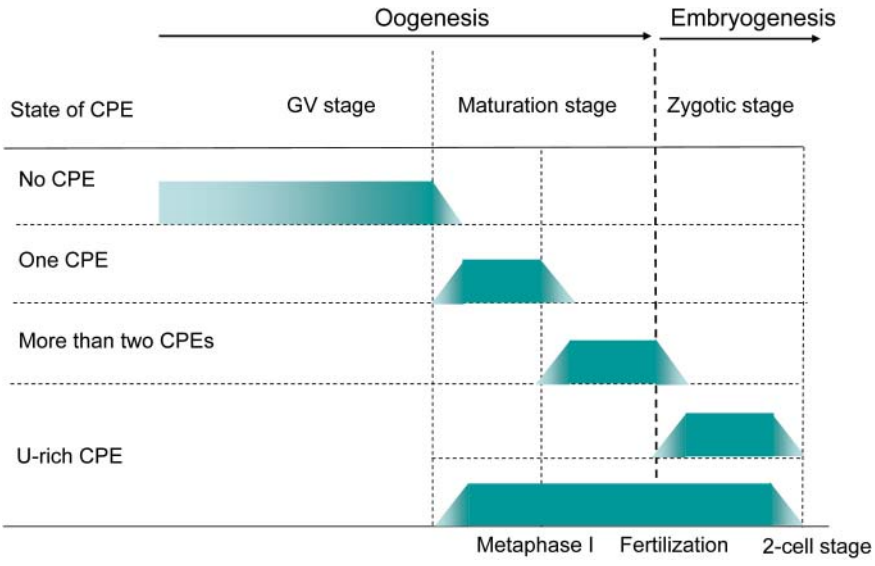

Fig. 3. Presumptive model for the polyadenylation and translation pattern in four sets of maternal mRNAs with different CPE states in their 3' UTR. A set of maternal mRNAs with no CPE loses the ability to gain poly(A) when oocytes enter the maturation stage. On the other hand, mRNAs having CPE acquire the ability to gain poly(A) during maturation. It was reported that maternal mRNAs having one CPE were preferentially adenylated in the first half of the maturation stage and that mRNAs having more than two CPEs were adenylated in the latter half of the maturation stage in *Xenopus*. Maternal mRNAs having a U-rich CPE are adenylated in the maturation stage and/or in the zygotic stage.

found to be localized not only in oocytes but also in the hippocampus in the mouse [62, 64, 65]. Moreover, CPE-containing cyclin B1 and cyclin B1 that lacks CPE were added to extracts of human breast cancer MCF7 cells synchronized at G2/M, S and G0/G1 and were found to cause G2/M phase-specific and G0/G1 phase-specific elongation of the poly(A) tail, respectively [66]. These results suggest that the CPE-mediated translational regulation is not a unique system in the period of oocyte to zygote transition.

Mechanism by which the poly(A) tail length of maternal mRNAs is adjusted in zygotes

After fertilization, among the maternal mRNAs that are actively adenylated and translated in the maturation period, some maternal mRNAs retain their activities of adenylation and translation, and others become deadenylated and translationally quiescent [9, 36]. On the other hand, the maternal mRNAs that are translationally quiescent in the maturation period become adenylated and translated after fertilization (Fig. 3) [6]. There have been many studies on the regulatory mechanism for adenylation and translation of maternal mRNAs after fertilization. Simon *et al.* [17] examined the mechanism regulating the timing and extent of adenylation in maternal mRNAs in *Xenopus* embryos after fertilization. They found that the length of the nucleotides between CPE and the nuclear poly(A) additional signal is an important factor in deciding the timing and extent of adenylation, because artificially produced mRNAs that have shorter nucleotides between CPE and the nuclear poly(A) additional signal showed more rapid adenylation and active translation compared with artificially produced mRNAs that have longer nucleotides [16]. Moreover, it was reported that although maternal mRNAs possessing conventional CPE were adenylated preferentially at the maturation stage, maternal mRNAs possessing U-rich CPE were adenylated preferentially after fertilization in *Xenopus* [17]. This difference observed between mRNAs that possess conventional CPE and those that possess U-rich CPE seems to be due to the presence of two different types of RNA-binding proteins for CPE and U-rich CPE. For example, a specific protein binding with U-rich CPE, ElrA protein, has been reported in *Xenopus* [67, 68]. Oh *et al.* [9] examined the relation of each

