



# ISFP

April 2012  
Volume 1 Issue 3

International Society for Fertility Preservation, 3901 Rainbow Blvd., Kansas City, KS 66160-7316  
<http://www.isfp-fertility.org/>, (913) 588-6201

## Letter from the Editors

### INSIDE THIS ISSUE

- 1 Letter from the Editors
- 2 Harvesting & Harnessing Ovarian Stem Cells
- 4 ISFP Practice Committee Recommendations
- 5 Latest in Books
- 6 Newsletter Submissions

---

*Every woman deserves  
the chance.*

---

Hello everyone,

This issue of the ISFP Newsletter features:

- A special editorial summarizing the recent publication reporting the isolation and identification of oocyte-producing germline stem cells. These experts also include a discussion on the clinical implications of these findings for fertility preservation.
- A report on "Recommendations for fertility preservation" developed by ISFP Practice Committee
- Announcements of new books, one recently published from the Moffitt Cancer Center on reproductive health issues for adolescent and young adult patients, and a manual of in vitro fertilization edited by ISFP Board member, Zsolt Peter Nagy.

We hope you take the time to peruse these important items to stay up-to-date on the most recent information in the field.

We welcome your submissions to the newsletter and your suggestions for topics of interest.

*Mary Zelinski, Ph.D.  
Sam Kim, M.D.*

## Harvesting and harnessing ovarian stem cells – is clinical application within reach?

Evelyn E Telfer<sup>1</sup> and David F Albertini<sup>2</sup>

<sup>1</sup>Institute of Cell Biology and Centre for Integrative Physiology. The University of Edinburgh, Edinburgh U.K.  
email: [Evelyn.Telfer@ed.ac.uk](mailto:Evelyn.Telfer@ed.ac.uk)

<sup>2</sup>Institute for Reproductive Health and Regenerative Medicine, Center for Reproductive Sciences, University of Kansas Medical Center, Kansas City, Kansas U.S.A email: [dalbertini@kumc.edu](mailto:dalbertini@kumc.edu)

It is a major tenet of, and a hopeful goal for, the evolving field of fertility preservation that restoring ovarian function in women lacking oocytes as a result of genetic or iatrogenic germ cell depletion could someday be achieved with safe and efficacious therapeutic management. The central problem reduces to a matter of either retaining functionality of a pre-existing population of follicles or restoring follicles in an ovary equivalent from the emergent toolkit of regenerative medicine. Stem cell biology looms heavily in the latter prospect and would be a welcomed alternative if brought within reach of a clinically tractable strategy. An important step in this direction has recently been announced.

A recent paper in Nature Medicine<sup>1</sup> from the Tilly group at Massachusetts General Hospital reports the isolation and identification of oocyte-producing germline stem cells [oogonial stem cells (OSC)] from ovaries of adult mice and humans. Some of these cells appear capable of forming oocyte like cells that take residence in follicle-like structures under specific *in vitro* and *in vivo* conditions<sup>1</sup>. The isolation of such rare cells from adult human ovaries makes this work significant in a biological context, offering a model to study the earliest stages of human oocyte development. It may also have important clinical implications for the field of fertility preservation.

The existence and physiological significance of mammalian female germ line stem cells has been a highly contentious area in the field of reproductive biology<sup>2,3,4</sup>. Over and above the fact that the mammalian ovary is a dynamic and regenerative organ during the reproductive lifespan of mammals, constantly requiring the birth and differentiation of an array of somatic cell types, the oocyte population, in contrast, is widely believed to be finite and incapable of *de novo* restoration. In fact, the premise for age-related ovarian failure and menopause occur takes origin in the belief that the mammalian ovary is unable to replenish the oocyte stockpile endowed at birth, and as a result there is a progressive and irreversible decline in follicle numbers until the pool is exhausted at some point during adult life<sup>5</sup>.

## Ovarian stem cells (continued)

Earlier studies by Zou *et.al* hinted at the presence of an extractable population of oocyte progenitor stem cells in mice<sup>6</sup> based on a magnetic cell sorting method that prompted criticism aimed at the reagents used for cell isolation. Tilly's group has improved this methodology and clarified the biomarker selection strategy in developing a purification scheme for these rare but potential oocyte progenitors from both adult mouse and human ovaries<sup>1</sup>. This study provides multiple lines of evidence demonstrating the existence of a rare population of cells within adult ovaries that divide mitotically *in vitro* and form cells expressing markers consistent with a germ line identity and yet distinct from pluripotent stem cells. Beyond the technological improvements for optimizing the isolation of these rare cells, the work details appropriate *in vitro* and *in vivo* conditions under which the production of oocytes capable of fertilisation and early embryonic development from mouse and the formation of "oocyte-like" cells in the human ovary can be achieved.

