

Journal of Andrology, Vol 16, Issue 1 36-46, Copyright © 1995 by The American Society of Andrology

---

## JOURNAL ARTICLE

# Characterization of two second messenger pathways and their interactions in eliciting the human sperm acrosome reaction

C. M. Doherty, S. M. Tarchala, E. Radwanska and C. J. De Jonge

Department of Obstetrics and Gynecology, University of Nebraska Medical Center, Omaha 68198-3255, USA.

The human sperm acrosome reaction (AR) occurs via the activation of at least two signal transduction pathways. The purpose of this investigation was to characterize two of the pathways, the protein kinase A (PKA) and C (PKC) pathways, and determine whether pathway "crosstalk" occurs between them in eliciting the AR in capacitated spermatozoa. Stimulators of each pathway were tested in a dose-dependent manner. AR<sub>max</sub>, ED<sub>50</sub>, and delta AR<sub>max</sub> (%AR<sub>max</sub>-%AR<sub>control</sub>) values were calculated. The PKA pathway stimulators forskolin and dibutyryl cyclic AMP (dbcAMP) induced an AR<sub>max</sub> at 1.0 microM and 1.0 mM, respectively. The ED<sub>50</sub> and delta AR<sub>max</sub> values were: 0.01 microM and 17% for forskolin and 0.069 mM and 13% for dbcAMP. Two stimulator types of the PKC pathway were tested: synthetic diacylglycerols (DG) and a phorbol diester. 1,2-dioleoyl -sn-glycerol and 1,2-dioctanoyl -sn-glycerol, analogues of the PKC-activating second messenger DG, each induced an AR<sub>max</sub> at 50 microM. The ED<sub>50</sub> and delta AR<sub>max</sub> values were: 33 microM and 24% for 1,2-dioleoyl and 34.8 microM and 34% for 1,2-dioctanoyl. 4 beta-Phorbol -12,13-didecanoate, a PKC stimulator, induced an AR<sub>max</sub> at 0.1 microM. The ED<sub>50</sub> and delta AR<sub>max</sub> were 0.021 microM and 26%. An inhibitor of each kinase was added at the end of the capacitation period and prior to stimulation by inducers at their AR<sub>max</sub> dose. KT5720, a PKA inhibitor, caused a dose-dependent reduction of the forskolin and dbcAMP-induced AR. Calphostin C, a PKC inhibitor, prevented stimulation of the AR by 1,2-dioleoyl and 4 beta-phorbol -12,13-didecanoate. To investigate pathway "crosstalk," the following experiments were conducted: (1) stimulators of each pathway were combined and tested at the AR<sub>max</sub> and ED<sub>50</sub> concentrations for each; (2) spermatozoa were pretreated with a kinase inhibitor and then stimulated using an alternative pathway stimulator; and (3) a PKA or PKC inhibitor and a combination of PKA and PKC stimulators, at ED<sub>50</sub> concentrations, were tested. The results for (1) indicate an additive AR response of ED<sub>50</sub> concentrations but not for AR<sub>max</sub> doses. The results for (2) demonstrate that a kinase inhibitor for one pathway prevents induction of the AR by a stimulator of the alternative pathway. Finally, the results for (3) show that a kinase inhibitor for one pathway prevents induction of the AR by the combined use of separate pathway stimulators. When taken collectively, the present results suggest a convergent mechanism of crosstalk between the PKA and PKC pathways leading to the human sperm AR.

### This Article

- ▶ [Full Text \(PDF\)](#)
- ▶ [Alert me when this article is cited](#)
- ▶ [Alert me if a correction is posted](#)

### Services

- ▶ [Similar articles in this journal](#)
- ▶ [Similar articles in PubMed](#)
- ▶ [Alert me to new issues of the journal](#)
- ▶ [Download to citation manager](#)

### Citing Articles

- ▶ [Citing Articles via HighWire](#)
- ▶ [Citing Articles via Google Scholar](#)

### Google Scholar

- ▶ [Articles by Doherty, C. M.](#)
- ▶ [Articles by De Jonge, C. J.](#)
- ▶ [Search for Related Content](#)

### PubMed

- ▶ [PubMed Citation](#)
- ▶ [Articles by Doherty, C. M.](#)
- ▶ [Articles by De Jonge, C. J.](#)



**Molecular Human Reproduction**

▶ HOME

A. Barbonetti, M.R.C. Vassallo, C. Antonangelo, V. Nuccetelli, A. D'Angeli, F. Pelliccione, M. Giorgi, F. Francavilla, and S. Francavilla  
RANTES and human sperm fertilizing ability: effect on acrosome reaction and sperm/oocyte fusion  
Mol. Hum. Reprod., July 1, 2008; 14(7): 387 - 391.  
[\[Abstract\]](#) [\[Full Text\]](#) [\[PDF\]](#)



**Reproduction**

▶ HOME

K S Sidhu, K E Mate, T Gunasekera, D Veal, L Hetherington, M A Baker, R J Aitken, and J C Rodger  
A flow cytometric assay for global estimation of tyrosine phosphorylation associated with capacitation of spermatozoa from two marsupial species, the tammar wallaby (*Macropus eugenii*) and the brushtail possum (*Trichosurus vulpecula*)  
Reproduction, January 1, 2004; 127(1): 95 - 103.  
[\[Abstract\]](#) [\[Full Text\]](#) [\[PDF\]](#)



**Molecular Human Reproduction**

▶ HOME

A. A. Schuffner, H. S. Bastiaan, H. E. Duran, Z.-Y. Lin, M. Morshedi, D. R. Franken, and S. Oehninger  
Zona pellucida-induced acrosome reaction in human sperm: dependency on activation of pertussis toxin-sensitive Gi protein and extracellular calcium, and priming effect of progesterone and follicular fluid  
Mol. Hum. Reprod., August 1, 2002; 8(8): 722 - 727.  
[\[Abstract\]](#) [\[Full Text\]](#) [\[PDF\]](#)



**Molecular Human Reproduction**

▶ HOME

R. Ain, K. Uma Devi, S. Shivaji, and P.B. Seshagiri  
Pentoxifylline-stimulated capacitation and acrosome reaction in hamster spermatozoa: involvement of intracellular signalling molecules  
Mol. Hum. Reprod., July 1, 1999; 5(7): 618 - 626.  
[\[Abstract\]](#) [\[Full Text\]](#) [\[PDF\]](#)



**Physiological Reviews**

▶ HOME

A. Darszon, P. Labarca, T. Nishigaki, and F. Espinosa  
Ion Channels in Sperm Physiology  
Physiol Rev, April 1, 1999; 79(2): 481 - 510.  
[\[Abstract\]](#) [\[Full Text\]](#) [\[PDF\]](#)