Table 1. Putative cytoplasmic polyadenylation elements(CPE) in maternal mRNAs

cDNA clone	Putative CPE Sequence	Polyadenylation
*spindlin I**	None	None
tPA	AUUUUAAU AUUUUAAU	Ovulated egg
Maid	AUUUUAA UUUUAUU	Ovulated egg
SSEC 51	AUUUUUA AUUUUUAAA	Ovulated egg
Ptp4a1	AUUUUUAA $(U)_8A(U)_{11}$	Ovulated egg and zygote
*spindlin II**	AUUUUUAU AUUUUAAU $(U)_{12}$	Ovulated egg and zygote

*In maternal mRNAs in mouse oocytes, there are types of *spindlin* mRNAs depending on the difference of their 3' UTR [9]. *Spindlin I* has no CPE in its 3' UTR. tPA, *Maid* and SSEC 51 possess two CPEs. *Ptp4a1* possesses one CPE and one U-rich CPE. *spindlin II* possesses two CPEs and one U-rich CPE [9].

adenylation profile and the presence of putative CPE and U-rich CPE in six maternal mRNAs in the mouse (Table 1). They demonstrated that maternal mRNAs possessing no CPE lost their poly(A) tail in the period of maturation but that maternal mRNAs possessing CPE were actively adenylated in the period of maturation. Maternal mRNAs possessing U-rich CPE tended to be adenylated in zygtotic stage. Although the regulatory mechanism has not been clarified, Zeng *et al*. [7] revealed that there is a set of maternal mRNAs that starts translation after fertilization possibly due to the the presence of U-rich CPE in their 3' UTR, in spite of their repressed translation of oogenesis and maturation (Table 1, Fig. 3). These findings suggest that CPE-mediated regulation of translation enables modulation of the timing and extent of polyadenylation and translation of maternal mRNAs, and helps to create the unique translation patterns in the oocyte to zygote transition of the *Xenopus* and mouse. Interestingly, the *Ptp4a1* mouse transcript contains a polyuridine tract in the range of 1,000 nucleotides from the poly(A) signal and has a putative U-rich CPE, but the rat homolog does not [9]. This suggests that the translation pattern during the oocyte to zygote transition differs depending on species and that the differences in the translation pattern causes a diversity of developmental processes in animals, such as differences in the timing of the start of transcription activation from zygotic genes.

The completion of the oocyte to zygote transition is accompanied by degradation of maternal mRNAs [6, 40]. The degradation of maternal mRNAs seems to be caused by the deadenylation activity that exists constantly in embryos as a default state [40]. The deadenylation allows exonuclease to access the body of mRNAs and inhibits the attachment of RNA-binding proteins such as PABP to mRNAs, and it facilitates interaction of the decapping enzyme to mRNAs [56]. These phenomena caused by deadenylation induce degradation of maternal mRNAs [39]. On the other hand, several studies have indicated that special short sequences in the 3' UTR of maternal mRNAs modulate not only adenylation but also deadenylation of maternal mRNAs in the period of oocyte to zygote transition in mammals. For example, A/U-rich elements (AREs) with repeats of the AUUUA motif in the 3' UTR have been widely reported in mammalian somatic cells, where they cause rapid deadenylation and regulate the cytoplasmic turnover of mRNAs encoding cytokines or proto-oncogenes [69, 70]. It has also been reported that injected reporter RNAs that contain AUUUA-type AREs are rapidly deadenylated in *Xenopus* embryos [71]. In addition, it has been reported that the embryo deadenylation element (EDEN) represented by several repeats of UGUA was localized within the 3' UTR of some maternal mRNAs and induced the repression of translation and promotion of deadenylation of maternal mRNAs by associating with its special binding protein named EDEN-BP in *Xenopus* [68, 72, 73]. Moreover, the increased activity of deadenylation caused by the degradation of some RNA-binding proteins may induce the rapid degradation of maternal mRNAs. In fact, CPEB has been reported to possess a PEST domain targeted by ubiquitination, and it was partially degraded when incubated with *Xenopus* egg extracts [60, 74]. These studies suggest that not only the default activity of deadenylation and degradation but also other mechanisms such as a sequence-specific mechanism or a ubiquitination-dependent mechanism may induce the rapid and complete degradation of maternal mRNAs at the late 2-cell stage in the mouse.

