

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Gianpiero D. Palermo

eRA COMMONS USER NAME (credential, e.g., agency login): GIPALERMO

POSITION TITLE: Professor of Reproductive Medicine, Director of Assisted Fertilization & Andrology

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.*)

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
University of Bari School of Medicine, Bari, Italy	MD	07/83	Medicine & Surgery
University of Bari, Bari, Italy	Ob/Gyn	07/88	Obstetrics & Gynecology
Brussels Free University, Brussels, Belgium	M.Sc.	06/90	Medical & Pharmaceutical Research
New York Presbyterian Hospital, New York, USA	Resident	06/02	Obstetrics & Gynecology
Monash University, Monash, Melbourne, Australia	PhD	05/05	Reproductive Science

A. Personal Statement

Since my early years, I displayed an investigative mind determined to understand the intimate mechanisms of a device or the intricate functions of an organism that brought me to pursue a career in medicine. It was during my training in Ob/Gyn that I developed a strong passion for Reproductive Science. I quickly became fascinated with reproductive technologies, one of the most fast moving and innovative fields of life sciences. This led me to seek a post-doc at the Brussels Free University where I developed a ground breaking procedure to treat male factor infertility, known as intracytoplasmic sperm injection (ICSI). This technique allowed me to investigate the different aspects of human fertilization and contribute to the understanding of sperm function. ICSI overcomes all problems related to number, parameter, and even function of the male gamete, the limitation being simply the presence of the sperm itself.

Through this proposal, we plan to investigate a mechanism of centriole dominance or repression (On&Off) that is active in androgenotes, and we aim to identify, characterise and validate the proteins/factors behind centriole On&Off. To achieve this goal, experimentation will be carried out in several mammalian models. I have the expertise, leadership and motivation necessary to successfully carry out the proposed work. In addition, I successfully conducted other projects in the past with other international collaborators involving nuclear transfer and somatic cell haploidization in the mouse and human and our group has recently reignited investigations into embryonic reprogramming. I have also conducted successful projects in the areas of molecular biology, epigenetics, and genetics. I have produced several peer-review publications from each project. The current application builds logically on our prior collaborative work and I believe that my experience and capabilities in conjunction with the co-applicants will provide a formidable team that will be well-suited to tackle this endeavor. In summary, I have a proven record of successful and prolific research projects in the areas of fertilization, micromanipulation, gamete function and interaction, and haploidization of somatic cells. I believe that my expertise as well as experience have prepared me to participate in and help guide the proposed investigation.

B. Positions and Honors

1988-1990 Post-doc, Centre for Reproductive Medicine, Brussels Free University, Brussels, Belgium

- 1994-1998 Assistant Professor, Embryology in Obstetrics & Gynecology, Cornell University Medical College, New York, NY, USA
- 1998-2008 Associate Professor, Reproductive Medicine, Weill Cornell Medical College, New York, NY, USA
- 2008-2010- Professor, Reproductive Medicine, Weill Cornell Medical College, New York, NY, USA
Blavatnik Distinguished Professor, Reproductive Biology, Weill Cornell Medical College, New York, NY, USA
- 2016- Diplomate, American Board of Obstetrics & Gynecology (ABOG)

Other Experience and Professional Memberships

- 1990 Member, European Society for Human Reproduction and Embryology
- 1994 Member, American Society for Reproductive Medicine
- 1999 Member, American Association for the Advancement of Science
- 2004-2009 CoEditor-in-Chief, Journal of Experimental and Clinical Assisted Reproduction
- 2007 Grant Reviewer, National Science Foundation (NSF)
- 2009 Associate Editor, Journal of Assisted Reproduction and Genetics
- 2009 Grant Reviewer, Direction de la Recherche Clinique et des Innovations (DRCI), University of Strasbourg
- 2011 Grant Reviewer, The Netherlands Organisation for Health Research and Development, Translational Adult Stem Cell Research Programme
- 2016 Member, American Board of Obstetrics & Gynecology (ABOG)

