Reprod Dev Biol 39(2) : 37-41 (2015)
http://dx.doi.org/10.12749/RDB.2015.39.2.37

ISSN : 1738-2432 (Print)
ISSN : 2288-0151 (Online)

Role of Golgi Apparatus on Regulation of Sec61β, COPG2 and Epidermal Growth Factor during Oocyte Maturation

Hae-In Oh[1], Sang-Hee Lee[1], Seunghyung Lee[1], Seung Tae Lee[1], Eunsong Lee[2] and Choon-Keun Park[1,†]

[1]*College of Animal Life Science, Kangwon National University, Chuncheon 200-701, Republic of Korea*

[2]*College of Veterinary Medicine, Kangwon National University, Chuncheon 200-701, Republic of Korea*

ABSTRACT

The oocyte undergoes various events during maturation and requires many substances for the maturation process. Various intracellular organelles are also involved in maturation of the oocyte. During the process glucose is essential for nuclear and cytoplasmic maturation, and adenosine triphosphate is needed for reorganization of the organelles and cytoskeleton. If mitochondrial function is lost, several developmental defects in meiotic chromosome segregation and maturation cause fertilization failure. The endoplasmic reticulum, a store for Ca^{2+}, releases Ca^{2+} into the cytoplasm in response to various cellular signaling molecules. This event stimulates secretion of hormones, growth factors and antioxidants in oocyte during maturation. Also, oocyte nuclear maturation is stimulated by growth factors such as epidermal growth factor. This review summarizes roles of organelles with focus on the Golgi apparatus during maturation in oocyte.

(Key words : Golgi apparatus, Oocyte maturation, Sec61β, COPG2, Epidermal growth factor)

INTRODUCTION

Generally, resumption and completion of the first meiotic division in oocyte are essential processing for successful fertilization (Eppig, 1996). Also, cytoplasmic and nuclear maturation of oocyte are related with oocyte activation, fertilization, and pre-implantation development (Eppig *et al.*, 1994). There are vairous physiological change of oraganelles during oocyte maturation, of these, cortical granules is regulated by amount of Ca^{2+} and released from smooth membrane vesicles (Ducibella *et al.*, 1988; Ducibella *et al.*, 1993). The smooth membrane vesicles exists cortical region that distributed at germinal vesicle stage in oocytes (Ducibella *et al.*, 1988). Exocytosis of cortical granules response increasing of Ca^{2+} ionophore for nuclear maturation (Ducibella *et al.*, 1990), the Ca^{2+} is temporary rised to fuse gamete during fertilization in Endoplasmic reticulum (ER) of metaphase II oocytes (Swann and Yu, 2008). Thus, cortical granules of cytoplasmic for oocytes maturation could be related with ER system for successful fertilization, this event influence on blastocyst development.

Practically, some studies have been reported that brefeldin A inhibited reversible oocyte maturation by blocking membrane traffic from ER to the Golgi apparatus (GA) (Moreno *et al.*, 2002). And brefeldin A or dominant mutants of the small guanosine triphosphatase adenosine diphosphate-ribosylation factor disaggregated from coat protein complex I (COPI) by GA caused blockage of the retrograde trafficking from GA to ER and these substances inhibit transported epidermal growth factor receptor (EGFR) from ER (Pepperkok *et al.*, 2000).

Sec61 beta (Sec61β) existence in ER-GA intermediate compartment/GA fractions of the gradient (Greenfield and High, 1999) and expression of EGFR level reduced in the nuclear pore portion of Sec61β knock-out cells, the Sec61β accumulated in the inner nuclear membrane portion (Wang *et al.*, 2010). Therefore, the purpose of this paper was focused to understating of organelles protein involved in ER system during oocyte maturation.

* This research was supported by Bio-industry Technology Development Program (IPET 31060-05-1-CG000), Ministry for Food, Agriculture, Forestry and Fisheries, Republic of Korea.

