THE ROLE OF PP60C-SRC TYROSINE KINASE IN SPERM CAPACITATION

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A protein kinase A-dependent tyrosine phosphorylation pathway in mammalian spermatozoa has been demonstrated to exist, and is unique to this cell type. As PKA is incapable of directly phosphorylating substrates on tyrosine residues, much research has focused on the identification of an intermediary tyrosine kinase which can be activated by serine/threonine phosphorylation via PKA. Inhibitory studies using genistein, tryphostin, erbstatin and herbimycin A, have demonstrated that the src family of kinases may be responsible for the tyrosine phosphorylation events seen during capacitation (1). Although one src family member, c-yes, has been implicated as the kinase responsible for these events (2), this has since been disputed (3). Another src family member, pp60c-src, can be activated by phosphorylation on Ser-17 by cAMP-dependent protein kinase and Ser-12 by calcium-phospholipid dependent protein kinase C (4), and may be the intermediary tyrosine kinase of interest. Western blot analysis demonstrated the presence of pp60c-src in rat sperm samples isolated from the caput and cauda epididymis. Furthermore, co-immunoprecipitation studies revealed a number of pp60c-src-associated proteins including outer dense fibre 2 (ODF2) and A-kinase anchoring protein 4 (AKAP4). Interestingly, both of these proteins become phosphorylated during capacitation of mouse sperm (data not shown) and AKAP4 is tyrosine phosphorylated in capacitated human sperm (5). These data implicate pp60c-src kinase activity in the phosphorylation of a number of sperm midpiece proteins, which may regulate hyperactivation during capacitation. Further research focusing on the activity of pp60c-src in non-capacitated and capacitated sperm will be conducted.

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