

## In Vitro Fertilization

Zsolt Peter Nagy  
Alex C. Varghese  
Ashok Agarwal  
*Editors*

# In Vitro Fertilization

A Textbook of Current and Emerging Methods and Devices

Second edition

*Editors*

**Zsolt Peter Nagy, MD, PhD**  
Reproductive Biology Associates – Prelude  
Atlanta, GA, USA

**Alex C. Varghese, PhD**  
Astra Fertility Group  
Mississauga, ON, Canada

**Ashok Agarwal, PhD**  
Cleveland Clinic  
Cleveland, OH, USA

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## Foreword

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Exactly 40 years following the birth of the first IVF baby, Louise Brown, the extended and fully updated second edition of *In Vitro Fertilization* will see the light of day. This new edition, again edited by Drs. Nagy, Varghese, and Agarwal, convincingly captures the many advances in assisted reproduction technology, especially in the IVF laboratory. It is overwhelming to see the wealth of added knowledge since the publication of its first edition in 2012.

It is a privilege for me, as a clinician, to be asked to write the foreword for such an excellent and scholarly textbook, mainly focusing on the many developments in the ART laboratory. Reviewing the advances in ART since the late 1970s, it seems to me that the first few decades have been dominated by progress in the IVF clinic. Beyond any doubt, however, we all have witnessed tremendous advances – away from the early days of “black box” fertilization and very early embryo development *in vitro* – in the laboratory during the most recent decade. I personally believe that a high-quality performance in the laboratory represents the key determinant for a successful IVF program. Quality management related to existing procedures, as well as the continued critical monitoring of possible benefits of novel technologies and the subsequent implementation of such new developments when proven beneficial, seem key determinants of a successful IVF laboratory.

The use of IVF continues to increase around the world, due to an ever-increasing global access to IVF care, the increasing use of ART in the treatment of different forms of infertility (like tubal disease, ovarian aging, or ovarian dysfunction), and – above all – the increasing central place of ART in conditions not directly related to infertility per se, such as the use of donor gametes in same-sex couples or singles; the cryopreservation of gametes, embryos, or gonadal tissue; genetic embryo testing in (often fertile) families suffering from genetic disease, and many others. Hence, the proportion of children born following ART will continue to increase in the years to come, and embryologists should be aware of their great responsibility toward the future health of ART offspring. Soon, at least one child in every primary school class will be generated by ART in the majority of countries worldwide.

Advances in the ART laboratory are everywhere, and they are all covered extensively in the 79 chapters of the current revised version of the book: the handling of sperm and oocytes, the many aspects of the process of fertilization, improved embryo culture media and culture conditions, and early embryo development. Moreover, many novel technologies have been developed for advanced embryo testing, and technologies are under way for automated and individualized embryo development assessment and handling (referred to by some as the “embryo hotel”).

Novel information is being unraveled, stimulating embryologists to think outside the box, such as the potential influence of the patient and ovarian stimulation regimens on the quality of oocytes entering the laboratory. In addition, knowledge is accumulating regarding effects of the quality of embryos leaving the laboratory on implantation, miscarriage rates, and even pregnancy complications, perinatal morbidity, and possibly future health of IVF offspring.

Needless to say, I can highly recommend this authoritative and comprehensive manual, primarily for everyone working in the IVF laboratory. Certainly, this book will also provide a wealth of useful information for everybody dealing with an IVF laboratory and may therefore fulfill the important role of bridging the gap between IVF clinicians and embryologists.

**Bart C.J.M. Fauser MD, PhD, FRCOG**

Emeritus Professor of Reproductive Medicine, University of Utrecht & University Medical Center Utrecht, The Netherlands

# Preface

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Ever since the first in vitro fertilization baby was born in Oldham, England, in 1978, the use of assisted reproductive technology (ART) to overcome infertility has increased exponentially with the simultaneous increase in the number of fertility centers in every part of the world. Since the first breakthrough, there have been several significant discoveries and improvements related to IVF technology, such as ICSI and vitrification (gametes, embryos, reproductive tissue), which has helped in increasing its efficiency severalfold.

The first edition of *Practical Manual of In Vitro Fertilization: Advanced Methods and Novel Devices* achieved an overwhelming success among clinical and laboratory professionals. It provided the most comprehensive update on all laboratory aspects of IVF, both theoretical and practical, in great detail and described several novel techniques that made the book also an outstanding reference for ART laboratory procedures.

The last six years has witnessed a steady stream of new discoveries and technological advancements in assisted reproduction laboratory methods and systems, such as automation, molecular testing, and gene editing, and with that growth, the necessity and demand for an updated new edition of this state-of-the-art textbook became readily apparent. For this second edition, the title shortened simply to *In Vitro Fertilization*, each section has been thoroughly revised and expanded to include the very latest evidence and practical guidelines, beginning with laboratory set-up, equipment, and management and moving on to detailed, thematic discussions of all relevant aspects of the IVF process: oocyte preparation and embryo culture methods, sperm processing and selection, insemination procedures, micromanipulation, embryo evaluation, grading and hatching, biopsy procedures, cryopreservation, and embryo transfer. The concluding sections present global perspectives on the regulation and licensing of ART laboratories; innovations, risks, and safety in ART; and molecular reproduction.

