

ROYAN INSTITUTE

THE NINETEENTH
ROYAN
INTERNATIONAL
RESEARCH AWARD

Reproductive Biomedicine & Stem Cell



AUGUST 2018

TEHRAN - IRAN



THE 20th ROYAN

INTERNATIONAL RESEARCH AWARD

TEHRAN - IRAN

DEADLINE FOR **APPLICATION**: 20 APRIL 2019

2019 KAZEMI PRIZE

In commemoration of Dr Kazemi,
the late founder of Royan Institute



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In the Name of

GOD

The Nineteenth

ROYAN

INTERNATIONAL RESEARCH AWARD



Dr Saeid Kazemi Ashtiani
The Late Founder of ROYAN Institute



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Neuronal Projections of
Human Embryonic Stem
Cell-derived Neural Cells

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FOREWORD



Hamid Reza Tayyebi, PhD, Eng
President of ACECR

The scientific progress of Islamic Republic of Iran, has drawn the attention of the world in recent years. The Academic Centre of Education, Culture and Research (ACECR) has paid special care to science production and technology development since its establishment in 1980, so that all human beings can enjoy the benefits of the scientists' endeavors. During almost four decades of ACECR's activity, it has focused on Reproductive Biomedicine, Stem Cell Biology and Technology, Regenerative Medicine, Biotechnology, Cancer Biology, and Herbal Medicine and has turned them into health services. In this regard, Royan Institute is one of the successful centers which has gained a national and international top rank for its unparalleled achievements.

Coming along with the innovative and hardworking scientists, establishing effective scientific collaborations via International Awards and Congresses is one of the most important factors of success at Royan Institute. Some of the previous participants have described these events by releasing essays in the journals, and some have written articles on their collaborative projects with Royan Institute. I hope the 19th Royan International Research Award can draw outlines in fields of Reproductive Biomedicine and Stem Cell Biology and Technology towards scientific society.

As the president of ACECR, I want to revive the memory of The Late founder of Royan Institute; Dr Saeid Kazemi Ashtiani who established Royan International Research Award, and express my appreciation to my colleagues in Royan Institute for their tremendous efforts in holding this prestigious Award as well as all scientists from all around the world who help us to evaluate the projects. I also want to deliver my special thanks to Dr Hamid Gourabi; previous president of Royan Institute, who conducted previous twelve Awards at high international levels. I express my sincere congratulation to Award winners and hope them success in all aspects of life. I also wish we could continue such a scientific event in the years to come.



INTRODUCTION

Abdolhossein Shahverdi, PhD

Award Chairman and
Royan Institute President



It is the final lap of our journey and we are about to wrap up the 19th Royan International Research Award (RIRA) in Regenerative Biomedicine and Stem Cells.

I would like to extend my heart felt gratitude to all who exerted utmost efforts to hold 19th RIRA in order to evaluate 191 submitted research papers from 38 countries. The success of this event is a reflection of dedication, passionate commitment and all-out devotion of scientists, researchers, jury committee members, executive committee and sponsors in ensuring the 19th RIRA success.

On behalf of all my colleagues in Royan Research Institute, I do hereby thank Dr Hamid Gourabi; well-deserved and competent successor of the late Dr Kazemi Ashtiani whose leadership capabilities paved the way of success, removed or diluted predicaments and opened new and bright horizon for future roadmaps of Royan Institute. Dr Gourabi could turn the former director's wishes and ideas into enduring reality. AT present, I, as the president of this prestigious and renowned research institute feel heavy responsibility to preserve the legacy of these two eminent and committed persons and provide necessary conditions for its flourishing.

In the world of science the means of communication is mutual understanding beyond nation, race and beliefs. This language mitigate the barriers that inhibit the cooperation and is the herald of friendship, mutual understanding, respect and love regardless of political insights and variety of notions. Royans' mission is to communicate with this language and to be the harbinger of friendship throughout the world. RIRA message is conveyed by using this language and I hope all participants disseminate Royans' amicable and friendly language in their own cities, countries and scientific communities.

As the final hours are looming, we think a little bit differently than we waked in, we identified some potential areas for concerted actions and recognized issues and bottlenecks about which we need to think far harder and much longer. I think our findings cast patches of light onto the darkness of ambiguities and uncertainties. This spark of hope makes our hearts imbued with joy and happiness. In this way our vision is ascertained.

The fruition of each gathering is the cooperation of those who actively engaged. This collaborations can be at academic level, joint publication, join projects and formal agreement among institutions. Royan Research institute extends its hand for cooperation and is open for new suggestions.



Royan Awards



Royan International Research Award was founded by the late director of Royan Institute, Dr Saeid Kazemi Ashtiani with the aim of encouraging researchers, appreciating their efforts and preparing a friendly scientific atmosphere for them to exchange their knowledge and experiences. Kazemi had wonderful ideas to bring researchers together and motivate them to increase their efforts and perform high level researches via this research award. Royan's staff lost their beloved director in January 2006 by heart attack, May he rest in peace.

This annual award is extending into a higher quality event every year, increasing the scientific level and number of the submitted papers. The research papers are evaluated through an intense jury procedure by Award's national and international Jury board to whom our special thanks goes. Each year the prominent researches with outstanding help in solving problems in reproduction and stem cell fields, are announced, appreciated and rewarded.

As comparing the researches in different fields is very difficult and finding the best researches with variations in methods, implements and results is almost impossible, from the eighth award the same prizes are distributed among winners in different fields of reproductive biomedicine and stem cell such as: female infertility, epidemiology, ethics, andrology, embryology, reproductive imaging, reproductive genetics, stem cell biology and technology, regenerative medicine, and biotechnology.

Nomination and Selection Procedure of Award

The submitted research articles are categorized according to ten scientific groups: female infertility, reproductive genetics, epidemiology, ethics, embryology, andrology, reproductive imaging, stem cell biology and technology, regenerative medicine and biotechnology. Each article is ranked according to its relevancy, impact factor, and an innovation score.

After the articles are sorted, each scientific group selects their nominees and sends them to national and international referees for evaluation.

Each referee evaluates the research articles related to his/her field of interest, qualitatively in Likert scale according to these norms:

- Relevancy to the award subjects
- Creativity and innovation
- Methodology and research design
- Problem solving
- Applicability on human

Evaluation of the articles by the juries is discussed in the board of juries and their decisions get approved by scientific board of the institute. Finally, international and national winners are selected and invited to present their researches in Royan twin congress on Reproductive Biomedicine and Stem Cell Biology and Technology which is held almost in August/September every year and receive their prizes in prize award ceremony.

Note: It is obligatory for the winners to attend the ceremony and present their research articles in the congress.



The
First
ROYAN
 International Research Award
 Reproductive Biomedicine & Stem Cell



September

2000

International Winners:

- **First Place: Mohamed Mitwally, Canada**
 Comparison of an Aromatase Inhibitor with Clomiphene Citrate for Induction of Ovulation
- **Second Place: Ali Ahmady, Canada**
 Cell and Molecular Investigation of the Fertilizing Ability of Dead Sperm
- **Third Place: Weihau Wang, USA**
 Spindle Observation in Living Human Eggs with Pollaries Microscope and Its Use in Assisted Human Reproduction
- **Fourth Place: Simon Marina Avendano, Spain**
 HIV-Seropositive Can Be Fathers without Infecting the Women or Child
- **Fifth Place: Jaffar Ali, Qatar**
 Formulation of a Protein-Free Medium for Human Assisted Reproduction

Iranian Winners:

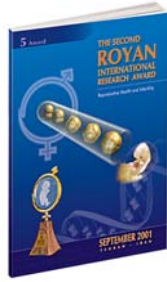
- **Mohammad Hossein Nasr-Esfahani**
 Sperm Chromatin Status and Male Infertility
- **Mahnaz Ashrafi**
 Effect of Metformin on Ovulation and Pregnancy Rate in Women with Clomiphene Resistant PCOS
- **Mohammad Ebrahim Parsanezhad**
 Section of the Cervical Septum Doesn't Impair Reproductive Outcome



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Received Papers: 72



The Second ROYAN

International Research Award
Reproductive Biomedicine & Stem Cell

September
2001

International Winners:

- **First Place: Ri-Cheng Chian, Canada**
A New Treatment for Women with Infertility Due to Polycystic Ovarian Syndrome: Immature Oocyte Retrieval Followed in-vitro Maturation
- **Second Place: Ma'asouma Makhseed, Kuwait**
The Possible Immunological Basis of Repeated Pregnancy Loss
- **Third Place: Esmail Behboodi, USA**
Production of Goats by Somatic Cell Nuclear Transfer
- **Fourth Place: Sayeed Unisa, India**
Reproductive, Demographic and Behavioral Causes of Infertility in India
- **Fifth Place: Ahmed Mohammed Saleh, Saudi Arabia**
Effect of Laparoscopic Ovarian Drilling on Serum Vascular Endothelial Growth Factor (VEGF), and on Insulin Response to Oral Glucose Tolerance Test in Women with PCOS

