Abstract
Meiotic division of a female germ cell, an oocyte, is more prone to segregation errors and consequently to aneuploidies than meiosis of a sperm. Aneuploidies and chromosomal aberrations in oocytes increase with higher maternal age in humans and also in mice. Meiotic maturation onset is connected with activity of cyclin dependent kinase 1 (CDK1) that leads to dissociation of nuclear membrane. Moreover regulation of translation of key transcripts is necessary for proper meiotic progression. In thesis findings from four scientific publications are interpreted.

We have analyzed the timing of nuclear envelope breakdown (NEBD) and polar body extrusion in mouse oocytes originating from two distinct female age groups: young (2 months old) and aged (12 months old). We found that meiotic maturation happens faster in aged females' oocytes due to early phosphorylation of Lamin A/C, a component of nuclear lamina, and rapid dissociation of nuclear membrane. Moreover aged females' oocytes presented unique characteristic invaginations of nuclear membrane and thus significantly increased circumference of the nuclear envelope compared to the oocytes from young females. These data combined with increased activity of CDK1 and Cyclin B, as well as increased translation of factors that regulate the translation itself, suggest that oocytes from aged females undergo a precocious meiotic division that can contribute to chromosomal errors in meiosis I.

To study the influence of CDK1 function during meiotic maturation in oocytes we have also elucidated the role of cyclin-dependent kinase subunit protein 2 (CKS2). *Cks2*$^{-/-}$ mice are infertile in both sexes with oocytes and spermatocytes arrested in metaphase of meiotic division I. These oocytes display reduced and delayed maturation-promoting factor (MPF) activity, leading to the delay of NEBD and defects in activation of the anaphase-promoting complex/cyclosome (APC/C) and meiotic spindle assembly. In *Cks2*$^{-/-}$ germ cells the expression of CDK1 and Cyclin A1/B1 is reduced.

We have observed that active CDK1 phosphorylates and activates mammalian target of rapamycin (mTOR). Activation of mTOR kinase leads to hyperphosphorylation and inhibition of translational repressor 4E-BP1. Inactive 4E-BP1 is released from eukaryotic initiation factor 4E (eIF4E), which can in turn form functional initiation complex eIF4F and start cap-dependent translation. In this manner CDK1 influences translation of a pool of RNAs during the meiosis onset. In addition to ongoing translation in the area of forming spindle we have observed specific localization of number of RNAs within the nucleus of oocytes before NEBD. Apart from RNAs, also active inhibitor of cap-dependent translation 4E-BP1 is localized in the nucleus, as well as the proteins connected with mRNA processing (hnRNPA1 and eIF4A3). As the specific localization of RNAs is a prerequisite for their subsequent translation, we propose that RNAs stored in the nucleus are translationally dormant and can be translated subsequently after NEBD.

Altogether, these observations show that MPF is an important regulator of many processes during meiotic maturation. It is also needed for full activation of mTOR, which inhibits 4E-BP1 and in this way allows initiation of translation. Inhibition of 4E-BP1 occurs post NEBD when previously dormant RNAs are available for cap-dependent translation. Aberrant MPF activity that occur in oocytes from aged females or in oocytes with *Cks2* deletion can lead to the increase in frequency of chromosome segregation errors, delay in the progression of meiotic maturation, or problems with polar body extrusion. Our findings should help to better understand the molecular basis of female reproductive physiology and can find usage in further research or practice.