Every effort has been made to ensure that the information contained in this second edition is as up-to-date as possible, written by the most acclaimed and acknowledged professionals of our field – more than 160 experts in total, representing all continents of the world. Because of the wide range of topics and the comprehensive theoretical and detailed practical descriptions, this second edition is an ideal reference for all who are involved with assisted reproduction, including clinical embryologists, andrologists, reproductive endocrinologists, and scientists, regardless if one wishes to obtain a basic understanding or to digest an in-depth presentation. We ensure that this textbook will be a valuable resource for university students pursuing clinical embryology courses, too – chapters include clear learning objectives as well as review questions for self-guided study or group review.

We are thankful to Kristopher Spring, Senior Editor at Springer, for his ready support and advice, and Kevin Wright, Developmental Editor, for his continuous efforts in the day-to-day management of this large book project. We are grateful to Professor Bart Fauser for reviewing our book and authoring an outstanding foreword for the second edition. Furthermore, we are thankful to all of the exceptional contributors for sharing their knowledge and for being part of this great project.

**Zsolt Peter Nagy, MD, PhD**

Atlanta, GA, USA

**Alex C. Varghese, PhD**

Mississauga, ON, Canada

**Ashok Agarwal, PhD**

Cleveland, OH, USA

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## Contributors

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### Ashok Agarwal, PhD

Department of Urology and American  
Center for Reproductive Medicine  
Cleveland Clinic  
Cleveland, OH, USA  
[agarwaa@ccf.org](mailto:agarwaa@ccf.org)

### Martha Aguirre, PhD

Fertility Center of Las Vegas  
Las Vegas, NV, USA  
[maguirre@ovationfertility.com](mailto:maguirre@ovationfertility.com)

### Robert John Aitken, PhD, ScD

Discipline of Biological Sciences and  
Priority Research Centre in Reproductive Science,  
School of Environmental and Life Sciences  
The University of Newcastle  
Callaghan, NSW, Australia  
[john.aitken@newcastle.edu.au](mailto:john.aitken@newcastle.edu.au)

### Carmela Albert Rodríguez, PhD

IVF Laboratory  
IVI Valencia  
Valencia, Spain

### Lucía Alegre Ferri

IVF Laboratory  
IVI Valencia  
Valencia, Spain

### Mina Alikani, PhD

Althea Science and IVFqc, ART Institute of Washington  
New York, NY, USA

### Akanksha Allahbadia, MD

A Rotunda – The Center for Human Reproduction  
Mumbai, India

### Gautam N. Allahbadia, MD

Indo Nippon IVF  
Mumbai, India  
[drallah@gmail.com](mailto:drallah@gmail.com)

### Swati Allahbadia, MD

A Rotunda – The Center for Human Reproduction  
Mumbai, India

### Siti Nornadhirah Amdani

Nuffield Department of Obstetrics and Gynaecology  
University of Oxford, Level 3, Women's Centre,  
John Radcliffe Hospital  
Oxford, UK

### Matteo A. Avella, PhD

Shady Grove Fertility, Reproductive Science  
Center of Pennsylvania, Department of Embryology  
Wayne, PA, USA  
[matteo.avella@integramed.com](mailto:matteo.avella@integramed.com)

### Doris J. Baker, PhD

Mercer University School of Medicine,  
Basic Medical Sciences  
Macon, GA, USA  
[dorisbkr@gmail.com](mailto:dorisbkr@gmail.com)

### Basak Balaban, MSc

VKE American Hospital of Istanbul,  
Assisted Reproduction Unit  
Istanbul, Turkey  
[basakbalaban@superonline.com](mailto:basakbalaban@superonline.com)  
[basakb@amerikanhastanesi.org](mailto:basakb@amerikanhastanesi.org)

### Tom Beckitt, BS

Genea Biomedx  
Sydney, NSW, Australia

### Barry Behr, PhD, HCID

Stanford University, Reproductive  
Endocrinology and Infertility  
Sunnyvale, CA, USA  
[behr1@stanford.edu](mailto:behr1@stanford.edu)

### Fabiola C. Bento, MBE

ANDROFERT, Andrology and Human Reproduction Clinic  
Campinas, SP, Brazil  
[fabiola.bento@androfert.com.br](mailto:fabiola.bento@androfert.com.br)

### Diana P. Bernal, DMV

Biotech INC  
Alpharetta, GA, USA  
[paticobernal@yahoo.com](mailto:paticobernal@yahoo.com)

### Jutimala Bhattacharyya, MD

Dispur Poly Clinic IVF  
Guwahati, India

### Kia Borg, BA

Livio Fertilitetscentrum Göteborg  
Göteborg, Sweden  
[kia.borg@fertilitetscentrum.se](mailto:kia.borg@fertilitetscentrum.se)

### Ching-Chien Chang, PhD

Reproductive Biology Associates – Prelude  
Atlanta, GA, USA  
[changivf@yahoo.com](mailto:changivf@yahoo.com)

**Alice A. Chen, PhD**

GRAIL, Inc  
Menlo Park, CA, USA

Hernest Institute for Reproductive Medicine  
Sunnyvale, CA, USA  
[aliceannchen@gmail.com](mailto:aliceannchen@gmail.com)

**Stephanie Cheung, BS**

Weill Cornell Medicine, The Ronald O. Perelman  
and Claudia Cohen Center for Reproductive Medicine  
New York, NY, USA  
[stc3001@med.cornell.edu](mailto:stc3001@med.cornell.edu)