Iranian Winners:

- **Hossein Baharvand**
Improvement of Blastocyst Development in-vitro and Overcoming the Blastocyst Collapse and Its Effective Factor(s) in Sequential Culture Media
- **Marzieh Nojomi**
Epidemiology of Infertility in the West of Tehran 2000-2001
- **Gholamreza Pourmand**
Effect of Renal Transplantation on Sperm Quality and Sex Hormones Level



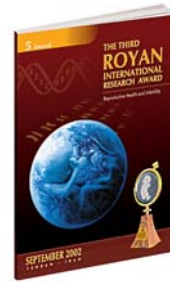
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Received Papers: 78



The
Third
ROYAN
 International Research Award
 Reproductive Biomedicine & Stem Cell



September **2002**

International Winners:

- **First Place: Marco Filicori, Italy**
 Novel Approaches to Ovulation Induction: The Critical Role of Luteinizing Hormone Activity in Regulating Folliculogenesis
- **Second Place: Klaus G. Steger, Canada**
 Influence of Histone-Prothmine-Exchange on Male Infertility
- **Third Place: Franck Pellestor, France**
 Chromosomal Investigations in Human Gametes: Study of the Interchromosomal Effect in Sperm of Chromosomal Rearrangement Carriers and Mechanisms of Non Disjunction in Oocytes
- **Fourth Place: Ghazala S. Basir, Hong Kong**
 The Effect of High Estradiol Levels on Endometrial Development in Assisted Reproduction Technology: Evaluation of Sonographic Doppler Haemodynamic and Morphometric Parameters
- **Fifth Place: Mohamed Ali Bedaiwy, USA**
 Transplantation of Intact Frozen-Thawed Mammalian Ovary with Vascular Anastomosis: A Novel Approach

Iranian Winners:

- **Saeed Alborzi**
 Laparoscopic Salpingoovulysis. Is There Any Place for Second Look Laparoscopy?
- **Saeed Rahbar**
 Laser Assisted Hatching in Young Women Significantly Increases Pregnancy and Implantation Rates
- **Shir Ahmad Sarani**
 Morphological Evidence for the Implantation Window in Human Luminal Endometrium
Special Winner in Reproductive Health

Special Winner:

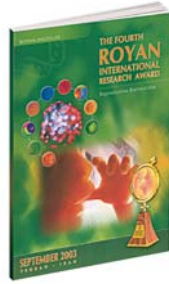
- **V. I. Sodestrom- Anttila, Finland**
 Embryo Donation-Outcome & Attitude Among Embryo Donors & Recipient



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Received Papers: 212



The Fourth ROYAN

International Research Award
Reproductive Biomedicine & Stem Cell

September
2003

International Winners:

- **First Place: Yong-Mahn Han**, South Korea
Abnormal Structural Integrity and Reprogramming in the Cloned Embryos
- **Second Place: Lucille E. Voullaire**, Australia
Chromosome Abnormality In Human Embryos Diagnosed Using Comparative Genomic Hybridization: Its Relationship to Infertility
- **Third Place: Mauro Maccarrone**, Italy
Low Fatty Acid Amide Hyrolase and Anandamide Levels Are Associated with Failure to Achieve an Ongoing Pregnancy after IVF and Embryo Transfer
- **Fourth Place: Ali Honaramooz**, USA
Sperm from Neonatal Mammalian Testes Grafted in Mice
- **Fifth Place: Jan M.R. Gerris**, Belgium
Elective Single Embryo Transfer Halves the Twinning Rate without Decrease in the Total Ongoing Pregnancy Rate of an AVF/ICSI Program



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Received Papers: 222

Iranian Winners:

- **Mohammad Ebrahim Parsanezhad**
Ovarian Stromal Blood Flow Changes After Laparoscopic Ovarian Cauterization in Women with Polycystic Ovary Syndrome
- **Mojdeh Salehnia**
Vitrification of Ovarian Tissue
- **Jaleh Zolghadri**
Successful Pregnancy Outcome with IUI in Patients with Unexplained Recurrent Miscarriage, Whose Male Partners Have Low Score Hypo-Osmotic Swelling Test



The
Fifth
ROYAN
International Research Award
Reproductive Biomedicine & Stem Cell



September

2004

International Winners:

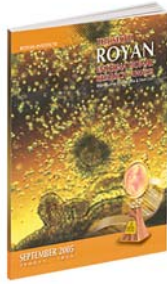
- **Second Place: Alfonso Guiterrez-Adan, Spain**
Long Term Effect of in vitro Culture of Mouse Embryos with Serum on mRNA Expression of Imprinting Genes, Development and Behavior
- **Second Place: Maciej K. Kurpisz, Poland**
Reactive Oxygen Species and "Male Factor" of Infertility
- **Third Place: Michel von Wolf, Germany**
Glucose Transporter Proteins (GLUT) in Human Endometrial-Expression, Regulation and Function through out the Menstrual Cycle and in Early Pregnancy
- **Fourth Place: Sophie Lambard, France**
Human Male Gamete Quality: Place of Aromatase and Estrogens
- **Fifth Place: Naojiro Minami, Japan**
A Novel Maternal Effect Gene, Oogenesis: Involvement in Zygotic Gene Activation and Early Embryonic Development in the Mouse

Iranian Winners:

- **Seyed Javad Mowla**
Catsper Gene Expression in Postnatal Development of Mouse Testis and in Subfertile Men with Deficient Sperm Motility
- **Mohammad A. Khalili**
Restoration of Spermatogenesis by Adenoviral Gene Transfer into Injured Spinal Cords of Rats
- **Mojdeh Salehnia**
Ultrastructural, Histochemical and Morphometric Studies of Mouse Reproductive Tract after Ovarian Induction

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Received Papers: 199



The
Sixth
ROYAN
International Research Award
Reproductive Biomedicine & Stem Cell

September
2005

International Winners:

- **First Place: Kathyjo Ann Jackson, USA**
Therapeutic potential of stem cells
- **Second Place: Carmen Belen Martinez-Madrid, Belgium**
Ficoll Density Gradient Method for Recovery of Isolated Human Ovarian Primordial Follicles
- **Third Place: Federico Alejandra Calegari, Germany**
Tissue-Specific Manipulating of Gene Expression of Mouse Embryos Using in Utero Electroporation
- **Fourth Place: Maryam Kabir-salmani, Japan**
Different Roles of $\alpha_5\beta_1$ and $\alpha_v\beta_3$ Integrins in the IGF-I-Induced Migration of the Human Extravillous Trophoblast Cells
- **Fifth Place: Zhenmin Lei, USA**
Testicular Phenotype in Luteinizing Hormone Knockout Animals and the Effect of Testosterone Replacement Therapy



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Iranian Winners:

- **Seyed Javad Mowla**
The Profile of Gene Expression Changes During the Neural Differentiation of Bone Marrow Stromal Cells (BMSCs)
- **Jaleh Zolghadri**
Pregnancy Outcome Following Laparoscopic Tubal Ligation of Hydrosalpinx Tube in Patients with Early Recurrent Abortion



Received Papers: 198



The Seventh ROYAN

International Research Award
Reproductive Biomedicine & Stem Cell



September
2006

International Winners:

- **First Place: James Affram Adjaye, Germany**
A) Whole-Genome Approaches for Large-Scale Gene Identification and Expression Analysis in Mammalian Preimplantation Embryos & B) Primary Differentiation in the Human Blastocyst: Comparative Molecular Portraits of Inner Cell Mass and Trophectoderm Cells
- **Second Place: Tian-hua Huang, China**
Detection and Expression of Hepatitis B Virus X Gene in One and Two-Cell Embryos from Golden Hamster Oocytes in-vitro Fertilized with Human Spermatozoa Carrying HBV DNA
- **Third Place: Adrian Richard Eley, UK**
Ooptosis of Ejaculated Human Sperm Is Induced by Co-Incubation with Chlamydia Trachomatis Lipopolysaccharide
- **Fourth Place: Lone Schmidt, Denmark**
Does Infertility Cause Marital Benefit? An Epidemiological Study of 2250 Women and Men in Fertility Treatment
- **Fifth Place: Louis Chukwuemeka Ajonuma, Hong Kong**
Molecular and Cellular Mechanisms Underlying Abnormal Fluid Formation in the Female Reproductive Tract: The Critical Role of Cystic Fibrosis Transmembrane Conductance Regulators

Iranian Winners:

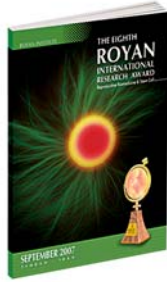
- **Mohammadreza Baghban Eslaminejad**
Polarized Culture Systems and Their Effects on Embryo Development
- **Mansoureh Movahedin**
New Approaches to Assess the Success and Enhance the Efficiency of Male Germ Cell Transplantation in the Mouse
- **Ashraf Alleyassin**
Comparison of Unilateral and Bilateral Transfer of Injected Oocytes into Fallopian Tubes: A Prospective Randomized Clinical Trial



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Received Papers: 221



The Eighth ROYAN

International Research Award
Reproductive Biomedicine & Stem Cell

September **2007**

International Winners:

Best research project in stem cell field

- **Chiba Shigeru**, Japan
Role of Notch Signaling in Normal and Neoplastic Hematopoietic Stem Cells and Clinical Application of Notch Signal Modifiers

Best research project in reproductive genetic field

- **Françoise Dantzer**, France
Poly (ADP-Ribose) Polymerase-2 Contributes to the Fidelity of Male Meiosis I and Spermiogenesis

Best research project in female infertility field

- **Seyed Mohammad Moazzeni**, Iran
Dendritic Cells and Pregnancy: A Bidirectional Relationship to Protect the Semiallogenic Fetus

Best research project in embryology field

- **Bjorn Johannes Oback**, New Zealand
Nuclear Donor Choice, Sperm Mediated Activation and Embryo Aggregation: A Multi-Pronged Approach to Sequentially Improve Cattle Cloning Efficacy

Best research project in andrology field

- **Reddanna Pallu**, India
Role of Cyclooxygenases in Male Reproduction

Iranian Winners:

- **Ramin Radpour**
Novel Mutations and (TG)M(T)N Polymorphism in Iranian Males with Congenital Bilateral Absence of the Vas Deferens
- **Mohammad Ebrahim Parsanezhad**
Hysteroscopic Metroplasty of the Complete Uterine Septum, Duplicate Cervix, and Vaginal Septum
- **Mehri Azadbakht**
Apoptosis in Mouse Embryos Co-Cultured with Polarized or Non-Polarized Uterine Epithelial Cells Using Sequential Culture Media



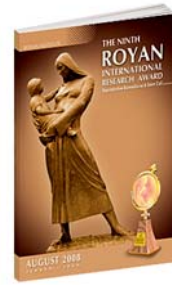
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Received Papers: 248



The
Ninth
ROYAN
 International Research Award
 Reproductive Biomedicine & Stem Cell



September **2008**

International Winners:

Best research project in stem cell field

- **Su-Chun Zhang, USA**
Human Embryonic Stem Cells As a Tool of Discovery

Best research project in reproductive genetic field

- **Smita Mahale, India**
Structural, Functional and Molecular Aspects of Follicle Stimulating Hormone Receptor: Applications in Designing Receptor Targets and Management of Female Infertility

Best research projects in female infertility field (share)

- **Federico Prefumo, Italy**
Uterine Doppler Investigations and Trophoblast Biology in Early Pregnancy
- **Saeed Alborzi, Iran**
Laparoscopic Metroplasty in Bicornuate and Didelphic Uterus

Best research project in embryology field

- **Leen.Vanhoutte, Belgium**
Nuclear and Cytoplasmic Maturation of in vitro Matured Human Oocytes After Temporary Nuclear Arrest by Phosphodiesterase 3-Inhibitor

Best research project in andrology field

- **T.O.Ogata, Japan**
Haplotype Analysis of the Estrogen Receptor Alpha Gene in Male Genital and Reproductive Abnormalities

Iranian Winners:

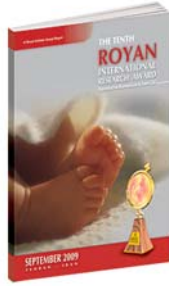
- **Ali Fathi**
The Molecular Mechanisms Controlling Embryonic Stem Cells (Escs) Proliferation and Differentiation
- **Fardin Fathi**
Characterizing Endothelial Cells Derived from the Murine Embryonic Stem Cell Line CCE



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Received Papers: 202



The
Tenth
ROYAN
International Research Award
Reproductive Biomedicine & Stem Cell

September
2009

International Winners:

Best research project in stem cell field

- **Yi Liu, China**
Dental Stem Cells-Based Tissue Regeneration in a Large Animal Model

Best research project in reproductive genetic field

- **Wai-sum OO, China**
Adrenomedullin in Male and Female Reproduction

Best research projects in female infertility field (share)

- **Sherman Silber, USA**
A Series of Monozygotic Twins Discordant for Ovarian Failure: Ovary Transplantation (Cortical versus Microvascular) and Cryopreservation
- **Melinda Halasz, Hungary**
What Harbours the Cradle of Life? The Progesterone-Dependent Immunomodulation

Best research project in embryology field

- **Geetanjali Sachdeva, India**
Molecular Assessment of the Uterine Milieu during Implantation Window in Humans and Non-human Primates

Best research project in andrology field

- **Paolo Chieffi, Italy**
PATZ1 Gene Has a Critical Role in the Spermatogenesis and Testicular Tumours

Iranian Winners:

- **Hossein Mozdarani**
Reduction of Induced Transgenerational Genomic Instability in Gametes Using Vitamins E and C, Observed As Chromosomal Aneuploidy and Micronuclei in Preimplantation Embryos
- **Seyed Javad Mowla**
OCT4 Spliced Variants Are Differentially Expressed in Human Pluripotent and Nonpluripotent Cells
- **Mohammad Reza Safarinejad**
Evidence Based Medicine on the Pharmacologic Management of Premature Ejaculation

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Received Papers: 253



The Eleventh ROYAN

International Research Award
Reproductive Biomedicine & Stem Cell



September

2010

International Winners:

Best research project in regenerative medicine field

- **Stefano Pluchino**, Italy
Human Neural Stem Cells Ameliorate Autoimmune Encephalomyelitis in Non-human Primates

Best research project in stem cell biology & technology field

- **Hooman Sadri-Ardekani**, Iran-The Netherlands
Propagation of Human Spermatogonial Stem Cells in vitro

Best research project in female infertility field

- **Louis Chukwuemeka Ajonuma**, Nigeria
New Insights into the Mechanisms Underlying Chlamydia Trachomatis Infection Induced Female Infertility

Best research project in reproductive genetic field

- **Anu Bashamboo**, France
Mutations in NR5A1 Associated with Ovarian Insufficiency

Best research project in embryology field

- **Mohammad Hossein Nasr-Esfahani**, Iran
New Era in Sperm Selection for ICSI Procedure

Iranian Winners:

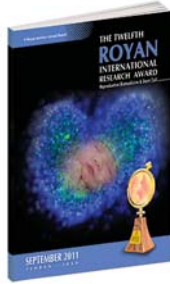
- **Serajoddin Vahidi**
Prevalence of Primary Infertility in the Islamic Republic of Iran in 2004-2005
- **Tahereh Ma'dani**
Improvement of Pregnancy Rate in ART Cycles
- **Mehrdad Noruzinia**
MTHFR Promoter Hypermethylation in Testicular Biopsies of Patients with Non-obstructive Azoospermia: The Role of Epigenetics in Male Infertility
- **Abbas Piryaee**
Differentiation Capability of Mouse Bone Marrow-Derived Mesenchymal Stem Cells into Hepatocyte-Like Cells on Artificial Basement Membrane Containing Ultraweb Nanofibers and Their Transplantation into Carbon Tetrachloride Injured Liver Model



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Received Papers: 358



The Twelfth ROYAN

International Research Award
Reproductive Biomedicine & Stem Cell

September **2011**

International Winners:

Best research project in regenerative medicine field

- **Lorenzo Piemonti, Italy**
Bone Marrow as Ideal Microenvironment for Human Islet Transplantation to Treat Type 1 Diabetes (ClinicalTrials.gov Identifier: NCT01345227)

Best research project in stem cell biology & technology field

- **Hiroimitsu Nakauchi, Japan**
Heterogeneity and Hierarchy Within the Most Primitive Hematopoietic Stem Cell Compartment

Best research project in female infertility field

- **Elizabeth Stewart, USA**
Safely Extending Focused Ultrasound Surgery for Uterine Leiomyomas to Women Who Desire Future Pregnancies

Best research project in reproductive genetic field

- **Paul Thomas, Australia**
Identification of SOX3 As an XX Male Sex Reversal Gene in Mice and Humans

Best research project in embryology field

- **Steve Tardif, UK**
Infertility with Impaired Zona Pellucida Adhesion of Spermatozoa from Mice Lacking TauCstF-64

Best research project in epidemiology & ethics fields

- **Heping Zhang, USA**
Decision Trees for Identifying Predictors of Treatment Effectiveness in Clinical Trials and Its Application to Ovulation in a Study of Women with Polycystic Ovary Syndrome