Honors

- 1995 Buckeye State of the Art Lecture, American Society of Andrology 20th Anniversary Annual Meeting, Raleigh, NC, USA.
- 1995 The Barbara Eck Menning Founders Award, National Resolve, New York, NY, USA.
- 1996 The Schackman Lecture, Baltimore, MD, USA.
- 1999 The Kokopelli Ball Award – FRABEL, The American Fertility Association, New York, NY, USA.
- 2009 Jacob Heskell Gabbay Award in Biotechnology and Medicine, Rosenstiel Basic Medical Sciences Research Center and Brandeis University, Waltham, MA, USA.
- 2010 The Crystal Tube Award. Russian Annual National Award created in honor of the achievements in Assisted Reproductive Technologies. December 11, 2010, Moscow, Russia.
- 2011 Francavilla Fontana Illustrious Citizen Award. An award created in honor of the outstanding citizens born from Francavilla Fontana, Brindisi, Italy in providing special services to society. 700 Anniversario della Nascita della Città di Francavilla (1310-2010). July 12, 2011, Francavilla Fontana, Italy.
- 2011, 2013 The ASRM Star Award. The Star Award is given to ASRM member, nominated by their peers, who have continuously contributed 10 or more years of presentation, beginning in 2000, at the ASRM's Annual Meeting. September 16, 2011; September 6, 2013. New York, USA.
- 2013 Stella d'Oro Accademica. The "Academic Gold Star" award is conferred to a candidate that demonstrates unselfish behavior, highly regarded by his colleagues in his profession, and have high morals and professional character. The award is given on behalf of the Cardinale Giuseppe Renato Imperiali of the *Accademia Imperiali Libero Sodalizio Letterario e Scientifico*. July 16, 2013. Francavilla Fontana, Brindisi, Italy.
- 2014-2021 The ASRM Star Award. The Star Award is given to ASRM member, nominated by their peers, who have continuously contributed 10 or more years of presentation, beginning in 2006, at the ASRM's Annual Meeting. September 5, 2014. New York, USA.

C. Contributions to Science

- 1. Proof of the paternal inheritance of the human centrosome:** The occurrence of severe chromosomal abnormalities in numerous embryos has been attributed to an abnormal mitotic spindle during syngamy related to centrosomal dysfunction. My team, through the genetic assessment of embryos generated from abnormally fertilized zygotes following in vitro fertilization and intra cytoplasmic sperm injection, was able to hypothesize and provide evidence of the paternal inheritance of the human centrosome. The centrosome has several implications for human infertility. It is possible that immotile or non-progressively motile spermatozoa may possess centriolar abnormalities or an

absence of centrioles. Similarly, anti-sperm antibodies against centrioles may be responsible for mitotic arrest. One way of solving this problem would be the use of donor centrosomes. To this end, my research has assessed the ability of embryos injected with physically separated sperm segments (head only, head and tail separated or isolated tail) to develop normally. Fluorescent in situ hybridization revealed an almost universal mosaicism in these embryos, suggesting that physical disruption of the spermatozoa compromises the ability of the centrosome to function in the zygote.

