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Proteasomal activity has multiple functions in oocyte meiosis, in cumulus expansion, in synthesis and processing of cumulus extracellular matrix and steroidogenesis

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Specifically, a hypothesis was tested whether proteasomal inhibitor MG132 affects the expression of cumulus expansion-related components (TNFAIP6, HAS2) and progesterone secretion by oocyte-cumulus complexes (OCC) and granulosa cells (GC).Terminal differentiation of OCC within the preovulatory follicle plays a crucial role in the ability of the oocyte to resume meiosis and attain full developmental competence. During this process, cumulus cells synthesize a large amount of hydrophilic hyaluronan (HA). This glycosaminoglycan is organized into a mucous-elastic matrix. For stabilization of expanded cumulus matrix in mouse and pig is essential the covalent linkage of heavy chains of inter-alpha-trypsin inhibitor to HA. We detected strong signal of HA in expanded porcine OCC after FSH/LH stimulation. In contrast, in the presence of MG132, no cumulus expansion, no signal of HA was detected. In addition the expression of HAS2 and TNFAIP6 was decreased. Moreover, we have shown that inhibition of proteasomal proteolysis with MG132 arrested >90% of oocytes in GV stage and blocked degradation of F-actin-rich transzonal projections (TZPs) interconnecting cumulus cells with the oocyte. Since maintenance of TZPs supports oocyte meiotic block and OCC remain unexpanded, we hypothesize that proteasomal proteolysis participates in the process of resumption of meiosis. It has been suggested that progesterone plays an indispensable role during the first 4 h of the ovulatory process by regulating proteolytic enzyme activities. Interestingly, our results show that the ability of gonadotropin-stimulated cumulus cells to produce progesterone to a level comparable with control OCC was not restored when MG132 was present 20 h in the culture but it was restored (50 %) when MG132 was present only 3 h. We conclude that specific proteasomal inhibitor, MG132, affects formation of expanded cumulus extracellular matrix, since it 1/ suppresses the production of progesterone 2/ reduces the expression of extracellular matrix-related components by porcine cumulus cells 3/ protects TZPs from breakdown 4/ prevents cumulus expansion and resumption of meiosis.

Biography

Eva Nagyova has completed her PhD at the age of 32 years from Academy of Sciences of the Czech Republic, Institute of Animal Physiology and Genetics in Prague and postdoctoral studies from -Norwegian College of Veterinary Medicine, Oslo, Norway (1992), and INSERM, Clamart, France (1994). In 1997, she obtained OECD Fellowship Award, and she moved to Cancer Research Center, Ottawa, Canada to collaborate with Professor B.C. Vanderhyden. During this period she studied different aspects of oocyte maturation and cumulus expansion. In 2002, she obtained again the OECD Fellowship Award, and she moved to Department of Public Health and Cell Biology, Faculty of Medicine, University of Rome, Italy; where she started to investigate organization of cumulus extracellular matrix in perfect collaboration with Prof .Salustri A, and Camaioni A. In years, 2002-2007, their collaboration was supported by - Program of Scientific and Technological Co-operation between the Government of the Italian Republic and Czech Republic. In 2013, she obtained OECD Fellowship Award again to continue her research in University of Rome, Italy. She published more than 40 papers in reputed journals.

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