**Ri-Cheng Chian, PhD**

Center for Reproductive Medicine,  
Shanghai 10th People's Hospital of Tongji University  
Shanghai, China  
[rchian@126.com](mailto:rchian@126.com)

**Chak-Lam Cho**

Department of Surgery, Union Hospital  
Hong Kong, China  
[chochaklam@yahoo.com.hk](mailto:chochaklam@yahoo.com.hk)

**Stephen Chow, BA**

Weill Cornell Medicine, The Ronald O. Perelman  
and Claudia Cohen Center for Reproductive Medicine  
New York, NY, USA  
[stc3004@med.cornell.edu](mailto:stc3004@med.cornell.edu)

**Ana Cobo, PhD**

IVI RMA  
Valencia, Spain  
[Ana.Cobo@ivi.es](mailto:Ana.Cobo@ivi.es)

**Jacques Cohen, PhD**

Althea Science and IVFqc,  
ART Institute of Washington  
New York, NY, USA  
[jc@embryos.net](mailto:jc@embryos.net)

**Giovanni Coticchio, BSc, MSc, MMedSci, PhD**

9.Baby, Family and Fertility Center  
Bologna, Italy  
[giovanni.coticchio@9puntobaby.it](mailto:giovanni.coticchio@9puntobaby.it)

**Kevin Coward, BSc, PhD**

Nuffield Department of Obstetrics and Gynaecology  
University of Oxford, Level 3, Women's Centre,  
John Radcliffe Hospital  
Oxford, UK

**Rachel Cutting, Bsc**

Sheffield Teaching Hospitals NHS Foundation Trust,  
Assisted Conception Department  
Sheffield, South Yorkshire, UK  
[rachel.cutting@sth.nhs.uk](mailto:rachel.cutting@sth.nhs.uk)

**Shir Dar, MD**

The IVF, Infertility and Reproductive Medicine Unit,  
Department of Obstetrics and Gynecology,  
Kaplan Medical Center  
Rehovot, Israel

**Madhab C. Das, PhD**

Kolkata Global IVF  
Kolkata, India  
[madhabcd@hotmail.com](mailto:madhabcd@hotmail.com)

**Adam Dawood**

Shady Grove Fertility, IVF  
Rockville, MD, USA  
[adam.dawood@gmail.com](mailto:adam.dawood@gmail.com)

**Shagufta Dawood, BS**

Shady Grove Fertility, IVF  
Rockville, MD, USA

**Lucia De Santis, Bsc, MSc, PhD**

IVF Unit, Department OB/GYN  
San Raffaele Scientific Institute, Vita-Salute University  
Milan, Italy  
[desantis.lucia@hsr.it](mailto:desantis.lucia@hsr.it)

**Tania R. Dias, MSc**

American Center for Reproductive Medicine  
Cleveland Clinic  
Cleveland, OH, USA

Universidade da Beira Interior  
Covilhã, Portugal

Department of Microscopy, Laboratory of Cell Biology  
Institute of Biomedical Sciences Abel Salazar  
and Unit for Multidisciplinary Research in Biomedicine,  
University of Porto  
Porto, Portugal

LAQV/REQUIMTE - Laboratory of Bromatology  
and Hydrology, Faculty of Pharmacy  
University of Porto  
Porto, Portugal  
[taniairdias@gmail.com](mailto:taniairdias@gmail.com)

**Enver Kerem Dirican, PhD**

Obstetrics and Gynecology, Center for Assisted  
Reproduction  
Akdeniz University, Faculty of Medicine  
Antalya, Turkey  
[keremdirican@gmail.com](mailto:keremdirican@gmail.com)

**Andrey V. Dolinko, MD**

Women and Infants Hospital,  
Obstetrics and Gynecology  
Providence, RI, USA  
[andolinko@gmail.com](mailto:andolinko@gmail.com)

**Marlena Duke, M.Sc., ELD**

Reproductive Medicine Associates of New York  
New York, NY, USA

**Damayanthi Durairajanayagam, MD**

Faculty of Medicine  
Universiti Teknologi MARA, Sungai Buloh Campus  
Sungai Buloh, Selangor, Malaysia

**Paula Dwan, WHPN-BC. BS, MS**

Third Party Reproduction  
Boston IVF  
Lexington, MA, USA  
[pdwan@bostonivf.com](mailto:pdwan@bostonivf.com)

**Thomas Ebner, PhD**

Kepler University, Department of Gynecology,  
Obstetrics, and Gynecological Endocrinology  
Linz, Austria  
[Thomas.Ebner@kepleruniklinikum.at](mailto:Thomas.Ebner@kepleruniklinikum.at)

**Thomas Elliott, BSc**

Reproductive Biology Associates – Prelude  
Atlanta, GA, USA  
[thomas@ivf.net](mailto:thomas@ivf.net)

**Marcos Meseguer Escrivá, PhD**

IVF Laboratory, IVI Valencia  
Valencia, Spain  
[Marcos.Meseguer@ivirma.com](mailto:Marcos.Meseguer@ivirma.com)

**Sandro C. Esteves, MD, PhD**

ANDROFERT, Andrology and Human Reproduction Clinic  
Campinas, SP, Brazil  
[s.esteves@androfert.com.br](mailto:s.esteves@androfert.com.br)

