Preventing Spontaneous Acrosome Reaction Depends on PI3K and PKA Activities

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In order to fertilize the egg the spermatozoon should undergo a process called acrosoma exocytosis or acrosome reaction (AR), a process which can take place only after a series of biochemical changes collectively called capacitation that the sperm undergo in the female reproductive tract. Polymerization of G-actin to F-actin which occurs during sperm capacitation prevents the occurrence of spontaneous-AR (sAR), which decreases fertilization rate. Calmodulin- kinase II (CaMKII) and phospholipase-D (PLD) mediate F-actin formation in two distinct pathways. The increase in sAR caused by the inactivation of the PLD-pathway, were reversed by activation of CaMKII using H_2O_2 or by inhibiting protein phosphatase 1 which enhance the dephosphorylation of CaMKII. This reversed activation is depended on activation of phosphatidyl-inositol-3-kinase (PI3K). Moreover, inactivation of protein-kinase A (PKA) using H-89 induces a significant increase in sAR which was mediated by CaMKII and could be reserved by inhibiting protein phosphatase 1. Spermine, activates phosphatidyl-inositol-4-kinase (PI4K) to produce phosphatidyl-inisitol-4,5-bisphosphate(PIP_2) a cofactor for PLD activation, was able to reverse the enhanced effect of CaMKII inhibition on sAR increase. We show that this effect of spermine was not apparent when sAR was induced by PKA inhibition, however this effect was reversed by adding phosphatidic acid (PA), the PLD product. These data clearly indicate that PLD is not activated when PKA is blocked. In summary, the data suggest that the prevention of sAR by CaMKII or PLD pathways depend of PI3K activity. Furthermore we propose that PKA activity is essential for PLD activation.

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