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# The Role of Cumulus Cells in Fertilization Process

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During ovulation process, cumulus cells produced and accumulated hyaluronan (HA) rich matrix within cumulus cell layers, called as cumulus expansion. The expanded cumulus oocyte complex is ovulated from follicle, and then fertilized in oviduct. It has been known that the fertilization rate of oocyte *in vitro* is higher when expanded COCs are used for *in vitro* fertilization as compared with that in denuded oocyte. However, the positive roles of cumulus cells in fertilization process were remained unclear.

Using mutant mouse models the functional relevance of HA and HA binding proteins has been documented by a wealth of biochemical data and physiological studies. Specifically, the level of *Tnfaip6* mRNA was significantly lower in mice null for either *Ptgs2* (prostaglandin synthase 2, also known as COX-2) or *Ptger2* (prostaglandin E2 receptor 2 known as EP2) than in their wild type littermates [1,2], indicating that *Tnfaip6* gene expression was dependent on prostaglandin E2 and its receptor pathway. Ovulation in both mouse models was reduced slightly, but cumulus expansion as well as fertilization was completely suppressed in these mutant mice. The fertilization defects of *Ptgs2* or *Ptger2* null mice were related to defective matrix stability/function because mature oocytes retrieved from these mutant mice could be fertilized *in vitro* by use of capacitated spermatozoa [3]. These reports suggest that the hyaluronan rich matrix produced by COCs is essential not only for ovulation but also for *in vivo* fertilization, and perhaps more specifically for sperm capacitation. Recently, we reported that cumulus cells express TLR2 and TLR4 that are well known to directly and selectively bind to bacteria released endotoxins, lipopolysaccharides and peptidoglycan. Both types of TLRs also recognize small hyaluronan fragments, less than 10 kDa, but not the high molecular hyaruronan polymer. During fertilization, the high molecular weight HA polymers are broken-down by sperm-head associated hyaluronidase to small fragments that then stimulate chemokine secretion from cumulus cells by TLR-dependent mechanisms [4]. The secreted chemokines, in turn, act on specific receptors present on the mid piece of sperm to enhance successful fertilization at least *in vitro*.

Therefore, the immune-related genes expressed in cumulus cells play important roles in oocyte maturation, COC expansion and fertilization.

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