**Stephen Fiser**

Althea Science and IVFqc, ART Institute of Washington  
New York, NY, USA

**Steven Fleming, PhD**

Origio, Copenhagen, Denmark  
  
University of Sydney, Sydney, Australia  
[sfleming@origio.com](mailto:sfleming@origio.com)

**Helena Fulka, PhD**

Department of Biology of Reproduction  
Institute of Animal Science  
Prague, Czech Republic

**Josef Fulka Jr, PhD**

Department of Biology of Reproduction  
Institute of Animal Science  
Prague, Czech Republic  
[fulka.josef@vuzv.cz](mailto:fulka.josef@vuzv.cz)

**Goral Gandhi, MA**

Indo Nippon IVF  
Mumbai, India

**David K. Gardner, BSc (Hons), PhD**

School of BioSciences  
University of Melbourne  
Parkville, VIC, Australia

Melbourne IVF  
Melbourne, VIC, Australia  
[david.gardner@unimelb.edu.au](mailto:david.gardner@unimelb.edu.au)

**Forest C. Garner, MS**

Fertility Center of Las Vegas  
Las Vegas, NV, USA

**Nicolás Garrido, PhD**

IVI Foundation  
Valencia, Spain  
[nicolas.garrido@ivi.es](mailto:nicolas.garrido@ivi.es)

**Brant C. Gibson, PhD**

ARC Centre of Excellence for Nanoscale  
BioPhotonics (CNBP)  
School of Science RMIT University  
Melbourne, VIC, Australia  
[brant.gibson@rmit.edu.au](mailto:brant.gibson@rmit.edu.au)

**Antonia Gilligan, BA**

Alpha Environmental  
New York, NY, USA

**Kathryn J. Go, PhD, HCLD**

Embryology Laboratory, Boston IVF – The Maine Center  
South Portland, ME, USA  
[KGo@bostonivf.com](mailto:KGo@bostonivf.com)

**Johan Guns, MSc**

UZ Brussel  
Brussels, Belgium  
[Johan.Guns@uzbrussel.be](mailto:Johan.Guns@uzbrussel.be)

**Tatsuya Harada, MD, PhD**

Kamaeda IVF Clinic Makuhari, Reproductive Medicine  
Chiba, Japan  
[harada.tatsuya@kameda.jp](mailto:harada.tatsuya@kameda.jp)

**Thorir Hardarson, PhD**

Livio AB  
Stockholm, Sweden  
[thorir.hardarson@fertilitetscentrum.se](mailto:thorir.hardarson@fertilitetscentrum.se)

**Ralf Henkel, B. ED, PhD, Habil**

Department of Medical Bioscience  
University of the Western Cape  
Bellville, South Africa  
[rhenkel@uwc.ac.za](mailto:rhenkel@uwc.ac.za)

**Christine Hennigan**

Department of Molecular, Cellular  
and Developmental Biology  
University of Colorado  
Boulder, CO, USA

**Linda Hillis, BA**

Donor Services, Boston IVF  
Lexington, MA, USA  
[lhillis@bostonivf.com](mailto:lhillis@bostonivf.com)

**Kenichiro Hiraoka, PhD**

Kameda Medical Center,  
Assisted Reproductive Technology Center  
Chiba, Japan  
[hiraoka@oct.email.ne.jp](mailto:hiraoka@oct.email.ne.jp)

**Julius Hreinsson, MSc, PhD**

Mount Sinai Fertility  
Toronto, Ontario, Canada  
[julius.hreinsson@gmail.com](mailto:julius.hreinsson@gmail.com)

**Louise Hyslop, BSc, PhD**

Newcastle Upon Tyne NHS Foundation Trust,  
Newcastle Fertility Centre  
Newcastle, UK  
[l.a.hyslop@newcastle.ac.uk](mailto:l.a.hyslop@newcastle.ac.uk)

**Romain Imbert**

IVF Center CHIREC  
Braine l'Alleud-Waterloo, Belgium

**Evgenia Isachenko**

University Maternal Hospital  
Department of Obstetrics and Gynecology,  
Cologne University  
Cologne, Germany

**Vladimir Isachenko, PhD**

University Maternal Hospital  
Department of Obstetrics and Gynecology,  
Cologne University  
Cologne, Germany  
[v.isachenko@yahoo.com](mailto:v.isachenko@yahoo.com)

**Tomonori Ishikawa, MD, PhD**

Tokyo Medical and Dental University,  
Comprehensive Reproductive Medicine  
Tokyo, Japan  
[t.ishikawa.crm@tmd.ac.jp](mailto:t.ishikawa.crm@tmd.ac.jp)

**Robert P. S. Jansen, MD CREI**

Sydney IVF  
Sydney, NSW, Australia

**Ronny Janssens, BSc**

Centre for Reproductive Medicine, UZ Brussel  
Brussels, Belgium  
[Ronny.Janssens@uzbrussel.be](mailto:Ronny.Janssens@uzbrussel.be)

**Kanna Jayaprakasan, PhD**

Division of Obstetrics and Gynaecology,  
Faculty of Medicine & Health Sciences  
University of Nottingham  
Nottingham, UK

Derby Fertility Unit  
Royal Derby Hospital  
Derby, UK

[kanna.jayaprakasan@nhs.net](mailto:kanna.jayaprakasan@nhs.net)  
[k.jayaprakasan@nottingham.ac.uk](mailto:k.jayaprakasan@nottingham.ac.uk)

