

Functional Assay for Male Infertility

CCTEC D-3290

Technology Overview:

There are over 73 million infertile couples globally, with 40% of the infertility being associated with the male. Despite current standards by which male fertility is assessed – sperm count, motility or morphology – approximately half of all male infertility is of an unknown origin and is only diagnosed by failed cycles of in vitro fertilization (IVF). Having the ability to diagnose sperm functional defects would allow clinicians to direct their patients toward a technology of assisted reproduction that is appropriate for their function. Unfortunately, most existing attempts to design functional assays are not clinically practical, as they take days to conduct, require special technical skill and/or equipment, and are uncontrolled.

Cornell researchers have discovered that they can assess the fertilizing ability of sperm by following the pattern of distribution of the ganglioside G_{M1} in response to exposure to stimuli for sperm capacitation. This provides a reliable and practical method to assess sperm quality and hence male fertility. Moreover, the pattern of G_{M1} redistribution appears to be conserved across many mammals, from mice to bulls to humans, providing opportunities for applications in human medicine, veterinary medicine, and production of agricultural animals.

Technical Merits:

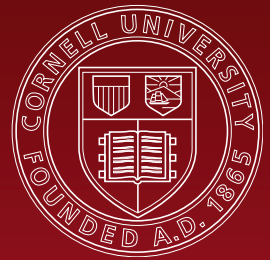
Ejaculated sperm are not immediately able to fertilize an egg. Rather, they must undergo a process of functional maturation known as "capacitation". Currently there are no sensitive and simple markers for capacitation that can be used in a clinical setting. For example, the appearance of protein tyrosine phosphorylation events during the process of capacitation has been described in many species. However, visualization of these events using polyacrylamide gel electrophoresis and immunoblotting can take upwards of 48 hours to perform, making it ill-suited for clinical purposes.

This invention describes the unique patterns of redistribution of G_{M1} ganglioside, in sperm induced to undergo capacitation, as a method for both diagnostic and predictive purposes, in assessing male reproductive fitness. The redistribution of G_{M1} during capacitation in distinct patterns has been seen in all mammalian species examined, including the bull, boar, stallion, and human.

Potential Applications & Advantages:

Assessing G_{M1} distribution patterns during capacitation can be used to:

- assess functional activity of sperm as part of a routine male fertility assay across mammalian species
- assess functional activity of sperm on the day of IVF to determine preferred procedure – classical IVF or intracytoplasmic sperm injection
- evaluate laboratory handling and cryopreservation techniques, thus addressing a major cause of unsuccessful IVF procedures – membrane damage during in vitro handling of sperm
- evaluate semen extenders and cryopreservation protocols in agricultural applications
- evaluate the effectiveness of topical contraceptives



Inventors:

Alexander J. Travis
Gregory S. Kopf

Patents:

US 7,160,676

Publications:

Buttke DE, Nelson JL, Schlegel PN, Hunnicutt GR, Travis AJ. (2006) Visualization of G_{M1} with cholera toxin B in live epididymal versus ejaculated bull, mouse, and human spermatozoa. *Biol Reprod.* 74(5):889-95.

Selvaraj V, Buttke DE, Asano A, McElwee JL, Wolff CA, Nelson JL, Klaus AV, Hunnicutt GR, Travis AJ. (2007) G_{M1} dynamics as a marker for membrane changes associated with the process of capacitation in murine and bovine spermatozoa. *J Androl.* 28(4):588-99.

Website:

<http://bakerinstitute.vet.cornell.edu/faculty/view.php?id=184>

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Contact:

Phillip Owh, MSc
Sr. Technology Commercialization
and Liaison Officer
Phone: (607) 254-4508
Email: po62@cornell.edu

Ref:

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