† Corresponding author : Phone: +82-33-250-8627, E-mail: parkck@kangwon.ac.kr

OOCYTE MATURATION

Meiosis

The oocytes resume meiotic cell division in gonadotropin dependent phase (Chesnel and Eppig, 1995), the oocyte meiosis initiated at fetus development phase and arrested at diplotene stage of the first meiotic prophase (Wang *et al.*, 2004). The meiosis resumption is initiated by homologous chromosome division, chromosome condensation and spindle assembly at metaphase I and meiosis is arrested at metaphase II stage (Liang *et al.*, 2007).

Sufficient nutrients are essential for nuclear maturation and cytoplasmic maturation necessary for fertilization and embryo development (Rieger and Loskutoff, 1994; Steeves and Gardner, 1999; Spindler *et al.*, 2000; Sutton-McDowall *et al.*, 2010; Sutton-McDowall *et al.*, 2005; Wongsrikeao *et al.*, 2006). Growth factors and hormones from follicular cells stimulate oocyte cytoplasmic maturation (Mattioli *et al.*, 1988). The activation of maturated oocyte (MII) is related with cytoplasmic maturation, ultimately, which has an effect on pre-implantation development in embryo (Eppig, 1996).

Cytoplasmic Maturation

Mitochondria

Mitochondrion found in most eukaryotic cells, optimal timing and location of adenosine triphosphate are essential for occurring organelle and cytoskeletal reorganization during oocyte maturation (Coticchio *et al.*, 2015). The mitochondrial function is disappeared, leading to failures in meiotic chromosome segregation, maturation and fertilization, and ultimately, development of oocytes is disturbed (Coticchio *et al.*, 2015). Mitochondria are accumulated in the perinuclear at germinal vesicle breakdown (GVBD) in anaphase I and many mitochondria were transported to the inner cytoplasm of matured oocytes (Sun *et al.*, 2001).

Endoplasmic Reticulum (ER)

ER is one of organelle in the eukaryotic cells and there are two types of ER, rough and smooth (Nikonov *et al.*, 2002). The rough ER of the surface ER is sites of protein synthesis(Walter and Johnson, 1994). The functions of smooth ER have several metabolic processes such as synthesization of lipids, phospholipids, and steroids. In case of oocytes maturation, the ER has the ability to store and release Ca^{2+} and acquires significance in the cytoplasm (Coticchio *et al.*, 2015). The centric function of ER temporary rises free Ca^{2+} concentration in intracellular by responded MII oocytes from gamete fusion at fertilization (Swann and Yu, 2008).

Golgi Apparatus (GA)

GA is one of organelles that is found in most eukaryotic cells. The GA release proteins in the extracellular or delivery to other intracellular by macromolecules post-translation, and contain lipid transport and lysosome formation (Higgins *et al.*, 1999). The duplication of centrosome and the couple of centrosomes are important for the mitotic spindle during the S phase (Green *et al.*, 2012). Commonly Large Golgi elements located in the inside oocyte at the GV stage which is replaced with smaller vesicular structures at MII stage oocyte during maturation (Moreno *et al.*, 2002). And brefeldin A treated mouse oocytes is inhibited reversible maturation by blocking membrane traffic from ER to the GA during *in vitro* maturation (Moreno *et al.*, 2002). However, investigation of functional GA has been rarely studied for oocyte maturation, GA could be considered point of regulatory mechanisms of oocyte and GA is suggested a potential role for oocyte maturation.

RELATION OF OOCYTE MATURATION AND GA

Effects of Epidermal Growth Factor (EGF) on Oocyte

EGF is a growth factor and stimulates cell growth, proliferation and differentiation by binding to EGFR (Yarden, 2001). MII oocyte is influenced by various growth factors during maturation (Tonetta and Dizerega, 1989) which stimulate oocyte nuclear maturation (Lorenzo *et al.*, 1994; Procházka *et al.*, 2000). Previous study reported that EGF stimulates nuclear maturation in porcine oocytes (Sommer *et al.*, 1992), porcine follicular fluid has significantly EGF level and ovary has the EGF binding sites (Feng *et al.*, 1987). Some studies were reported that effect of EGF on supporting development of eight-cell stage (Paria and Dey, 1990) and contribution of blastocyst production (Harper and Brackett, 1993) in bovine oocyte during *in vitro* maturation. Willingham and Pastan (1982) reported that bound EGF to cell surface receptor in lysosome was involved in GA. Thus, we expect that EGF and GA are closely relation in oocyte during maturation.

