

Perspective Article

Sperm Associated Oocyte Activating Factor

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Sperm associated oocyte activating factor (SAOAF) activates the oocyte to initiate embryogenesis¹. Oocyte activation involves a rise in Ca^{+} release and followed by a series of Ca^{+} oscillations¹. Ca^{+} oscillations modulate multifaceted events which include cortical granule exocytosis, release of meiotic arrest, regulate gene expression, recruit maternal mRNA and initiate embryogenesis¹.

Different empiricists have purported many sperm factors like oscillin, truncated c-kit receptor(tr-kit), post-acrosomal sheath WW domain binding protein(PAWP) and Phospholipase c zeta^{2,3,4}. Although many factors have been proposed, none of them meet all the criteria of SAOAF.

A sperm factor should meet certain basic criteria to be considered as SAOAF. Activation of oocyte takes place after sperm delivers a testis-specific, sperm-borne oocyte activating factor(SAOAF) into ooplasm⁵. Sperm factor should have a molecular weight of 30-100k Da found in association with isolated sperm heads and capable of inducing Ca^{+} oscillations resembling those seen at fertilization^{2,6,7,8,9}. Blocking of sperm factor should stop activation if it is a physiological activator of the oocyte. Microinjection of recombinant sperm protein should induce oocyte activation¹⁰.

Several proteins were proposed to be the SAOAF. Oscillin was proposed as oocyte activating factor by Parrington et al in 1996¹¹. Microinjection of sperm extracts of 33K protein showed Ca oscillations which was considered as oscillogen¹¹. Oscillin was homologous to glucosamine 6-phosphate isomerase, an enzyme involved in hexose phosphate metabolism¹². Injection of recombinant glucosamine 6-phosphate isomerase into fura-2-dextran-loaded metaphase II(MII) oocytes didn't showed any Ca^{+} oscillations¹².

Truncated c-kit receptor(tr-kit) which was known to cause Ca^{+} oscillations was offered by Sette et al in 1997¹³. Microinjection of sperm extracts showed Ca^{+} oscillations but recombinant protein didn't show any oscillations. Research by Mehlmann et al 1998, and Sette et al 1998 had proposed that mechanism of Tr-kit induced activation of oocyte appears to be different from that utilized by sperm^{14,15}. In addition, Tr-kit is associated with the residual cytoplasm of sperm tail, not with the sperm head¹³.

Phospholipase c zeta(PLC ζ) was propounded by Saunders et al in 2002¹⁶. Experiments done by Aarabi et al states that PLC ζ is not a cytosolic protein localised over the surface of the post-acrosomal region of mouse/bull sperm and over the entire head of human sperm which contradicts other studies which states that SAOAF is a cytosolic protein specified to acrosomal, equatorial, and post-acrosomal regions of rodent and human sperm^{1,10}. Moreover, PLC ζ is also secreted by epididymal cells which contradicts SAOAF as testis-specific protein and is not incorporated into ooplasm for activation^{5,10}. Although clinical evidence supports that deficiency of PLC ζ leads to Oocyte activation deficiency(OAD), it doesn't necessarily support PLC ζ alone¹⁷. Globozoospermia which lacks sperm perinuclear theca and acrosome which is a predominant site of PLC ζ lacks another protein PAWP¹⁷.

Post-acrosomal sheath WW domain binding protein(PAWP) was proposed by Wu et al in 2007¹⁹. Nomikos et al injected recombinant mouse PAWP protein, or the complementary RNA encoding either untagged PAWP, or the complementary RNA encoding either untagged PAWP, or YFP-PAWP, or PAWP-luciferase failed to show Ca^{+} oscillations¹⁷. Aarabi et al contradicts study of Nomikos et al¹⁸. Aarabi et al states that tagging on a protein to PAWP prevents its binding with oocyte WW domain containing proteins, which is a compulsory first step in the signal cascade that PAWP initiates in the oocyte cytoplasm¹⁸. Working injection concentration of Aarabi et al PAWP CRNA was 0.002 which was 600times lesser than Nomikos et al. Initial dilution trials by Aarabi et al has found that higher concentrations of PAWP failed to induce Ca^{+} oscillations^{17,18}. Nevertheless Nomikos et al refute Aarabi et al study by stating that generation of Ca^{+} oscillations by PAWP protein pathway is unknown¹⁷. Aarabi et al concluded that we need further investigations to conclude PAWP as SAOAF¹⁸.

None of the above mentioned sperm protein factors satisfy Sperm Factor Hypothesis. However PLC ζ and PAWP protein are still in debate. We need further investigations to conclude the novel SAOAF protein which could gratify the conditions of Sperm Factor Hypothesis.

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