Iranian Winners:

- **Morteza S. Hosseini**
Development of an Optimized Zona-Free Method of Somatic Cell Nuclear Transfer in the Goat

- **Jaleh Zolghadri**
Relationship Between Abnormal Glucose Tolerance Test and History of Previous Recurrent Miscarriages, and Beneficial Effect of Metformin in These Patients: A Prospective Clinical Study

- **Batool Rashidi**
Simvastatin Effects on Androgens, Inflammatory Mediators, and Endogenous Pituitary Gonadotropins Among Patients with PCOS Undergoing IVF: Results from a Prospective Randomized Placebo-Controlled Clinical Trial



ROYAN Institute



Received Papers: 280



The
Thirteenth
ROYAN
 International Research Award
 Reproductive Biomedicine & Stem Cell



September

2012

International Winners:

Best research project in stem cell biology & technology field

- **Chengcheng (Alec) Zhang, USA**
 Ex Vivo Expanded Hematopoietic Stem Cells Overcome the MHC Barrier in Allogeneic Transplantation

Best research project in andrology field

- **Kristian Almstrup, Denmark**
 Screening of Subfertile Men for Testicular Carcinoma in Situ by an Automated Image Analysis-based Cytological Test of the Ejaculate

Best research projects in female infertility field (share)

- **Wenjie Zhu, China**
 Transvaginal Ultrasound-guided Ovarian Interstitial Laser Treatment in Anovulatory Women with Polycystic Ovary Syndrome: A Randomized Clinical Trial on the Effect of Laser Dose Used on the Outcome
- **Kaei Nasu, Japan**
 Role of Mevalonate-Ras Homology (Rho)/Rho-associated Coiled-Coil-Forming Protein Kinase-mediated Signaling Pathway in the Pathogenesis of Endometriosis-associated Fibrosis

Best research project in reproductive genetic field

- **Signe Atlmäe, Sweden**
 Interactome of Human Embryo Implantation: Identification of Gene Expression Pathways, Regulation, and Integrated Regulatory Networks

Best research project in embryology field

- **Laura Cecilia Giojalas, Argentina**
 Sperm Chemotaxis towards Progesterone, a Guiding Mechanism That May Be Used to Select the Best Spermatozoa for Assisted Reproduction

Iranian Winner:

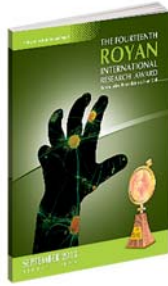
- **Alireza Pouya**
 Human Induced Pluripotent Stem Cells Differentiation into Oligodendrocyte Progenitors and Transplantation in a Rat Model of Optic Chiasm Demyelination



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The
Fourteenth
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September

2013**International Winners:**

Best research project in stem cell biology & technology field

- **Antonio Uccelli**, Italy
Mesenchymal Stem Cells Shape Microglia Effector Functions Through the Release of CX3CL1

Best research project in reproductive genetic & andrology fields

- **Pierre F Ray**, France
Search for Genetic Causes of Male Infertility

Best research project in female infertility field

- **Paola Panina Bordignon**, Italy
The Selective Vitamin D Receptor Agonist Elocalcitol Reduces Development of Endometriosis and Formation of Peritoneal Adhesion in a Mouse Model

Best research project in embryology field

- **Mariano Buffone**, USA
Role of Actin Cytoskeleton During Mouse Sperm Acrosomal Exocytosis

Iranian Winners:

- **Ashraf Moini**
Risk Factors Associated with Endometriosis Among Iranian Infertile Women

- **Malek Hossein Asadi**
OCT4B1, A Novel Spliced Variant of OCT4, Is Highly Expressed in Gastric Cancer and Acts as an Antiapoptotic Factor

- **Hossein Mozdarani**
Genome Instability and DNA Damage in Male Somatic and Germ Cells Expressed as Chromosomal Microdeletion and Aneuploidy Is a Major Cause of Male Infertility

- **Armin Towhidi**
Omega-3 Fatty Acids Accompanied with A-Tocopherol Improved Fresh and Post-thaw Sperm Quality in Ruminants

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The Fifteenth ROYAN

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September

2014

International Winners:

Best research project in regenerative medicine field

- **Anne S. Baron-Van Evercooren**, France
Role of Endogenous Neural Precursor Cells in Multiple Sclerosis

Best research project in stem cell biology & technology field

- **Milena Bellin**, Netherlands
Human Pluripotent Stem Cells for Modelling and Correcting Long-QT Syndrome

Best research project in andrology & reproductive genetic fields

- **Sophie Rousseaux**, France
Male Genome Programming, Infertility and Cancer

Best research project in female infertility field

- **Christiani Andrade Amorim**, Belgium
New Steps Towards the Artificial Ovary

Best research project in embryology & biotechnology fields

- **Guoping Fan**, USA
Transcriptome Dynamics of Human and Mouse Preimplantation Embryos Revealed by Single Cell RNA-sequencing

Best research project in ethics field

- **Kristien Hens**, Netherlands
Towards the Transparent Embryo? Dynamics and Ethics of Comprehensive Pre-implantation Genetic Screening

Iranian Winners:

- **Seyedeh Nafiseh Hassani**
The Augmented BMP Pluripotency Pathway via TGF- β Suppression Maintains the Ground State of Embryonic Stem Cells Self-Renewal
- **Rouhollah Fathi**
Optimal Strategy Toward Fertility Preservation: In vivo and in vitro Post-thaw Options in Gamete, Embryo and Ovarian Tissue Cryostorage



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The Sixteenth ROYAN

International Research Award
Reproductive Biomedicine & Stem Cell

September
2015

International Winners:

Best research project in female infertility field

- **Geetanjali Sachdeva**, India
Endometrial Secretome and Its Role in Uterine Functions

Best research project in embryology field

- **Priyanka Parte**, India
Tubulin Reversible Acetylation – Driving the Moves and the Moves Behind the Drive

Best research project in biotechnology field

- **Zhang**, USA
Identifying and Overcoming an Epigenetic Barrier for SCNT Reprogramming

Best research project in reproductive genetic field

- **Masoud Zamani Esteki**, Belgium
Concurrent Whole-Genome Haplotyping and Copy Number Profiling of Single Cells

Best research project in stem cell biology and technology field

- **Guoliang Xu**, China
DNA Oxidation Towards Totipotency in Mammalian Development

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- **Maryam Shahhoseini**
Expression Profile of Macrophage Migration Inhibitory Factor (MIF) Signaling Pathway as a Potential Biomarker in Pathophysiology of Endometriosis

- **Morteza Mahmoudi**
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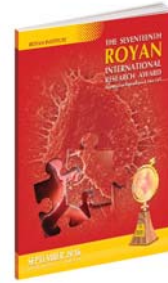
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The
Seventeenth
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International Research Award
Reproductive Biomedicine & Stem Cell



September

2016

International Winners:

Best research project in biotechnology field

- **Jianguo Zhao**, China
High Efficient Genome Editing in Pigs for Making Human Disease Models

Best research project in embryology field

- **Peter Koopman**, Australia
Validation of Retinoic Acid as the Master Inducer of Meiosis in Fetal Germ Cells

Best research project in regenerative medicine field

- **Mohammad Sharif Tabebordbar**, USA
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Best research project in reproductive genetic field

- **Miguel Ramalho-Santos**, USA
Hira-Mediated H3.3 Incorporation Is Required for DNA Replication and Ribosomal RNA Transcription in the Mouse Zygote

Best research project in stem cell biology and technology field

- **Xiaohua Shen**, China
Cis-regulatory Roles of lncRNAs in Transcription Regulation and Stem Cell Differentiation

Iranian Winners:

- **Mohsen Sharafi**
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- **Anahita Mohseni Meybodi**
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- **Kamran Ghaedi**
Utilization of Pioglitazone as a Novel Approach to Increase the Colony Formation Efficiency of Individualized Human Pluripotent Stem Cells

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The
Eighteenth
ROYAN
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Reproductive Biomedicine & Stem Cell

August

2017

International Winners:

Best research project in stem cell biology and technology field

- **Thomas Braun**, Germany
Compaction of Chromatin Seals Quiescence of Muscle Stem Cells

Best research project in embryology field

- **David Greening**, Australia
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Best research project in regenerative medicine field

- **Riccardo Fodde**, Neatherlands
Diet, Inflammation, and Stem Cells: Trading off Regenerative Response with Cancer Risk

Best research project in reproductive genetics field

- **Kaei Nasu**, Japan
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Best research project in female infertility field

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Winners

Female Infertility

INTERNATIONAL WINNER

A Bioprosthetic Ovary Created Using 3D Printed Microporous Scaffolds Restores Ovarian Function in Sterilized Mice

Objective:

Emerging additive manufacturing techniques enable investigation of the effects of pore geometry on cell behavior and function. Here, we 3D print microporous hydrogel scaffolds to test how varying pore geometry, accomplished by manipulating the advancing angle between printed layers, affects the survival of ovarian follicles.