Some of the previous criticisms aimed at the demonstration of proliferative, meiosis-entry, follicle formation, and embryo generation capabilities of purported stem cells have been addressed in an albeit broad and evocative data sets linking molecular and developmental manifestations of what appear to be oocytes with a credible identity. The study represents a major breakthrough in identifying cells with apparent germ line potential in both mouse and human ovary. Despite being an accomplishment of measurable proportions, many challenges remain including independent verification before a practical and convincing demonstration of developmental potential of the oocyte-like structures derived from human cells is obtained. Clearly these "oocyte-like" cells that form from the progenitor population *in vitro* require somatic cell support to form follicles and develop into functional oocytes. Melding the use of these cells with conventional human ovarian culture models<sup>8</sup> may improve the incidence of follicle reassembly and growth enabling a more detailed analysis and genetic testing of any resulting oocytes<sup>9</sup>.

Whilst this work represents an advance with the potential to change the face of infertility treatments in the future, many practical and conceptual obstacles remain before clinical utility could be realised. Much effort can be anticipated towards improving the efficiency of isolation and transformation into oocytes and a more detailed characterisation of genetic, epigenetic, and developmental integrity is fully warranted if clinical application is to materialize over the coming years.

Questions remain as to the meiotic competence of these cells and whether they acquire and/or manifest germ line status after activation *in vitro* or during *de novo* neo-oogenesis *in vivo*. Much experimentation is required before these questions will be fully answered. However, the results reported in this paper should change the tone of future discourse towards measured enthusiasm and most importantly prompt speculation and tempered progress into what remains a nearly intractable and significant obstacle in the treatment of various forms of human infertility<sup>10</sup>.

## Ovarian stem cells (continued)

- 1 White YR, Woods DC, Takae, M, Ishihara O, Seki H, Tilly JL. Oocyte formation by mitotically-active germ cells purified from ovaries of reproductive age women. (2012) *Nature Medicine* 18: 413-421.
- 2 Johnson J, Canning J, Kaneko T, Pru JK, Tilly JL. Germline stem cells and follicular renewal in the postnatal mammalian ovary. (2004) *Nature* 428: 145–150.
- 3 Telfer EE, Gosden RG, Byskov AG, Spears N, Albertini D, Andersen CY, Anderson R, Braw-Tal R, Clarke H, Gougeon A, McLaughlin E, McLaren A, McNatty K, Schatten G, Silber S, Tsafirri A. On regenerating the ovary and generating controversy. (2005) *Cell* 122: 821–822.
- 4 Tilly JL, Niikura Y, Rueda BR. The current status of evidence for and against postnatal oogenesis in mammals: a case of ovarian optimism versus pessimism? (2009) *Biol Reprod* 80: 2–12.
- 5 Faddy MJ, Gosden RG, Gougeon A, Richardson SJ, Nelson JF. Accelerated disappearance of ovarian follicles in mid-life: implications for forecasting menopause. (1992) *Hum Reprod* 7: 1342–1346.
- 6 Zou K, Yuan Z, Yang Z, Luo H, Sun K, Zhou L, Xiang J, Shi L, Yu Q, Zhang Y, Hou R, Wu J. Production of offspring from a germline stem cell line derived from neonatal ovaries. (2009) *Nat Cell Biol* 11: 631–636.
- 7 Tilly JL and Telfer EE Purification of germline stem cells from adult mammalian ovaries: a step closer towards control of the female biological clock? (2009) *Mol Hum Reprod*. 15(7): 393–398.
- 8 Telfer EE, McLaughlin M, Ding C, Thong KJ. A two-step serum-free culture system supports development of human oocytes from primordial follicles in the presence of activin. (2008) *Hum Reprod* 23: 1151–1158.
- 9 Rodrigues P, Limback D, McGinnis LK, Plancha CE, Albertini DF Oogenesis: Prospects and challenges for the future. (2008) *J.Cell Physiol* 216: 355-365
- 10 Telfer EE and Albertini DF. The quest for human ovarian stem cells. (2012) *Nature Medicine* 18: 353-354.

## Recommendations For Fertility Preservation

Recommendations for fertility preservation have been developed by the ISFP Practice Committee. These recommendations will be published in June 2012 in the *Journal of Assisted Reproduction and Genetics*. As soon as the link is available we will send an email with that information to the membership.

## Books in the News

### Moffitt Cancer Center Researchers Publish Book on Reproductive Health and Cancer in Adolescents and Young Adults

*Text examines advances in the experimental medicine and biology*

**TAMPA, Fla. (Jan. 26, 2012)** – Advances in treatment, screening and early diagnosis of cancer have turned a historically fatal diagnosis for children and adolescents into an 80 percent survival rate. The increase in adolescent and young adult (AYA) cancer survivors during the past 40 years demands a critical examination of the quality-of-life issues in survivorship, including fertility preservation and other reproductive health issues. This newly released book from Springer Press, "[Reproductive Health and Cancer in Adolescents and Young Adults](#)," by [Gwendolyn Quinn](#), Ph.D., and [Susan Vadaparampil](#), Ph.D., analyzes the advances in reproductive health and fertility preservation options available to AYA oncology patients.