**Lars Johansson, PhD**

NewLifeAid-Global  
Torgny Segerstedts Alle21  
Uppsala, Sweden  
[newlifeaidlj@gmail.com](mailto:newlifeaidlj@gmail.com)

**Celine Jones**

Nuffield Department of Obstetrics and Gynaecology  
University of Oxford, Level 3, Women's Centre,  
John Radcliffe Hospital  
Oxford, UK

**Hubert Joris**

Vitrolife Sweden AB  
Göteborg, Sweden  
[HJoris@vitrolife.com](mailto:HJoris@vitrolife.com)

**Kiyotaka Kawai, MD**

Kameda Medical Center, Assisted Reproductive  
Technology Center  
Chiba, Japan  
[kawai.kiyotaka@kameda.jp](mailto:kawai.kiyotaka@kameda.jp)

**Jonathan Kort, PhD, HCLD**

Department of Reproductive  
Endocrinology and Infertility  
Stanford University  
Stanford, CA, USA

**Borut Kovačič, PhD**

University Medical Centre Maribor,  
Department of Reproductive Medicine  
and Gynaecological Endocrinology  
Maribor, Slovenia  
[borut.kov@ukc-mb.si](mailto:borut.kov@ukc-mb.si)  
[borut.kov63@gmail.com](mailto:borut.kov63@gmail.com)

**Michelle Lane, PhD**

Robinson Research Institute, School of Paediatrics  
and Reproductive Health, University of Adelaide  
Adelaide, SA, Australia

Repromed, Dulwich, SA, Australia  
[michelle.lane@adelaide.edu.au](mailto:michelle.lane@adelaide.edu.au)

**Christine Leary**

Hull IVF Unit, East Riding Fertility Services  
The Women and Children's Hospital, Hull Royal Infirmary  
Hull, UK

**Henry J. Leese**

Hull York Medical School,  
University of Hull, Hertford Building  
Hull, UK

**Don Leigh, PhD (UNSW)**

Sydney IVF  
Sydney, NSW, Australia

**Juergen Liebermann, MS, PhD, HCLD**

Fertility Centers of Illinois  
Chicago, IL, USA  
[Juergen.Liebermann@integrated.com](mailto:Juergen.Liebermann@integrated.com)

**Georgios Liperis, PhD, M Med Sci, MSc, BSc**

Westmead Fertility Centre  
Institute of Reproductive Medicine, University of Sydney  
Westmead, NSW, Australia  
[gliperis@westmeadivf.com](mailto:gliperis@westmeadivf.com)

**Christa Mackenzie, BSc**

Reproductive Science Center of the  
San Francisco Bay Area  
San Ramon, CA, USA

**Roberta Maggiulli, PhD**

Clinca Valle Giulia, Genera  
Rome, Italy  
[maggiulli@generaroma.it](mailto:maggiulli@generaroma.it)

**Peter Mallmann, MD**

University Maternal Hospital  
Department of Obstetrics and Gynecology,  
Cologne University  
Cologne, Germany

**James Marshall, BAppSc (UTS)**

Sydney IVF  
Sydney, NSW, Australia

**David Jareno Martinez**

IVF Center CHIREC  
Braine l'Alleud-Waterloo, Belgium

**Ana D. Martins, MSc, PhD Candidate**

Department of Urology and American Center  
for Reproductive Medicine  
Cleveland Clinic  
Cleveland, OH, USA

Department of Microscopy,  
Laboratory of Cell Biology and Unit  
for Multidisciplinary Research in Biomedicine  
Abel Salazar Institute of Biomedical Sciences (ICBAS),  
University of Porto  
Porto, Portugal

**Steven J. McArthur, BSc**

Sydney IVF  
Sydney, NSW, Australia  
[stevenmcarthur@y7mail.com](mailto:stevenmcarthur@y7mail.com)  
[Steve.mcarthur@sydneyivf.com](mailto:Steve.mcarthur@sydneyivf.com)

**Marius Meintjes, PhD, HCLD**

Frisco Institute for Reproductive Medicine  
Frisco, TX, USA  
[mmeintjes@friscoinfertility.com](mailto:mmeintjes@friscoinfertility.com)

**Rubina Merchant**

A Rotunda – The Center for Human Reproduction  
Mumbai, India

**Kristine A. Milne, BS Biology**

Shady Grove Fertility, IVF  
Rockville, MD, USA  
[kristine.milne@integrated.com](mailto:kristine.milne@integrated.com)

**Markus Montag, PhD**

ilabcomm GmbH  
Sankt Augustin, Germany  
[mmontag@ilabcomm.com](mailto:mmontag@ilabcomm.com)

**Dean E. Morbeck, PhD, HCLD, MBA**

Fertility Associates  
Auckland, New Zealand  
[dmorbeck@fertilityassociates.co.nz](mailto:dmorbeck@fertilityassociates.co.nz)

**Santiago Munné, PhD**

CooperGenomics, a Cooper Surgical Company  
School of Biosciences, University of Kent  
Canterbury, UK  
[munne@reprogenetics.com](mailto:munne@reprogenetics.com)

**Maximillian Murtinger**

NextClinic IVF Centers. Prof. Zech  
Bregenz, Austria



**Zsolt Peter Nagy, MD, PhD**

Reproductive Biology Associates – Prelude  
Atlanta, GA, USA  
[zsolt.peter.nagy@gmail.com](mailto:zsolt.peter.nagy@gmail.com)