Material and Methods:

30° and 60° scaffolds provide corners that surround follicles on multiple sides while 90° scaffolds have an open porosity that limits follicle–scaffold interaction. As the amount of scaffold interaction increases, follicle spreading is limited and survival increases.

Results:

Follicle-seeded scaffolds become highly vascularized and ovarian function is fully restored when implanted in surgically sterilized mice. Moreover, pups are born through natural mating and thrive through maternal lactation.

Conclusion:

These findings present an in vivo functional ovarian implant designed with 3D printing, and indicate that scaffold pore architecture is a critical variable in additively manufactured scaffold design for functional tissue engineering.

Keywords:

Biomaterials, Preclinical Research, Translational Research, Fertility



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Teresa K Woodruff is the Dean and Associate Provost for Graduate Education in The Graduate School at Northwestern University. She is also the Thomas J. Watkins Professor of Obstetrics & Gynecology, the Vice Chair for Research and the Chief of the Division of Reproductive Science in Medicine in the Department of Obstetrics and Gynecology, Feinberg School of Medicine. She is Professor of Molecular Biosciences in the Weinberg College of Arts and Sciences, and Professor of Biomedical Engineering in the McCormick School of Engineering. She is the Director of the Center for Reproductive Science (CRS), Founder and Director of the Women's Health Research Institute (WHRI), and Director of the Oncofertility Consortium. She is an internationally recognized expert in ovarian biology and, in 2006, coined the term "oncofertility" to describe the merging of two fields: oncology and fertility. She now heads the Oncofertility Consortium, an interdisciplinary team of biomedical and social scientist experts from across the country. She has been active in education not only at the professional level but also with high school students. To this end, she founded and directs the Oncofertility Saturday Academy (OSA), one of several high school outreach programs that engages girls in basic and medical sciences. She was awarded the Presidential Award for Excellence in Science Mentoring in an oval office ceremony by President Obama (2011). Widely recognized for her work, Woodruff holds 10 U.S. Patents, and in 2013 she was named to Time magazine's "Most Influential Persons" list. Some of her recent awards and honors include a Guggenheim Fellowship (2017), a National Academy of Inventors Fellowship (2017), the Society for Endocrinology Transatlantic Medal (2017), and a Leadership Award from the Endocrine Society (2017). She has two honorary degrees including one from the University of Birmingham, College of Medical, UK (2016). She is an elected fellow of the American Institute of Medical and Biological Engineering and the American Association for the Advancement of Science (AAAS). She is past-president of the Endocrine Society and championed the new NIH policy that mandates the use of females in fundamental research. She is civically active and is an elected member of The Economic Club of Chicago and on the school board of the Chicago-based Young Women's Leadership Charter School.





INTERNATIONAL WINNER

Embryology and Andrology



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Dr Reza Nosrati is an Assistant Professor (Lecturer) in the Department of Mechanical and Aerospace Engineering at Monash University. Prior to joining Monash University, he was an NSERC postdoctoral fellow in the Department of Chemical Engineering at Queen's University (2016-2018). Dr Nosrati received his PhD in Mechanical Engineering from the University of Toronto (2016), his MSc in Mechanical Engineering from the University of Tehran (2010), and his BSc in Mechanical Engineering from Amirkabir University of Technology (2007). Dr Nosrati is a pioneer in microfluidics for male fertility and assisted reproduction. His research interests include the study and application of small-scale fluid mechanics for use in assisted reproduction, fundamental biology, translational medicine, biosensing, and environmental sciences.

Dr Nosrati's research efforts to date have resulted in several articles in top-tier scientific Journals like Nature Communications, Nature Reviews Urology, Clinical Chemistry, and Lab on a Chip. His work, including his ground-breaking discovery of the 2D slither swimming mode of sperm, has been highlighted several times in renowned journals such as Nature Reviews Urology, and has featured routinely in news sources worldwide, including LA Times, Daily Mail, and The Scientist. Dr Nosrati has received numerous prestigious awards and recognitions, including the 2016 Douglas R. Colton Medal for research excellence in Microsystems and Nanotechnology in Canada.

 **Microfluidics for Male Fertility****Objective:**

Infertility is a growing global health issue with far-reaching socioeconomic impacts, affecting >50 million couples worldwide. Semen analysis and sperm selection are cornerstones of infertility diagnosis and treatment. However, current clinical methods for sperm analysis and selection are insufficient, costly, time-consuming, and prone to operator error, resulting in sub-optimal pregnancy outcomes. The global trend of rising infertility motivates immediate attention to infertility issues, and highlights the fundamental challenges of making both diagnosis and treatment affordable and accessible. Here, rapid and low-cost microfluidic methods are demonstrated for the study, analysis, and selection of sperm for male infertility diagnosis and treatment.

Material and Methods:

Microfluidics provides several fruitful opportunities for infertility diagnosis and treatment. Microfluidic methods were applied here to (a) understand the biophysics of sperm motion, (b) develop paper-based strategies for semen analysis, and (c) develop rapid technologies for high-quality sperm selection. First, microfluidics and total internal reflection fluorescence microscopy were used to capture and describe full 3D dynamics of sperm motion near surfaces with nanoscale resolution for the first time. Second, by leveraging biochemical and electrokinetic capabilities in paper-based assays, affordable and accessible technologies were developed for at-home semen analysis and sperm DNA integrity testing. Finally, by leveraging the natural swimming characteristics of sperm to follow boundaries in a parallel array of 500 microchannels, a rapid sperm selection device was developed that reflects the natural in vivo process. These microfluidic devices were clinically tested with human samples against current best practices.

Results:

A distinct 2D 'slither' swimming mode was discovered for sperm within 1 μm of a surface, in which the full sperm body is aligned parallel to the surface and the flagellum beats in a 2D plane. Human sperm swims 50% faster in the slither mode, suggesting a strategy that is well-suited to the confined portions of the reproductive tract. With respect to semen analysis, a rapid (10 min) and low-cost (US\$0.05/device) paper-based technology was developed for at-home male fertility testing that simultaneously quantifies three critical semen parameters (concentration, vitality, and motility) using a colorimetric enzymatic assay. The paper-based device provided 100% agreement with conventional CASA and dye exclusion vitality assay in terms of clinical outcome for patients. Additionally, a rapid, sensitive, and low-cost paper-based approach was developed for sperm DNA integrity analysis that provides identical clinical outcome as flow cytometry-based SCSA, with two orders of magnitude less overall capital and operating costs. With respect to sperm selection, a high-throughput microfluidic technology was developed for one-step semen purification and high DNA integrity sperm selection, by on-chip processing of 1 ml of raw semen in <20 min. Clinical tests with raw human semen samples showed >80% improvement in DNA integrity of selected sperm, considerably outperforming the best practices in current use.

Conclusion:

Microfluidics has led to new biological insights into sperm behaviour, and developments in microfluidic devices show the most promise for near-term medical advances in male fertility. These technologies are scalable alternatives to conventional clinical testing and provide novel opportunities to alleviate major emotional and financial burdens for families dealing with infertility worldwide.

Keywords:

Male Infertility, Microfluidics, Sperm, Semen Analysis, Assisted Reproduction



Stem Cell Biology and Technology

INTERNATIONAL WINNER

Two-Way Conversion Between Lipogenic and Myogenic Fibroblastic Phenotypes Marks the Progression and Resolution of Lung Fibrosis

Objective:

Idiopathic pulmonary fibrosis (IPF) is a form of progressive interstitial lung disease with unknown etiology. Due to a lack of effective treatment, IPF is associated with a high mortality rate. The hallmark feature of this disease is the accumulation of activated myofibroblasts that excessively deposit extracellular matrix proteins, thus compromising lung architecture and function and hindering gas exchange. Here we investigated the origin of activated myofibroblasts and the molecular mechanisms governing fibrosis formation and resolution.

Material and Methods:

Genetic engineering in mice enables the time-controlled labelling and monitoring of lipogenic or myogenic populations of lung fibroblasts during fibrosis formation and resolution.

Results:

Our data demonstrate a lipogenic to- myogenic switch in fibroblastic phenotype during fibrosis formation. Conversely, we observed a myogenic-to-lipogenic switch during fibrosis resolution. Analysis of human lung tissues and primary human lung fibroblasts indicates that this fate switching is involved in IPF pathogenesis.

Conclusion:

These results open the way for potential therapeutic avenues to treat IPF patients.

