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#### Review

Second Messengers, Steroids and Signaling Cascades: Crosstalk in Sperm Development and Function

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## ACCEPTED MANUSCRIPT

#### 1 Second Messengers, Steroids and Signaling Cascades: Crosstalk in Sperm Development and

- 2 Function
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#### 6 **Abstract**:

- 7 Signaling cascades control numerous aspects of sperm physiology, ranging from creation to
- 8 fertilization. Novel aspects of several kinases and their influence on sperm development will be
- 9 discussed in the first section and cover proliferation, chromatin remodeling and morphology.
- 10 In the second section, protein kinases (A, B and C)<sup>1</sup> that affect sperm function and their
- 11 regulation by second messengers, cyclic-AMP and phosphoinositides, as well as steroids will be
- 12 featured. Key areas of integration will be presented on the topics of sperm motility,
- 13 capacitation, acrosome reaction and fertilization.
- 14

<sup>1</sup> List of Abberviations: AC, Adenylyl cyclase; AKT, Protein kinase B; AMPK, AMP-activated protein kinase; AnR, Androgen receptor; ARF6, ADP ribosylation factor 6; CaMK, Ca2+-calmodulin dependent kinase; CaMKK, CaMK kinase; cAMP, Cyclic adenosine 3',5'-monophosphate; CDK5, Cyclin-dependent kinase 5; CFTR, Cystic fibrosis transmembrane conductance regulator; CREB, cAMP-response element (CRE) binding protein; CREM, CRE modulator; Ck2, Casein kinase II; DAPK-3, Death-associated protein kinase-3; DHT, Dihydrotestosterone; EGFR, Epidermal growth factor receptor; Epac, Exchange protein directly activated by cAMP; ER, Estrogen receptor; ERK/MAPK, Extracellular signal-regulated protein kinases or Mitogen-activated protein kinases; FAK, Focal adhesion kinase; GABA, y-aminobutyric acid; GSK3, Glycogen synthase kinase-3; IGF, Insulin-like growth factor; IGFR, IGF-1 Receptor; IP3, Inositol 1,4,5-trisphosphate; JNK1, c-Jun N-terminal kinase; MARCKS, Myristoylated alanine-rich C-kinase substrate; MEK, MAPK kinase; MRP4, Multidrug resistance associated protein 4; Nek2, Neverin-Mitosis (NIMA)-related kinase 2; NO, Nitric oxide; NOS, Nitric oxide synthase; Odf, Outer dense fibers; P4, Progesterone; PDGF, Platelet-derived growth factor; PDK1, Phosphoinositide-dependent kinase 1; Pl(3,4,5)P3, Phosphatidylinositol-3,4,5-trisphosphate; PI3K, Phosphoinositide-3 kinase; PIP(2), Phosphatidylinositol 4,5bisphosphate; PKA, Protein Kinase A; PKC, Protein Kinase C; PLC, Phospholipase C; PLD, Phospholipase D; PTEN, Phosphatase and tensin homologue deleted on chromosome 10; PTP, Protein tyrosine phosphorylation; PTP-PEST, Protein tyrosine phosphatase/ proline-glutamic acid-serine-threonine; PYK2, Proline-rich tyrosine kinase 2; RAPGEF, Rap guanine nucleotide exchange factor; ROS, Reactive oxygen species; Rsk2, Ribosomal S6 kinase; StAR, Steroidogenic acute regulatory protein; Syk, Spleen tyrosine kinase; TCP10L, Transcription factor T-complex 10 like; ZIP kinase, Zipper interacting protein kinase

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