**Laszlo Nanassy**

Human Reproduction Institute  
Budapest, Hungary  
[nanassyl@hotmail.com](mailto:nanassyl@hotmail.com)

**Liesl Nel-Themaat, PhD**

Department of Advanced Reproductive Medicine  
University of Colorado Denver  
Stapleton, CO, USA  
[liesl.nel-themaat@ucdenver.edu](mailto:liesl.nel-themaat@ucdenver.edu)  
[lnthemaat@gmail.com](mailto:lnthemaat@gmail.com)

**Queenie V. Neri, PhD**

Weill Cornell Medicine, The Ronald O. Perelman  
and Claudia Cohen Center for Reproductive Medicine  
New York, NY, USA  
[qneri@med.cornell.edu](mailto:qneri@med.cornell.edu)

**Willem Ombelet, MD, PhD**

Genk Institute for Fertility Technology  
Genk, Belgium

**Akira Onishi, PhD**

Transgenic Pig Research Unit  
National Institute of Agrobiological Sciences  
Tsukuba, Japan  
[onishi@affrc.go.jp](mailto:onishi@affrc.go.jp)

**Yuval Or, MD**

The IVF, Infertility and Reproductive Medicine Unit,  
Department of Obstetrics and Gynecology,  
Kaplan Medical Center  
Rehovot, Israel

**Gianpiero D. Palermo, MD PhD**

Weill Cornell Medicine, The Ronald O. Perelman  
and Claudia Cohen Center for Reproductive Medicine  
New York, NY, USA  
[gdpalerm@med.cornell.edu](mailto:gdpalerm@med.cornell.edu)

**Pasquale Patrizio, MD, MBE, HCLD**

Department of Obstetrics, Gynecology and  
Reproductive Sciences  
Yale University School of Medicine, Yale Fertility Center  
New Haven, CT, USA  
[pasquale.patrizio@yale.edu](mailto:pasquale.patrizio@yale.edu)

**Nigel Pereira, MD**

Weill Cornell Medicine, The Ronald O. Perelman  
and Claudia Cohen Center for Reproductive Medicine  
New York, NY, USA  
[nip9060@med.cornell.edu](mailto:nip9060@med.cornell.edu)

**Sonia Pérez Albalá**

IVF Laboratory, IVI Valencia  
Valencia, Spain

**Anthony C. F. Perry, BSc, PhD**

Laboratory of Mammalian Molecular Embryology,  
Centre for Regenerative Medicine  
University of Bath, Bath, UK

Department of Biology and Biochemistry  
University of Bath, Bath, UK  
[perry135@aol.com](mailto:perry135@aol.com)

**Adrienne K. Pope, PhD**

Adrienne Pope Consulting  
Brisbane, QLD, Australia  
[apopeconsulting@gmail.com](mailto:apopeconsulting@gmail.com)

**Catherine Pretty, BSc (bons), PhD**

Nuffield Health, Woking Hospital,  
Assisted Conception Unit  
Woking, UK  
[catherine.pretty@gmail.com](mailto:catherine.pretty@gmail.com)

**Catherine Racowsky, PhD**

Brigham and Women's Hospital, Obstetrics, Genecology,  
and Reproductive Biology  
Boston, MA, USA  
[cracowsky@partners.org](mailto:cracowsky@partners.org)

**Gohar Rahimi, MD**

University Maternal Hospital  
Department of Obstetrics and Gynecology,  
Cologne University  
Cologne, Germany

**Vanesa Y. Rawe**

REPROTEC, Diagnóstico y Tratamiento Reproductivo  
Buenos Aires, Argentina

**Michael L. Reed, PhD**

Fertility Center of New Mexico  
Albuquerque, NM, USA  
[mleeroyreed@gmail.com](mailto:mleeroyreed@gmail.com)

**Philipp Reineck, PhD**

ARC Centre of Excellence for Nanoscale BioPhotonics  
(CNBP), School of Science, RMIT University  
Melbourne, VIC, Australia  
[philipp.reineck@rmit.edu.au](mailto:philipp.reineck@rmit.edu.au)

**Don Rieger, BSc, PhD**

LifeGlobal LLC, Research and Development  
Guelph, ON, Canada  
[DonRieger@LifeGlobal.com](mailto:DonRieger@LifeGlobal.com)

**Laura Francesca Rienzi, BSc, MSc**

G.E.N.E.R.A. Centre for Reproductive Medicine  
of Valle Giulia Clinic  
Rome, Italy  
[rienzi@generaroma.it](mailto:rienzi@generaroma.it)

**Rocio Rivera-Egea, MSc**

Andrology Laboratory and Sperm Bank, IVIRMA Valencia  
Valencia, Spain  
[Rocio.Rivera@ivi.es](mailto:Rocio.Rivera@ivi.es)

**Zev Rosenwaks, MD**

Weill Cornell Medicine, The Ronald O. Perelman  
and Claudia Cohen Center for Reproductive Medicine  
New York, NY, USA  
[zrosenw@med.cornell.edu](mailto:zrosenw@med.cornell.edu)

**Tammie Roy, PhD**

Genea Biomedx  
Sydney, NSW, Australia  
[tammie.roy@geneabiomedx.com](mailto:tammie.roy@geneabiomedx.com)