Sec61 Beta (Sec61β)

Transport protein Sec61 subunit beta (Sec61β) is encoded by human-Sec61 beta gene and membrane of ER, translocation organ, consist of Sec61 complex (Kalies *et al.*, 1998). Transmembrane channel is formed by oligo-

mers of the Sec61 complex that integrated with ER membrane in opposite side. The Sec61 complex is consisted of three type membrane proteins which are alpha, beta, and gamma (Samuelson *et al.*, 2000). Wild-type Sec61 alpha, beta and gamma existence in ER and ER-GA intermediate compartment/GA fractions of the gradient, thus, Sec61 translocon is expected to location in the ER and ER-Golgi intermediate position (Greenfield and High, 1999). However, Sec61β proteins has not been reported to be associated with oocyte maturation, therefore, we expect experiment to detect mechanism for relation of Sec61β and oocyte maturation in mammal using *in vitro* maturation system.

Coatomer Subunit Protein Complex Gamma-2 (COPG2)

COPG2 is a protein that encoded by the COPG2 gene, which interact with Dopamine receptor D1 and COPB1 in human (Linebach *et al.*, 2014). Recently, the COPG2 was reported to be a novel imprinted gene that overlaps the 3*-untranslated region (3*-UTR) of MEST in a tail-to-tail orientation (Yamasaki *et al.*, 2000). Representative role of COPG2 is membrane traffic protein on mouse oocyte (Cui *et al.*, 2007), and COPG2 is a required for GA membranes, and is essential to the transport of proteins from the ER to GA (Mendis *et al.*, 2008).

CONCLUSION

Cytoplasmic organelle and protein such as mitochondria, ER, GA, Sec61β and COPG2 is important to oocyte maturation for preparation of fertilization. Also, various growth factor and hormones influence to oocyte during maturation. The growth factors regulate mechanism of oocyte maturation, especially, EGF is essential for nuclear oocyte maturation by binding to the EGFR for activation. Also, combined EGFR with EGF plays a larger role interaction and transportation various proteins in oocyte. We observed that the Sec61β is activated by EGFR system, this event are occurred in the ER and the ER-GA intermediate compartment. Therefore, the relationship between the EGF and sec61β would be related with the transport of GA and ER. Also, the GA and the ER would be activated by the increased Sec61β and EGF in oocyte during maturation. The COPG2 activate increasing trafficking from GA to ER which membrane traffic protein. Overall, the COPG2 would be essential for proteins transport from the ER to GA in GA membranes during oocyte maturation. Therefore, study of EGF, Sec61β, GA and COPG2 may provide understating of novel mechanism for relation of ER system and growth factor in oocyte.