Based on the increasing availability of fertility preservation options and ethical guidelines of approaching AYA patients, this critical quality-of-life issue must be integrated into the overall AYA patient care. The authors provide an extensive review of the impact of cancer on reproductive health and options for maintaining reproductive health as a means of disseminating and raising awareness for these significant issues.

Brad Zebrack, associate professor of social work at the University of Michigan and cancer survivor, noted that "as a researcher and advocate whose work focuses on the quality of life for cancer survivors and their loved ones, I feel that this text is an invaluable educational resource that targets unique needs and issues faced by young adults fighting cancer during their reproductive years."

For more information on the book, please contact Nicole Hutchins at (813) 745-6941 or [Nicole.Hutchins@moffitt.org](mailto:Nicole.Hutchins@moffitt.org). The book can be purchased at <http://www.amazon.com/Reproductive-Adolescents-Advances-Experimental-Medicine/dp/9400724918>.

#### About Moffitt Cancer Center

Follow Moffitt on Facebook: [www.facebook.com/MoffittCancerCenter](http://www.facebook.com/MoffittCancerCenter)

Follow Moffitt on Twitter: [@MoffittNews](https://twitter.com/MoffittNews)

Follow Moffitt on YouTube: [MoffittNews](http://www.youtube.com/MoffittNews)



**Reproductive Health and Cancer in Adolescents and Young Adult**

**Series: Advances in Experimental Medicine and Biology, Vol. 732**

**Quinn, Gwendolyn P.; Vadaparampil, Susan T. (Eds.)**

**2012, 2012, XV, 220 p. 8 illus.**

**Hardcover, ISBN 978-94-007-2491-4**

#### ABOUT THIS BOOK

- Summarizes the latest research in this field
- Each chapter written by expert in the field
- Covers broad array of reproductive health issues
- Unique population of AYA (adolescent and young adult)
- Each chapter has vignette and list of recommendation for providers

Reproductive medicine is a growing field with new technology emerging faster than we can assess consumer's perceptions of –the number of cancer survivors are growing and there is a great need to attend to their quality of life–this book addresses the needs of males and females, identifies effective communication strategies and proactive measures for health care professionals and researchers to use as well as identifying gaps in the literature where more research is needed.

## Books in the News



### Practical Manual of In Vitro Fertilization

Nagy, Zsolt Peter; Varghese, Alex C.; Agarwal, Ashok (Eds.)

2012, 2012, XVIII, 842 p. 139 illus., 104 in color.

Hardcover, ISBN 978-1-4419-1779-9

Due: April 30, 2012

#### ABOUT THIS BOOK

- Unique, practical manual for day-to-day use in clinic and laboratory
- Written by a team of international experts in the field of human reproduction
- Discusses all current and commonly used techniques as well as the majority of novel, promising procedures
- Provides overview of novel technologies still in the developmental stage

The *Practical Manual of In Vitro Fertilization: Advanced Methods and Novel Devices* is a unique, accessible title that provides a complete review of the most well-established and current diagnostic and treatment techniques comprising in vitro fertilization. Throughout the chapters, a uniform structure is employed, including a brief abstract, a keyword glossary, a step-by-step protocol of the laboratory procedures, several pages of expert commentary, key issues of clinical concern, and a list of references. The result is a readily accessible, high quality reference guide for reproductive endocrinologists, urologists, embryologists, biologists and research scientists. The Manual also offers an excellent description of novel procedures that will likely be employed in the near future. An indispensable resource for physicians and basic scientists, the *Practical Manual of In Vitro Fertilization: Advanced Methods and Novel Devices* is an invaluable reference and addition to the literature.

## Newsletter Submissions

#### Instructions for submissions

**Deadline for Submissions** : The 1<sup>st</sup> of the month prior to the next issue: (December 1, March 1, June 1 and September 1).

**Submissions**: ≤ 6 pages, double-spaced; consist of a concise summary of new findings and future directions; avoid extensive review of past literature; include relevant peer-reviewed references. Submissions will be reviewed by the President of the ISFP and the Editor for content and accuracy.

**Editorials**: ≤ 2 pages, double-spaced; clear statement of position and sources to support this position; employ insight, diplomacy and respect; inflammatory statements will not be allowed.

**Send to**: Mary Zelinski at [zelinski@ohsu.edu](mailto:zelinski@ohsu.edu)

International Society for Fertility Preservation  
3901 Rainbow Boulevard  
Department of Ob/Gyn  
Kansas City, KS 66160-7316

Phone: (913) 588-6201 Fax: (913) 588-6271

E-mail: [info@isfp-fertility.org](mailto:info@isfp-fertility.org) or nturner@kumc.edu