Keywords:

IPF, Lipofibroblast, Myofibroblast, Lineage Tracing, Fgf10



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Dr Saverio Bellusci is internationally recognized as a leader in the field of fibroblast growth factors (FGFs) and stem cells in lung development and regeneration/repair after injury.

He has published so far 145 papers including papers in Cell Stem Cell, Journal of Clinical Investigation, Molecular Cell, American Journal of Critical Care and Respiratory Medicine, PLoS Pathogens, Development and BMC Biology. He has a total of 10458 citations, his h-index is 51 and his i10-index is 109.

As an illustration of his leadership in this field, he has been the chair of the Gordon Research conference on FGFs in Development and Disease organized in Ventura, California in 2014. He has also organized a similar conference in Cancun, Mexico (Fusion meeting on FGF signaling in 2015 and 2017) and currently, he is co-chairing another Fusion meeting on stromal-epithelial stem cells interaction in lung health and disease in 2019. In 2010, he was recruited as a Professor with a chair in the field of stem cells and lung development and regeneration/repair after injury. He has established a world class, research facility at Justus Liebig University in Giessen (Germany), within the internationally recognized and highly competitive Excellence Cluster in Cardio-pulmonary system (ECCPS).

His lab is interested in the role of Lipofibroblasts in lung homeostasis and disease. LIFs are mesenchymal cells which are tightly associated with alveolar type II stem/progenitor epithelial cells and their function is primarily to provide the triglycerides needed for the elaboration of surfactant. It has emerged recently that these cells may indeed also represent a "niche" for the alveolar type II epithelial stem/progenitor cells. Their hypothesis is that this interaction is at the center of lung regeneration after injury. In addition, they are also evaluating the fate of the lipofibroblasts once the niche is disturbed by injury. They have recently published that lipofibroblasts can transdifferentiate into activated myofibroblasts in the context of lung fibrosis.

In summary, he has a proven expertise in the field of stem/progenitor cells in development and regeneration/repair after injury. He has also a very strong expertise in mouse genetics. Finally, he is interacting closely with clinicians to investigate the cellular and molecular bases of lung diseases.





INTERNATIONAL WINNER

Reproductive Genetics | Shared Winner |

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Dr Amir Amiri-Yekta has been working in Royan research Institute on full time basis as of 2006. He has been actively engaged in research and educated related activities. He completed his PhD program at Royan Institute and Grenoble-Alpes University in the field of human molecular genetics in 2017. The title of his dissertation is Genetics and molecular characterization of the multiple morphological abnormalities of the sperm flagella (MMAF) syndrome. Not only has Dr Amiri-Yekta identified and introduced some genes, but he also has launched a survey into the effects of these genes by recruiting different models. He has conducted several projects in the field of biotechnology such as transgenic animals. So far Dr Amiri-Yekta, Royan institute faculty member, has published some valuable articles in authentic journals such as Nature communications, The American Journal of Human Genetics, and EMBO Molecular Medicine. He has been the author of some books in the field of genetics as well as biotechnology. He has registered some patents. Nowadays, he has devoted most of his research activities on genetics infertility by applying NGS technology.

Genetics and Molecular Characterization of the Multiple Morphological Abnormalities of the Sperm Flagella (MMAF) Syndrome

Objective:

Male infertility is a complex disorder that affects more than 20 millions men worldwide and has become a global concern that affects many aspects of human life. Many cases of infertile males are categorized to be idiopathic, indicating that the cause is unknown and the mechanisms responsible for their condition are to be found. To date, a very short list of genes was identified which is in sharp contrast with the fact that several hundreds of genes are estimated to be involved in spermatogenesis and male reproduction. Multiple morphological abnormalities of the flagella (MMAF), previously described as “dysplasia of the fibrous sheath”, “short tails” or “stump tail syndrome”, is one of the most severe forms of asthenozoospermia and is characterized by the simultaneous presence of five morphological defects of the sperm flagella (absent, short, bent, coiled flagella and flagella of irregular width). The abundance of potential candidate genes makes identification of pathogenic mutations difficult and complex. However, gene identification is the key to improving knowledge of the pathophysiology of MMAF and opens new perspectives for diagnosis and treatment of infertile patients. Further genetic studies are therefore warranted to identify other genes involved in MMAF to better characterize the genetic etiology of the MMAF phenotype and to improve the management of patients diagnosed with flagellar defects. In this study, Whole Exome Sequencing (WES) has led to the identification of new genes involved in MMAF and exploit the WES data to the benefit of the patients.

Material and Methods:

In our study, we analyzed 78 MMAF patients using WES and showed that in addition to mutations in DNAH1, mutations in CFAP43 and CFAP44, two tryptophan-aspartic acid repeat (WDR) containing proteins, and also in CFAP69 are responsible for MMAF syndrome. The effect of all candidate variants was confirmed by RT-PCR and immunochemistry. Most importantly, we investigated the role of these novel genes by performing gene invalidation and silencing in two evolutionary distant models sharing an extremely conserved flagellar structure, Trypanosoma, and mouse.

Results:

Using this original approach we demonstrate the importance of WDR proteins for the axonemal structure of the flagella throughout evolution. Overall, DNAH1, CFAP43, CFAP44, and CFAP69 mutations were identified in 30% of the analyzed sporadic subjects (24 out of 78 patients) originating from North Africa, Europe, and the Middle East.

Conclusion:

Altogether, our results underline the global importance of these 4 genes in the MMAF syndrome and will improve the genetic diagnosis efficiency of infertile MMAF patients. In our study, WES revealed that CFAP43, CFAP44, CFAP69, and DNAH1 are the main genes involved in MMAF phenotypes. Our work illustrates the efficiency of the combination of WES with original workflow for the validation of the candidate genes that are identified in male infertility due to the MMAF phenotype.

Keywords:

Male Infertility, Genetic Diagnosis, Exome Sequencing, Gene Mutations, MMAF



Reproductive Genetics | Shared Winner |

INTERNATIONAL WINNER

Epigenetic Regulation of Coding and Non-coding RNA Expression During the 1st Wave of Spermatogenesis

Objective:

Spermatogenesis is a highly regulated process in which undifferentiated spermatogonial stem cells differentiate to form highly specialized sperm cells capable of fusing with the ovum to form a zygote. This is achieved through tightly controlled regulation of gene expression which depends on transcriptional, post-transcriptional, translational and epigenetic mechanisms. Using the first wave of spermatogenesis in mouse as a model, we profiled the transcriptome, mirnome and histone methyl marks in relation to gene expression in the testis during initiation of spermatogenesis. We integrated these three big data sets to generate a network of H3K4Me3 marks on the promoter/ transcription start sites (TSS) and its impact on the expression miRNAs and their target transcripts. Further, we evaluated the effect of silencing of a Meisetz, a known meiosis specific H3K4 methyl transferase, in germ cell line to assess the validity of the networks thus generated.

Material and Methods:

Mice of age groups Day 8, Day 16 and Day 24 were used for this study. RNA extraction was done using miRNAeasy kit (Qiagen). miRNA microarray was done using mercury LNA array, Version 11.0 (Exiqon) containing capture probes targeting all miRNAs for human, mouse or rat (miRBASE 13.0, Exiqon). Whole transcriptome analysis was done on a GeneChip 1.0 ST array (Affimetrix) containing 28853 well-annotated genes. For chromatin immunoprecipitation (ChIP), isolated genomic DNA was crosslinked with bound proteins, sheared and immunoprecipitated using anti-H3K4Me3 antibodies. The ChIPed fraction was decrosslinked and libraries were prepared, which were subjected to next-generation sequencing on HiSeq 2500 (Illumina). The input DNA (Non ChIP'd genomic DNA) was used as the control. Quality check of the raw reads was performed using SeqQCv2.2. Filtered high quality reads from INPUT and IP files were aligned to reference genome (mm10) using Bowtie-0.12.8 alignment tool using Mouse (*Mus musculus*) reference genome downloaded from UCSC and indexed using Bowtie-build. These three data sets were integrated using Cytoscape Version 2.8.3 (Cytoscape Consortium).

Results:

Out of a total of 6244 promoters of protein coding genes that were identified to be H3K4 trimethylated Day 8 and Day 24 mice testes in our data set, transcription profile of 3105 genes could be identified in the microarray data set. We also detected 1267 H3K4Me3 peaks of non-coding RNAs, out of which 314 were of miRNAs. The prominent members were miR34b, miR34c, miR199b, miR184, miR762 and miR475. miR34b and miR34c were especially important in that they made strong networks with mRNAs relevant to spermatogenesis. We further demonstrated that ablation of Meisetz in germ cells resulted in aberrant expression of spermatogenesis related genes, thus emphasizing the role of Meisetz dependent H3K4 trimethylation during spermatogenesis. Some of the genes analyzed such as Gpx4, Zfp35, Ccin, Theg and Zfp37, are known to be crucial to spermatid development.