Conclusions

In metazoan animals, the oocyte to zygote transition is a specific event for the development of new progeny. During the period of oocyte to zygote transition, specific phenomena that do not occur in somatic cells, such as arrest of meiosis at the MII stage, fertilization, fusion of pronuclei and replacement of the maternal transcripts

with newly synthesized transcripts, are observed. These phenomena are required for triggering the reprogramming of differentiated germ cells into totipotent embryos. Since development only proceeds under the condition of post-transcriptional regulation from the inherited maternal mRNAs in the cytoplasm in the period of oocyte to zygote transition, investigation of the features in the process of the translation in this period will provide the key to answer the question why oocytes can develop into new progenies but other cells cannot [5]. Moreover, although post-transcriptional regulation of maternal mRNAs in amphibians and *Drosophila* has been extensively studied and discussed more frequently than in mammals, their post-transcriptional regulation seems to be different from that in mammals; for example, the period of oocyte to zygote transition continues past the differentiation stage in *Xenopus* [1, 4]. For these reasons, we focused on the mechanism of post-transcriptional regulation of maternal mRNAs in the period of oocyte to zygote transition in the mouse in this review.

The main feature of the translation of maternal mRNAs in the period of oocyte to zygote transition is that the promotion or repression of translation does not start in unison and each mRNA seems to wait its turn to begin or end its translation. To achieve this temporal and selective translation regulation, the state of deadenylation and adenylation activity during oocyte to zygotic transition appears to be important. Considering that the polyadenylation and the translation of maternal mRNAs are promoted under the condition of constant deadenylation activity in the period of oocyte to zygote transition, a mechanism to promote adenylation at the appropriate time during oocyte to zygote transition is important for the formation of a unique temporal translation pattern in this period [39, 40]. RNA-binding proteins, such as MSY2, RCK/p54 protein and CPEB, are suitable candidates for this mechanism because these proteins can interact with maternal mRNAs to protect them from inappropriate adenylation and deadenylation. This protection occurs from the oocyte growing phase and continues to an appropriate stage depending on the difference of RNA-binding proteins; for example, MSY2 protein and RCK/p54 protein appear to release maternal mRNAs after the 4-cell stage, and CPEB releases them during maturation [13, 14, 46]. Since these proteins seem to release maternal mRNAs when their phosphorylation states are changed by cell-cycle specific kinases, the selective activation and repression of translation observed during oocyte to zygote transition is regulated by the cell cycle of oocytes or zygotes. That is, some maternal mRNAs are preferentially translated at the M phase (corresponding to meiosis in oocytes) and their translation is repressed, or they are even degraded, at the S phase (corresponding to oocytes in GV stage or 1-cell embryo immediately after fertilization), while others are translated in the S phase and their translation ceases at the M phase [66]. This cell cycle-dependent switching of translation mediated through the RNA-binding proteins has been observed in other cells such as male germ cells [14, 28], neuron dendrites in the brain [33, 51, 65], and human somatic cells [66]. These findings suggest that the selective translation regulation mechanism observed in maternal mRNAs is not a specific mechanism working only in the period of oocyte to zygote transition, and that the diverse RNA-binding proteins, or the short sequences encoded in the 3' UTRs of maternal mRNAs, contained in oocytes create the unique translation pattern in the oocyte to zygote transition.

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