Alternative pathways of acrosome reaction induction

Dear Sir,

The acrosome reaction of mammalian spermatozoa can occur spontaneously or in response to natural or artificial stimuli. It is now generally accepted that the fertilizing spermatozoon undergoes a stimulus-induced rather than a spontaneous acrosome reaction, which ensures a proper timing of this exocytotic event (reviewed in Cummins, 1994). Two physiological acrosome reaction inducers are known: progesterone and a zona pellucida glycoprotein termed ZP3 (reviewed in Yanagimachi, 1994). Both are associated with the ovulated oocyte and each of them can alone induce a complete acrosome reaction. The fact that the two physiological inducers of the acrosome reaction, progesterone and ZP3, coincide at fully effective concentrations at the site of fertilization and that each of these inducers is capable of stimulating a complete sequence of the acrosome reaction events raises an intriguing question of what the biological significance of this unusual biligand cell activation system is and how it functions.

In spite of the molecular dissimilarity of the two physiological acrosome reaction inducers, both can activate the same signal transduction pathways (reviewed in Tesarik et al., 1996) namely those involving calcium influx through plasma membrane calcium channels and protein tyrosine phosphorylation. Interestingly, recent studies suggest that each of the two physiological inducers can activate at least two different types of calcium channels, one reacting rapidly, and thus probably activated directly by the inducer molecule, and the other responding after a lag period and probably regulated by the inducer indirectly via a cell signalling cascade (Florman, 1994; Mendoza et al., 1995; Tesarik et al., 1996). Because the channels mediating the rapid calcium response to progesterone and the zona pellucida share some biological characteristics, one may ask whether both ligands do not in fact operate the same channel.

Similarly, a 94-95 kDa protein of human spermatozoa is phosphorylated on tyrosine in response to both solubilized zona pellucida and progesterone, and a recent study has shown that this protein is a unique, germ cell-specific receptor PTK localized at the sperm plasma membrane in the acrosomal region and enhancing its kinase activity in response to ZP3 binding to its extracellular domain. Because no other major sperm head-specific Triton soluble phosphoprotein was detected in the corresponding molecular weight region (Tesarik et al., 1996), these observations suggest that the same PTK molecule may behave as a receptor PTK with regard to ZP3 and a non-receptor PTK with regard to progesterone (Figure 1). This PTK may thus be activated either by ZP3 binding or by interaction with cross-linked progesterone receptor.

Consequently, there does not appear to be a real complementarity between the progesterone- and ZP3-activated acrosome reaction mechanisms, but both rather represent alternative pathways capable of autonomously carrying out the whole process. This situation may have arisen by superimposition of two pathways of different evolutionary origin thus creating a backing mechanism for this biologically extremely important process. The possibility of substitution of one acrosome reaction induction pathway by the other must be taken into account with regard to eventual contraceptive strategies using the acrosome reaction as target.

References


Florman, H.M. (1994) Sequential focal and global elevations of sperm intracellular Ca\(^{2+}\) are initiated by the zona pellucida during acrosomal exocytosis. Dev. Biol., 165, 152-164.


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