Conclusion:

This study establishes that H3K4 trimethylation is important in establishing spermatogenesis specific gene expression pattern by its direct effect on transcription of both coding and non-coding RNAs. Our study shows that H3K4 trimethylation is necessary for the transcription of the genes important to spermatogenesis and therefore, may play a crucial role in determining the fertility status.

Keywords:

Spermatogenesis, miRNA, Transcriptome, Histome Methylation, Testis

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Dr Pradeep Kumar G is a Scientist at Rajiv Gandhi Centre for Biotechnology (RGCB), Trivandrum, India, one of the Autonomous Research Institutes under Department of Biotechnology, Government of India. Before relocating to RGCB, he worked as Lecturer and Reader in School of Life Sciences at DA University, Indore; Fellow-in-Residence at The Rockefeller University, New York; Post-Doctoral Fellow at University of Virginia and Visiting Faculty at University of Florida.

He is a recipient of National Fellowships from UGC and CSIR (1984), International Post-Doctoral Fellowship from The Rockefeller Foundation New York (1994) and a fellowship from National Institute of Health, Maryland (2000). He has won several awards including National Bioscience Award from Department of Biotechnology, India (2006), Department of Biotechnology Overseas Associateship (2008), Labhsetwar Award (2015), DrTC Anand Kumar Memorial Oration Award and Gold medal (2016) and Subhas Mukherjee Oration Award (2016)

He leads a research unit pursuing studies to understand the development and differentiation of testicular germline stem cells, factors regulating control of cell division through meiosis and the structural organization of spermatozoa making it capable to fuse with the oocyte.



INTERNATIONAL WINNER

Animal Biotechnology



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Dr Ali Fouladi Nashta was trained as a Veterinarian in Tehran University and served for about 7 years as a Lecturer in Animal Reproduction before moving to the United Kingdom for further education. He gained his MSc in 1995 and PhD in 1999 from the University of Edinburgh in Scotland. Dr Fouladi undertook his PhD studies at the Roslin Institute under supervision of late Professor Keith Campbell, creator of Dolly the cloned sheep from differentiated cells. Following this he undertook post-doctoral positions at Manchester and Nottingham universities. In June 2006, he accepted a Lectureship position at the Royal Veterinary College, University of London. He was promoted to Senior Lecturer in 2012 and then to Reader in 2016. He is a member of the Reproduction Research Group. His research is focused in the area of oocyte biology and embryology of domesticated animal species, uterine embryo interaction and mechanism of embryo implantation.

Impact of Sperm Hyaluronidase and VLMWHA on Sheep Blastocyst Formation *in vitro*, Viability After Cryopreservation and Pregnancy Rate After Embryo Transfer

Objective:

Recent research in our laboratory has reported the presence of members of the hyaluronan (HA) system including HA synthases and receptors and hyaluronidase (hyals) in reproductive system and embryos and the critical role of *hyal2* in early stage embryo development. We hypothesised that very low molecular size HA fragments (VLMWHA; <10kDa) produced during degradation by sperm hyaluronidase (PH20), function as a survival factor and growth stimulator during preimplantation embryo development.

Material and Methods:

Sheep oocytes were collected from slaughterhouse derived ovaries and matured and fertilized *in vitro*. Experiment 1: Cleaved embryos were cultured in the absence (control) or presence of 10ng/ml PH20, or 100µg/ml VLMWHA or anti HA cell membrane receptors CD44 and RHAMM for 6 days when development to blastocyst was recorded and the number of hatched blastocysts counted. Experiment 2 assessed quality of the blastocysts based on survival after cryopreservation by vitrification of early blastocyst stage embryos. Experiment 3 analysed pregnancy and live birth rates after embryo transfer to oestrus synchronised recipient ewes. Pregnancy was assessed by ultrasound scanning on day 35, and number and normality of lambs were recorded.

Results:

Significantly higher percentage of blastocysts were produced in PH20 (56.8 ± 6.9) or VLMWHA (63.6 ± 4.0) versus control (32.4 ± 3.4 %). Similarly higher proportion of these blastocysts were hatched (PH20; 21.6 ± 3.1 , VLMWHA; 22.6 ± 4.4 , Control; 7.2 ± 1.2) $P < 0.05$). These effects were abrogated in the presence anti-CD44 and RHAMM. Higher percentage of the blastocysts cultured in PH20 or VLMWHA survived after vitrification as observed by re-expansion and hatching after re-culture (76.2% and 80% v. 52.2%, $P < 0.05$). Higher number of pregnancies and live birth was observed in the ewes receiving blastocysts developed in the presence of PH20 (8/11; 73%) or VLMWHA (9/12; 75%) versus control (6/11; 55%). No abnormality was observed in the lambs weight, behaviour and survival.

Conclusion:

These studies have defined a new role for sperm in supporting early stage embryos and provided evidence for a receptor-mediated role of sperm hyaluronidases or VLMWHA in enhancing embryo development and quality during the preimplantation period.

Keywords:

Hyaluronan, Hyaluronidase, Sperm, Blastocyst, Pregnancy and Live Birth



Winners

Stem Cell Biology and Technology

NATIONAL WINNER

Bioengineering of a Humanized Heart by Seeding of hiPSC-Derived Cardiovascular Progenitor Cells into Growth Factor-Tethered Rat Heart Matrix

Objective:

Millions of people worldwide suffer from cardiovascular diseases. Although current interventional and pharmacological approaches provide efficient therapies, curative treatment of end-stage heart failure is limited to heart transplantation. Bioengineering of whole hearts using human embryonic stem cells (hESCs)-derived cardiovascular progenitor cells (CPCs) and natural matrices is a promising approach to overcome organ donor shortage threatening millions of patients awaiting for heart transplantation.

Material and Methods:

Here, we developed a novel strategy for generation of heart constructs by repopulating engineered decellularized rat hearts using hESCs-derived CPCs. We modified decellularization protocol to improve efficacy which was confirmed by multiple tests including DNA content analysis as well as biochemical studies. The decellularized hearts were recellularized by hESC-derived CPCs, which were generated in a scalable suspension bioreactor system. To improve CPCs proliferation and differentiation, we immobilized bFGF onto heart ECM prior to cell perfusion. Further optimization of seeding density and loading intervals allowed uniform recellularization of the heart scaffold. At day 12 post seeding, functional studies were performed on recellularized hearts. The beating rhythm was evaluated using a multielectrode array system. Contraction motions were recorded using video microscopy and analyzed using a custom-made matlab macro. qRT-PCR and immunostaining was performed for cardiac specific markers. In-depth examination of the ultrastructure of seeded CPCs and CPC-derived cells were investigated by transmission electron microscopy (TEM).

Results:

We demonstrated that perfusion-decellularization of whole heart allows the generation of a heart ECM scaffold with a perfusable vascular tree and intact 3D architecture, which acts as an efficient template to generate synchronously beating heart tissue. Comprehensive characterization of the decellularized heart matrix demonstrated preservation of complex ECM proteins, 3D spatial orientation and the micro-structure of native heart. Careful expansion of CPCs in a scalable stirred-suspension bioreactor combined with step-wise seeding (60 million cells in 3 steps of 20 million per 1.5 hour) onto decellularized hearts containing immobilized bFGF resulted in improved retention of CPCs and differentiation to cardiomyocytes, smooth muscle cells and endothelial cells as evaluated by immunohistochemistry and qRT-PCR. We observed spontaneous and synchronous contractions of humanized hearts after 12 days of perfusion as well as advanced alignment of myofilaments.

Conclusion:

While clinical implementation of engineered heart tissues is recently examining in clinical trials, the whole heart bioengineering science is evolving quickly in order to circumvent the heart transplantation obstacles in patients with end stage heart failure. Nevertheless, heart organogenesis via decellularization/recellularization is still facing multiple technological challenges before commercialization. Selection and large scale production of clinical grade starting cell ingredients, supplying heart natural scaffold, and more importantly improving cell repopulation procedure efficacy as well as the functionality of lab grown hearts are the main challenges which need to be addressed. Our study provides a robust platform for generation of artificial human hearts and resolves major bottlenecks hindering further development of this technology. Bioengineered hearts might soon find their way toward clinical application.

Keywords:

Bioengineering, bFGF, Heart



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Sarah Rajabi was born in Iran in 1983. She received the BSc degree in General Biology from the university of Payam Noor, Sari, Iran, the MSc and PhD degrees from Kharazmi University, Tehran, Iran, in 2008 and 2013 respectively. Since 2009, she was joined Royan institute and completed her postdoctoral research fellow on Bioengineering in 2017. Her research interests include the design and fabrication variety of biomaterials and analysis of interaction of stem cells with different scaffolds for cardiovascular, skin and muscle tissue engineering. Now, she is one of the academic staff of cardiovascular group of Royan Institute.