1. **Palermo G**, Munné S, Cohen J. The human zygote inherits its mitotic potential from the male gamete. *Hum Reprod* 1994;9(7):1220-5.
 2. **Palermo GD**, Munné S, Colombero L, Cohen J, Rosenwaks Z. Genetics of abnormal human fertilization. *Hum Reprod* 1995;10(Suppl 1):120-7
 3. **Palermo GD**, Colombero LT, Rosenwaks Z. The human sperm centrosome is responsible for normal syngamy and early embryonic development. *Rev Reprod* 1997;2(1):19-27.
 4. Colombero LT, Takeuchi T, Sills ES, Breed WG, Rosenwaks Z, **Palermo GD**. A comparison of human spermatozoa immunolabeling features using xenogenic reagents for centrosomal proteins. *Clin Exp Obstet Gynecol* 1999;26(3-4):141-6.
2. **Advancement in the understanding of spermatozoal dysfunction as a contributing factor for fertilization failure:** Since the inception of in vitro fertilization, it became clear that proper fertilization of an oocyte requires the presence of a functional spermatozoon. Several factors can indeed interfere with male gamete function. This ranges from immunological factors such as the presence of anti-sperm antibodies to a dysfunction or complete absence of the acrosome. My team has performed several groundbreaking investigations to actually understand the function and at the same time to test methods to enhance acrosomal activity. This work led to the understanding, together with outstanding researchers in the field, of the area within the sperm nucleus where the soluble cytosolic factor responsible for oocyte activation is located.
1. **Palermo G**, Van Steirteghem A. Enhancement of acrosome reaction and subzonal insemination of a single spermatozoon in mouse eggs. *Mol Reprod Dev* 1991;30(4):339-45.
 2. **Palermo G**, Joris H, Devroey P, Van Steirteghem AC. Induction of acrosome reaction in human spermatozoa used for subzonal insemination. *Hum Reprod* 1992;7(2):248-54.
 3. **Palermo GD**, Avrech OM, Colombero LT, Wu H, Wolny YM, Fissore RA, Rosenwaks Z. Human sperm cytosolic factor triggers Ca²⁺ oscillations and overcomes activation failure of mammalian oocytes. *Mol Hum Reprod* 1997;3(4):367-74.
 4. Lee B, **Palermo G**, Machaca K. Downregulation of store-operated Ca²⁺ entry during mammalian meiosis is required for the egg-to-embryo transition. *J Cell Sci* 2013;126(Pt 7):1672-81.
3. **Development of the ultimate treatment of human male infertility:** Male-factor infertility represents half of the causes for the inability of couples to reproduce. Since 1980, several micro manipulation techniques were attempted to achieve fertilization with gametes from men with severe male-factor infertility. In 1992, I succeeded to report the first four human pregnancies with intracytoplasmic sperm injection (ICSI). With this procedure, couples with almost all aspects of male infertility, from the presence of anti-sperm antibodies to complete absence of the acrosome, can be successfully treated. Indeed, only one spermatozoon is required, as long as it is viable, to be able to achieve a zygote and therefore provide a chance for conception. Today, there are over 3 million offspring generated from ICSI throughout the world.
1. **Palermo G**, Joris H, Devroey P, Van Steirteghem AC. Pregnancies after intracytoplasmic injection of single spermatozoon into an oocyte. *Lancet* 1992;340(8810):17-8.
 2. **Palermo G**, Joris H, Derde MP, Camus M, Devroey P, Van Steirteghem A. Sperm characteristics and outcome of human assisted fertilization by subzonal insemination and intracytoplasmic sperm injection. *Fertil Steril* 1993;59(4):826-35.
 3. **Palermo GD**, Cohen J, Alikani M, Adler A, Rosenwaks Z. Intracytoplasmic sperm injection: a novel treatment for all forms of male factor infertility. *Fertil Steril* 1995;63(6):1231-40.

4. **Palermo GD**, Cohen J, Alikani M, Adler A, Rosenwaks Z. Development and implementation of intracytoplasmic sperm injection (ICSI). *Reprod Fertil Dev* 1995;7(2):211-7.

4. **Refined treatment of men with severe oligozoospermia and various forms of azoospermia:**

The consistent pregnancies achieved with ICSI across the arrays of dysfunctional spermatozoa have allowed the possibility to push the boundaries of this technique towards the most extreme aspect of male infertility, when only few spermatozoa can be identified as often encountered in cryptozoospermia, virtual azoospermia or when surgical specimens are retrieved in cases of absolute azoospermia. The ability to obtain pregnancies with these scarce spermatozoa has introduced another variable: the injection of the non-ideal and unselected spermatozoon. My team as characterized these spermatozoa as euploid with a functional centrosome albeit with abnormal morphology. In subsequent follow-ups, we have found that cases performed with these spermatozoa have resulted in healthy children. My team has highlighted that utilization of such scarce and unselected spermatozoa can still yield rewarding pregnancy rates and reassuring offspring health.