REFERENCES

1. Eppig JJ (1996): Coordination of nuclear and cytoplasmic oocyte maturation in eutherian mammals. Fertil Dev 8:485-489.
2. Eppig JJ, Schultz RM, O'Brien M, Chesnel F (1994): Relationship between the developmental programs controlling nuclear and cytoplasmic maturation of mouse oocytes. Dev Biol 164:1-9.
3. Ducibella T, Rangarajan S, Anderson E (1988): The development of mouse oocyte cortical reaction competence is accompanied by major changes in cortical vesicles and not cortical granule depth. Dev Biol 130:789-792.
4. Ducibella T, Kurasawa S, Duffy P, Kopf GS, Schultz RM (1993): Regulation of the polyspermy block in the mouse egg: maturation-dependent differences in cortical granule exocytosis and zona pellucida modifications induced by inositol 1,4,5-trisphosphate and an activator of protein kinase C. Biol Reprod 48:1251-1257.
5. Ducibella T, Kurasawa S, Rangarajan S, Kopf GS, Schultz RM (1990): Precocious loss of cortical granules during mouse oocyte meiotic maturation and correlation with an egg-induced modification of the zona pellucida. Dev Biol 137:46-55.
6. Swann K, Yu Y (2008): The dynamics of calcium oscillations that activate mammalian eggs. Int J Dev Biol 52:585.
7. Moreno RD, Schatten G, Ramalho-Santos J (2002): Golgi apparatus dynamics during mouse oocyte *in vitro* maturation: effect of the membrane trafficking inhibitor brefeldin A. Biol Reprod 66:1259-1266.
8. Pepperkok R, Whitney JA, Gomez M, Kreis TE (2000): COPI vesicles accumulating in the presence of a GTP restricted arf1 mutant are depleted of anterograde and retrograde cargo. J Cell Sci 113:135-144.
9. Greenfield J, High S (1999): The Sec61 complex is located in both the ER and the ER-Golgi intermediate compartment. J Cell Sci 112:1477-1486.
10. Wang YN, Yamaguchi H, Huo L, Du Y, Lee H-J, *et al.* (2010): The translocon Sec61β localized in the inner nuclear membrane transports membrane-embedded EGF receptor to the nucleus. J Biol Chem 285:38720-38729.
11. Chesnel F, Eppig JJ (1995): Synthesis and accumulation of p34cdc2 and cyclin B in mouse oocytes during acquisition of competence to resume meiosis. Mol Reprod Dev 40:503-508.

