# Perspective Article

## Sperm Associated Oocyte Activating Factor

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Sperm associated oocyte activating factor (SAOAF) activates the oocyte to initiate embryogenesis[1]. Oocyte activation involves a rise in $Ca^+$ release and followed by a series of $Ca^+$ oscillations[1]. $Ca^+$ oscillations modulate multifaceted events which include cortical granule exocytosis, release of meiotic arrest,regulate gene expression, recruit maternal mRNA and initiate embryogenesis[1].

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 ooplasm[5]. 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 activation[10].

Several proteins were proposed to be the SAOAF. Oscillin was proposed as oocyte activating factor by Parrington et al in 1996[11].Microinjection of sperm extracts of 33K protein showed Ca oscillations which was considered as oscillogen[11]. Oscillin was homologous to glucosamine 6-phosphate isomerase, an enzyme involved in hexose phosphate metabolism[12]. Injection of recombinant glucosamine 6-phosphate isomerase into fura-2-dextran–loaded metaphase II(MII) oocytes didn't showed any $Ca^+$ oscillations[12].

Truncated c-kit receptor(tr-kit) which was known to cause $Ca^+$ oscillations was proffered by Sette et al in 1997[13]. 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 head[13].

Phospholipase c zeta(PLC ζ) was propounded by Saunders et al in 2002[16]. 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 alone[17]. Globozoospermia which lacks sperm perinuclear theca and acrosome which is a predominant site of PLC ζ lacks another protein PAWP[17].

Post-acrosomal sheath WW domain binding protein(PAWP) was proposed by Wu et al in 2007[19]. 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 $Ca^+$ oscillations[17]. Aarabi et al contradicts study of Nomikos et al[18]. Arabi 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 cytoplasm[18]. Working injection concentration of Arabi et al PAWP CRNA was 0.002 which was 600times lesser than Nomikos et al. Initial dilution trials by A arabi et al has found that higher concentrations of PAWP failed to induce $Ca^+$ oscillations[17,18]. Neverthless Nomikos et al refute Aarabi et al study by stating that generation of $Ca^+$ oscillations by PAWP protein pathway is unknown[17]. Aarabi et al concluded that we need further investigations to conclude PAWP as SAOAF[18].

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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