1. **Palermo GD**, Schlegel PN, Colombero LT, Zaninovic N, Moy F, Rosenwaks Z. Aggressive sperm immobilization prior to intracytoplasmic sperm injection with immature spermatozoa improves fertilization and pregnancy rates. *Hum Reprod* 1996;11(5):1023-9.
2. **Palermo GD**, Schlegel PN, Sills ES, Veeck LL, Zaninovic N, Menendez S, Rosenwaks Z. Births after intracytoplasmic injection of sperm obtained by testicular extraction from men with nonmosaic Klinefelter's syndrome. *N Engl J Med* 1998;338(9):588-90.
3. **Palermo GD**, Schlegel PN, Hariprashad JJ, Ergün B, Mielnik A, Zaninovic N, Veeck LL, Rosenwaks Z. Fertilization and pregnancy outcome with intracytoplasmic sperm injection for azoospermic men. *Hum Reprod* 1999;14(3):741-8.
4. **Palermo GD**, Neri QV, Schlegel PN, Rosenwaks Z. Intracytoplasmic sperm injection (ICSI) in extreme cases of male infertility. *PLoS One* 2014;9(12):e113671.

D. Additional Information: Research Support and/or Scholastic Performance

Completed Research Support

Jan. 1988-Nov. 1988	Consortium of the University of Bari (10,000.00 USD). <i>Principal Investigator</i> .
Dec. 1988-Mar.1990	Center for Reproductive Medicine, Brussels Free University Hospital (5,000.00 USD). <i>Principal Investigator</i> .
1992-1996	Scientific research grant 3.0018.92 "Experimental and clinical assisted fertilization by subzonal insemination of spermatozoa" of the Belgian Fund for Medical Scientific Research (130,000.00 USD). <i>Principal Investigator</i> .
1996	Unrestricted educational grant from Serono Laboratories, Inc. (2,500.00 USD).
1999, 2000	Scientific research grant from Organon for the "Follow-up of Pregnancies, Neonatal and Pediatric Outcomes after Intracytoplasmic Sperm Injection and <i>In Vitro</i> Fertilization", Protocol No. 0399-613 (50,000 USD/year). <i>Principal Investigator</i> .
1999	Unrestricted educational grant from Serono Laboratories, Inc. (2,500.00 USD).
2000, 2001	Scientific research grant from Bertarelli Foundation, Serono Pharma for the "Follow-up of pregnancies, neonatal, and pediatric outcome of five year old children born through intracytoplasmic sperm injection and <i>in vitro</i> fertilization", Protocol No. 0299-581 (150,000 USD/year). <i>Principal Investigator</i> .
2002, 2003	Scientific research grant from Serono for the "Follow-up of Pregnancies, Neonatal and Pediatric Outcomes after Intracytoplasmic Sperm Injection and <i>In Vitro</i> Fertilization", Protocol No. 0399-613 (10,000 USD/year). <i>Principal Investigator</i> .
2006-2007	Tri-Institutional Stem Cell Initiative of The Rockefeller University, Weill Medical College of Cornell University, and Sloan Kettering Institute Research Program for the project "Laying the foundations for integrated therapeutic cloning and globin gene transfer to treat β -thalassemia", (62,700 USD/year). <i>Principal Investigator</i> .

- 2010-2012 National Priorities Research Program (NPRP), Qatar National Research Fund for the project "Calcium signaling mechanisms in oocyte development and pathology", (250,000/year). *Co-Principal Investigator*.
- 2012-2014 New York City Partnership Foundation, Inc., NYC BioAccelerate (OSP # 65774) for the project "Assay of sperm function to diagnose male infertility", (250,000/year). *Co-Principal Investigator*.
- 2021- Weill Cornell Medicine. Clinical & Translational Science Center. CTSC Pilot Award "ICSI-on-a-Chip", (50,000/year). *Co-Principal Investigator*.
- 2021- Memorial Sloan Kettering Cancer Center, The Rockefeller University, and Weill Cornell Medical College. Tri-Institutional Stem Cell Initiative. The STARR Foundation Grant "Large scale production and maturation of human primordial germ cell derived from hESCs or hiPSCs gastruloids", (188,000/year). *Co-Principal Investigator*.