12. Wang QT, Piotrowska K, Ciemerych MA, Milenkovic L, Scott MP, *et al.* (2004): A genome-wide study of gene activity reveals developmental signaling pathways in the preimplantation mouse embryo. Dev Cell 6:133-144.
13. Liang C-G, Su Y-Q, Fan H-Y, Schatten H, Sun Q-Y (2007): Mechanisms regulating oocyte meiotic resumption: roles of mitogen-activated protein kinase. Mol Endocrinol 21:2037-2055.
14. Rieger D, Loskutoff N (1994): Changes in the metabolism of glucose, pyruvate, glutamine and glycine during maturation of cattle oocytes *in vitro*. J Reprod Fertil 100:257-262.
15. Steeves T, Gardner D (1999): Metabolism of glucose, pyruvate, and glutamine during the maturation of oocytes derived from pre-pubertal and adult cows. Mol Reprod Dev 54:92-101.
16. Spindler RE, Pukazhenthi BS, Wildt DE (2000): Oocyte metabolism predicts the development of cat embryos to blastocyst *in vitro*. Mol Reprod Dev 56: 163-171.
17. Sutton-McDowall ML, Gilchrist RB, Thompson JG (2010): The pivotal role of glucose metabolism in determining oocyte developmental competence. Reproduction 139:685-695.
18. Sutton-McDowall ML, Gilchrist RB, Thompson JG (2005): Effect of hexoses and gonadotrophin supplementation on bovine oocyte nuclear maturation during *in vitro* maturation in a synthetic follicle fluid medium. Reprod Fertil Dev 17:407-415.
19. Wongsrikeao P, Otoi T, Yamasaki H, Agung B, Taniguchi M, *et al.* (2006): Effects of single and double exposure to brilliant cresyl blue on the selection of porcine oocytes for *in vitro* production of embryos. Theriogenology 66:366-372.
20. Mattioli M, Galeati G, Seren E (1988): Effect of follicle somatic cells during pig oocyte maturation on egg penetrability and male pronucleus formation. Gamete Res 20:177-183.
21. Coticchio G, Dal Canto M, Renzini MM, Guglielmo MC, Brambillasca F, *et al.* (2015): Oocyte maturation: gamete-somatic cells interactions, meiotic resumption, cytoskeletal dynamics and cytoplasmic reorganization. Hum Reprod Update: dmv011.
22. Sun Q, Wu G, Lai L, Park K, Cabot R, *et al.* (2001): Translocation of active mitochondria during pig oocyte maturation, fertilization and early embryo development *in vitro*. Reproduction 122:155-163.
23. Nikonov AV, Snapp E, Lippincott-Schwartz J, Kreibich G (2002): Active translocon complexes labeled with GFP-Dad1 diffuse slowly as large polysome arrays in the endoplasmic reticulum. J Cell Biol 158: 497-506.
24. Walter P, Johnson AE (1994): Signal sequence recognition and protein targeting to the endoplasmic reticulum membrane. Annu Rev Cell Biol 10:87-119.
25. Higgins ME, Davies JP, Chen FW, Ioannou YA (1999): Niemann-Pick C1 is a late endosome-resident protein that transiently associates with lysosomes and the trans-Golgi network. Mol Genet Metab 68:1-13.
26. Green RA, Paluch E, Oegema K (2012): Cytokinesis in animal cells. Annu Rev Cell Dev Biol 28: 29-58.
27. Yarden Y (2001): The EGFR family and its ligands in human cancer: signalling mechanisms and therapeutic opportunities. Eur J Cancer 37:3-8.
28. Tonetta SA, Dizerega GS (1989): Intragonadal regulation of follicular maturation. Endocr Rev 10:205-229.
29. Lorenzo P, Illera M, Illera J, Illera M (1994): Enhancement of cumulus expansion and nuclear maturation during bovine oocyte maturation *in vitro* by the addition of epidermal growth factor and insulin-like growth factor I. J Reprod Fertil 101:697-701.
30. Sommer P, Rath D, Niemann H (1992): *In vitro* maturation of porcine oocytes in the presence of follicular granulosa cells, FSH and/or EGF. Proc. 12th International Congress on Animal Reproduction, Vol. 1. Dublin, Ireland, pp 378-380.
31. Feng P, Knecht M, Catt K (1987): Hormonal control of epidermal growth factor receptors by gonadotropins during granulosa cell differentiation. Endocrinology 120:1121-1126.
32. Procházka R, Sršeň V, Nagyova E, Miyano T, Flechon JE (2000): Developmental regulation of effect of epidermal growth factor on porcine oocyte-cumulus cell complexes: Nuclear maturation, expansion, and F-actin remodeling. Mol Reprod Dev 56: 63-73.
33. Paria B, Dey S (1990): Preimplantation embryo development *in vitro*: cooperative interactions among embryos and role of growth factors. Dev Biol 87: 4756-4760.
34. Harper KM, Brackett BG (1993): Bovine blastocyst development after follicle-stimulating hormone and platelet-derived growth factor treatment for oocyte maturation *in vitro*. Zygote 1:27-34.
35. Willingham MC, Pastan IH (1982): Transit of epidermal growth factor through coated pits of the Golgi system. J Cell Biol 94:207-212.
36. Kalies K-U, Rapoport TA, Hartmann E (1998): The β subunit of the Sec61 complex facilitates cotranslational protein transport and interacts with the signal peptidase during translocation. J Cell Biol 141: 887-894.
37. Samuelson JC, Chen M, Jiang F, Möller I, Wiedmann M, *et al.* (2000): YidC mediates membrane protein insertion in bacteria. Nature 406:637-641.

38. Linebach M, Murphy M, Hiner M, Staab R (2014): Differentiating gene expression profiles of staphylococcal enterotoxin B and lipopolysaccharide in induced human PBMCs. J Res Development 2:2.
39. Yamasaki K, Hayashida S, Miura K, Masuzaki H, Ishimaru T, *et al.* (2000): The novel gene, γ2-COP (COPG2), in the 7q32 imprinted domain escapes genomic imprinting. Genomics 68:330-335.
40. Cui XS, Li XY, Shen XH, Bae YJ, Kang JJ, *et al.* (2007): Transcription profile in mouse four-cell, morula, and blastocyst: Genes implicated in compaction and blastocoel formation. Mol Reprod Dev 74:133-143.
41. Mendis C, Campbell K, Das R, Yang D, Jett M (2008): Effect of 5-lipoxygenase inhibitor MK591 on early molecular and signaling events induced by staphylococcal enterotoxin B in human peripheral blood mononuclear cells. FEBS J 275:3088-3098.

(Received: May 16 2015/ Accepted: May 25 2015)