**Amparo Ruiz, MD**

IVI Valencia, Insitituto Valenciano De  
Infertilidad (IVI Valencia)  
Valencia, Spain  
[Amparo.Ruiz@ivi.es](mailto:Amparo.Ruiz@ivi.es)

**Thamara Viloria Samochin, Phd MSc**

IVF Laboratory, Instituto Universitario IVI Valencia  
Valencia, Spain  
[thamara.viloria@ivi.es](mailto:thamara.viloria@ivi.es)

**Raul Sanchez, MD**

Department of Preclinical Science  
Faculty of Medicine, Universidad de La Frontera  
Temuco, Chile

**Sarthak Sawarkar**

MedAnswers, University of Kent  
Canterbury, UK  
[Sarthak.Sawarkar@coopergenomics.com](mailto:Sarthak.Sawarkar@coopergenomics.com)

**Heide Schatten, PhD**

Department of Veterinary Pathobiology  
University of Missouri-Columbia  
Columbia, MO, USA  
[SchattenH@missouri.edu](mailto:SchattenH@missouri.edu)

**Tim Schimmel, BA**

Cooper Surgical  
New York, NY, USA

**Manesh Kumar Panner Selvam, PhD**

American Center for Reproductive Medicine,  
Cleveland Clinic  
Cleveland, OH, USA

**Bruce S. Shapiro, MD PhD**

Fertility Center of Las Vegas  
Las Vegas, NV, USA  
[bsshapiro@aol.com](mailto:bsshapiro@aol.com)

**Rakesh Sharma, PhD**

Department of Urology and American Center  
for Reproductive Medicine  
Cleveland Clinic  
Cleveland, OH, USA  
[sharmar@ccf.org](mailto:sharmar@ccf.org)

**Shehua Shen, MD**

Hernest Institute for Reproductive Medicine  
Sunnyvale, CA, USA  
[shehuashen@gmail.com](mailto:shehuashen@gmail.com)  
[shen.shehua@hernest.com](http://shen.shehua@hernest.com)

**Zeev Shoham, MD**

The IVF, Infertility and Reproductive Medicine Unit,  
Department of Obstetrics and Gynecology,  
Kaplan Medical Center  
Rehovot, Israel  
[zeev1@mail.huji.ac.il](mailto:zeev1@mail.huji.ac.il)

**Sherman Silber, MD**

Infertility Center of St. Louis  
St. Louis, MO, USA

**Sankalp Singh, MD**

CRAFT Hospital and Research Centre  
Kodungalloor, Kerala, India  
[sankalp489@gmail.com](mailto:sankalp489@gmail.com)

**Charalampos S. Siristatidis, MD**

Assisted Reproduction Unit  
"Attikon" Hospital, Medical School,  
National and Kapodistrian University of Athens  
Athens, Greece  
[harrysiri@yahoo.gr](mailto:harrysiri@yahoo.gr)

**Cecilia Sjoblom, MSc, PhD**

Westmead Fertility Centre  
Institute of Reproductive Medicine, University of Sydney  
Westmead, NSW, Australia  
[cecilia.sjoblom@sydney.edu.au](mailto:cecilia.sjoblom@sydney.edu.au)

**Danielle G. Smith, PhD**

Leeds Institute of Molecular Medicine,  
University of Leeds, St James's University Hospital  
Leeds, UK

**Gary D. Smith, PhD**

Departments of Obstetrics and Gynecology, Physiology,  
and Urology, University of Michigan  
Ann Arbor, MI, USA  
[smithgd@med.umich.edu](mailto:smithgd@med.umich.edu)

**James J. Stachecki, PhD**

Innovative Cryo Enterprises LLC  
Linden, NJ, USA  
[jstachecki@gmail.com](mailto:jstachecki@gmail.com)

**James Stanger, PhD**

FertAid Pty Ltd  
Newcastle, NSW, Australia  
[office@fertaid.com](mailto:office@fertaid.com)

**Astrid Stecher**

NextClinic IVF Centers. Prof. Zech  
Bregenz, Austria

**Karl Sterzik, MD**

Department of Reproductive Medicine  
Christian-Lauritzen Institute, Ulm, Germany

**Roger G. Sturme, MD**

Centre for Cardiovascular and Metabolic Research  
Hull York Medical School, University of Hull,  
Hertford Building  
Hull, UK  
[rgs102@york.ac.uk](mailto:rgs102@york.ac.uk)

**Qing-Yuan Sun, PhD**

State Key Laboratory of Stem Cell  
and Reproductive Biology  
Institute of Zoology, Chinese Academy of Sciences  
Beijing, China

**Arne Sunde, PhD**

Department of Clinical and Molecular Medicine  
Norwegian University of Science and Technology  
Trondheim, Norway  
[Trondheimivf@gmail.com](mailto:Trondheimivf@gmail.com)

**Jason E. Swain, PhD, HCLD**

CCRM IVF Network  
Lone Tree, CO, USA  
[jswain@ccrmivf.com](mailto:jswain@ccrmivf.com)

**Lei Tan, PhD**

Celmatix, Inc.,  
New York, NY, USA  
  
Hernest Institute for Reproductive Medicine  
Sunnyvale, CA, USA  
[ltan0729@gmail.com](mailto:ltan0729@gmail.com)

**Jeremy G. Thompson, CNBP**

ARC Centre of Excellence for Nanoscale BioPhotonics (CNBP)  
The Robinson Research Institute, Adelaide Medical  
School, The University of Adelaide  
Adelaide, SA, Australia  
[jeremy.thompson@adelaide.edu.au](mailto:jeremy.thompson@adelaide.edu.au)

**Alan R. Thornhill, PhD HCLD**

Department of Gynaecology and Genetics Centre  
The London Bridge Fertility  
London, UK  
[arthornhill@aol.com](mailto:arthornhill@aol.com)

**Akansha Tiwari, MD MSc**

Yale University School of Medicine,  
Obstetrics and Gynecology  
New Haven, CT, USA  
[akansha.tiwari@yale.edu](mailto:akansha.tiwari@yale.edu)

**Giles Tomkin, PhD**

Althea Science and IVFqc  
ART Institute of Washington  
New York, NY, USA

**Maria Traversa, BSc, Msc, (MED)**

Sydney IVF  
Sydney, NSW, Australia

**Michael J. Tucker, PhD**

Shady Grove Fertility, IVF  
Rockville, MD, USA  
[mtucker@ivf.com](mailto:mtucker@ivf.com)

**Filippo Maria Ubaldi, MD**

G.E.N.E.R.A. Centre for Reproductive  
Medicine of Valle Giulia Clinic  
Rome, Italy  
[ubaldi@generaroma.it](mailto:ubaldi@generaroma.it)

**Jonathan Van Blerkom, MD**

Department of Molecular, Cellular and  
Developmental Biology  
University of Colorado  
Boulder, CO, USA

Colorado Reproductive Endocrinology  
Rose Medical Center  
Denver, CO, USA  
[jonathan.vanblerkom@colorado.edu](mailto:jonathan.vanblerkom@colorado.edu)

**Pierre Vanderzwalmen, Bio-Eng**

IVF Center CHIREC  
Braine l'Alleud-Waterloo, Belgium  
  
NextClinic IVF Centers. Prof. Zech  
Bregenz, Austria  
[pierrevdz@hotmail.com](mailto:pierrevdz@hotmail.com)

**Sabine Vanderzwalmen**

IVF Center CHIREC  
Braine l'Alleud-Waterloo, Belgium

**Anne Vansteenbrugge**

IVF Center CHIREC  
Braine l'Alleud-Waterloo, Belgium

**Alex C. Varghese, PhD**

Astra Fertility Group  
Mississauga, ON, Canada  
[alexcv2008@gmail.com](mailto:alexcv2008@gmail.com)

**Sidney Verza Jr, MSc**

ANDROFERT, Andrology & Human Reproduction Clinic,  
Referral Center for Male Infertility  
Campinas, SP, Brazil  
[labfiv@androfert.com.br](mailto:labfiv@androfert.com.br)

**Ling Wang, BSc**

Center for Reproductive Medicine  
Shanghai 10th People's Hospital of Tongji University  
Shanghai, China

**Leslie Weikert, BSc**

A.R.T. Institute of Washington, Inc.  
Rockville, MD, USA

A.R.T. Institute of Washington, Inc.,  
Rockville, MD, USA  
[leslieweikert@gmail.com](mailto:leslieweikert@gmail.com)

**Klaus E. Wiemer, PhD**

Poma Fertility  
Kirkland, WA, USA  
[kewiemer@comcast.net](mailto:kewiemer@comcast.net)  
[kwiemer@pomafertility.com](mailto:kwiemer@pomafertility.com)

**Matts Wikland, PhD**

Department of Obstetrics and Gynecology  
University of Gothenburg  
Gothenburg, Sweden

**Barbara Wirleitner, MSc, PhD**

IVF Centers Prof. Zech, IVF Laboratory  
Bregenz, Austria

**Graham Wright, PhD**

Reproductive Biology Associates  
Atlanta, GA, USA

**Wolfgang Würfel, MD**

KCM (Kinderwunsch Centrum München) –  
Fertility Center Munich  
Munich, Germany  
[prof.w.wuerfel@ivf-muenchen.de](mailto:prof.w.wuerfel@ivf-muenchen.de)

**Liyang Yan**

Department of Obstetrics and Gynecology  
Peking University Third Hospital  
Beijing, China

**Zhi-Yong Yang, MD**

Center for Reproductive Medicine  
Shanghai 10th People's Hospital of Tongji University  
Shanghai, China

**Marc Yeste, PhD**

Department of Biology, Unit of Cell Biology,  
Faculty of Sciences, University of Girona  
Girona, Spain  
[marc.yeste@udg.edu](mailto:marc.yeste@udg.edu)

**Peng Yuan, PhD**

Department of Obstetrics and Gynecology  
Peking University Third Hospital  
Beijing, China

# Abbreviations

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<b>ART</b>	Assisted reproduction technology	<b>ICM</b>	Inner cell mass
<b>DOHaD</b>	Developmental Origins of Health and Disease	<b>ICSI</b>	Intracytoplasmic sperm injection
<b>FET</b>	Frozen embryo transfer	<b>IVC</b>	In vitro culture
<b>GM-CSF</b>	Granulocyte-macrophage colony-stimulating factor	<b>IVF</b>	In vitro fertilization
<b>hsA</b>	Human serum albumin	<b>LGA</b>	Large for gestational age
<b>HTF</b>	Human tubal fluid	<b>TE</b>	Trophectoderm
		<b>VOC</b>	Volatile organic compounds