NATIONAL WINNER

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Mazdak Razi received his DVM degree from Islamic Azad University, Urmia Branch in 2006, and his PhD in Comparative Histology in 2011 from Urmia University, Iran. His PhD thesis was about long-time varicocele-induced molecular and biochemical pathogenesis, and effect on in-vitro fertilization potential. Currently, he is assistant professor in the Department of Basic Sciences, Division of Histology and Embryology, Faculty of Veterinary Medicine, Urmia University, Urmia, Iran. Also, he is director and dean of AYANDEH center, now one of the leading developmental research and diagnosis institutes, and member of Iranian Society of Reproductive Biology and Embryology. Since 2008, he has been working in the field of male infertility, by focusing on molecular, biochemical, genetic and epigenetic alterations, in-vitro fertilization, experimental varicocele, spermatogonial stem cells self-renewal, the cell cycle machinery of germinal epithelium, reproductive cytotoxicity. He developed and supervised several pre-clinical and experimental studies for varicocele-induced genetic, epigenetic, biochemical and molecular alterations, and recently, he and his team could show the reinforcing effect of antioxidant chemicals on Leydig-Sertoli cells network, as well as spermatogonial stem cells self-renewal process, by performing pre-clinical trials on varicocele rats.

Reproductive Biomedicine

Antioxidant, Anti-inflammatory and Testosterone Therapy Reinforces Spermatogonial Stem Cells Self-Renewal in Experimentally-Induced Varicocele; Possible Mechanisms**Objective:**

The varicocele (VCL) has been known as one of the infertility problems in 15-20% of the male population, which severely affects the spermatogenesis via inducing oxidative, inflammatory stresses and suppressing testicular endocrine potential. Thus, the antioxidant, anti-inflammatory and testosterone boosting chemicals (herbal and/or synthetic) have been considered as the alternative therapeutic methods. Thus, the VCL-induced damages can be divided into a-failed endocrine network between Leydig and Sertoli cells, b-the cytokines-induced effects on transcriptional factors and encoding genes, c-the oxidative stress-related molecular changes at cell cycle machinery.

Material and Methods:

To analyze mentioned three mechanisms, the experimental VCL was induced in Wistar rats, then the animals were divided into VCL-sole and antioxidant, anti-inflammatory and testosterone treated VCL-induced groups. Following 2 months, the animals were euthanized and the testicular glial cell line-derived neurotrophic (GDNF), its receptors *Gfr α 1* and *C-ret*, the encoding active genes of spermatogonial stem cells (SSCs) self-renewal *Bcl-6b* and *Etv5*, and genes involving in cell cycle machinery including, *Cylin D1*, *CDK-4*, *p21*, and the inflammatory mediators, tumor necrosis factor- α (*TNF- α*), interleukin-6 (*IL-6*), cyclooxygenases (*COX-II*) and nitric oxide (*NO*), and the homeostatic factors heat shock protein70-2 (*Hsp70-2*), *E2f1* expressions, serum levels of testosterone and inhibin B, the testicular total antioxidant capacity (TAC), malondialdehyde (MDA), glutathione peroxidase (*GSH-px*), superoxide dismutase (*SOD*), catalase, total thiol molecules (TTM) were investigated, using different RT-PCR, immunohistochemical, western blot and ELISA methods. The germinal cells DNA fragmentation was assessed using TUNEL staining. Moreover, the sperm parameters including, sperm count, viability, motility, DNA integrity, chromatin condensation were assessed. All results were compared between VCL-sole and treatment groups.

Results:

Observations revealed that, administrating antioxidant and anti-inflammatory chemicals in association with testosterone boosting agents significantly ameliorates the VCL-impaired Leydig-Sertoli network, amplify the VCL-diminished GDNF, *Gfr α 1*, *C-ret*, *Bcl-6b* and *Etv5* expression, and finally through this mechanism promote the SSCs self-renewal. Moreover, we showed that promoting the testicular endocrine and antioxidant system remarkably down regulates the DNA fragmentation, suppresses the *p21* expression, amplifies the *Cylin D1* and *CDK-4* expression, and through this mechanism promotes cell cycle progression in SSCs. More observations revealed a remarkable reduction in inflammatory mediators expression/synthesis/activity in treated groups. the animals in antioxidant and anti-inflammatory chemicals-treated groups exhibited enhanced testicular *Hsp70*, TAC, *GSH-px*, *SOD*, catalase and TTM levels and represented diminished *E2f1* and apoptosis indices versus VCL-sole group. Finally, the VCL-treated groups exhibited improved sperm parameters compared to VCL-sole group.

Conclusion:

The antioxidant and anti-inflammatory therapies in association with testosterone boosting agents (in sole and simultaneous form of administration) promote the Leydig-Sertoli cells physiologic interactions, which in turn a- amplifies the Sertoli-related niche factors expression/synthesis and affect on SSCs self-renewal, b- downregulates the inflammatory mediators expression/synthesis and affect on SSCs self-renewal, c- reduces DNA fragmentation both at germ cells and sperm levels and amplifies the homeostatic factors *Hsp70-2* expression and suppresses the *E2f1* protein level and d- improves the sperm parameters resulting in enhanced fertilization potential.

Keywords:

Varicocele, Spermatogonial Stem Cells, Self-Renewal, Cell Cycle



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Kazemi Prize 2018

About Kazemi Prize

Dr Saeid Kazemi Ashtiani was born in March 1961 in Tehran. Upon completion of his high school at the age of 18, he was admitted to Iran Medical University to pursue his studies in the field of Physiotherapy. He graduated in 1991 and subsequently in 1993 he started his postgraduate education in the field of Anatomy (Embryology branch) in Tarbiat Modares University. He received his Doctorate Degree with Distinction in 1998.

Dr Kazemi established Royan Research Institute in 1991. This institute renders advanced medical services to infertile couples. The center is also one of the most important and active research centers in the Middle East. Dr Kazemi and his colleagues at Royan Infertility Research Center could achieve a tremendous success in 2003 by establishing human embryonic stem cell line. This great scientific achievement has earned a high position for Iran among the other top 10 countries having access to this advanced technology at that time.

He was not only a scientist who led a lot of principle research projects in the field of stem cell and cloning but a great manager as well. He was the head of ACECR, Iran Medical University branch, head of Royan Research Institute, guest instructor and lecturer of many Iranian medical universities, manager and chief of quarterly scientific and research journal of Yakhteh, head of ethical research committee in Royan Institute, and an active member of Iranian Society for Reproductive Biomedicine as well as Iran Anatomical Science Society. Dr Saeid Kazemi also presided Royan International Award, which was held six times from 2000-2005. His short fruitful life was ended in 2006 when he died of a sudden heart attack.

To respect his efforts and revive his memories amongst national and international scientists as well as nonscientists, Iran supreme leader, Ayatollah Khamenei recommended establishing a yearly prize in biology entitled "Kazemi Prize" which will be awarded to a scientist who made an extraordinary progress in the biological sciences. Kazemi Research Award is for appreciation of extreme effort of the scientist who dedicates his/her life to make progress in human life and relief people's pain.

A nomination committee consisting of prominent national and international scientists is the working body that evaluates the nominees and presents its recommendations to the scientific board of the institute. The scientific board is responsible for the final selection of the prize laureates. In 2010 the first Kazemi Prize was awarded to Prof Rudolf Jaenisch one of the most innovative and creative scientists in the field of developmental biology, gene regulation, stem cell biology and stem cell-mediated therapies. In 2011 the second Kazemi Prize was awarded to Prof Hans Robert Schöler a world-renowned researcher who has made significant contributions to the field of stem cell biology over the past 40 years. The third Kazemi Prize was awarded to Prof Robert S. Langer; one of the most important individuals in biotechnology in the world and one of the best innovators worldwide. In 2016 the fourth Kazemi Prize recipient was Professor Hans Clevers; a geneticist, physician, medical researcher and a professor in molecular genetics who was the first to identify stem cells in the intestine and one of the world's leading researchers on normal stem cells and their potential for regenerative therapy. This year this prize will be awarded to Professor Michele De Luca.



Michele De Luca
Kazemi Prize 2018

Michele De Luca is Full Professor of Biochemistry, University of Modena and Reggio Emilia, and Director of the Centre for Regenerative Medicine of the same University. He is Scientific Director of Holostem Terapie Avanzate S.r.l.

Prof De Luca was Scientific Director of the Veneto Eye Bank Foundation (2002-2007), Director of the Laboratory of Tissue Engineering at the Istituto Dermopatico dell'Immacolata, Rome (1996-2002), adjunct Professor of Cell Biology of the Medical School of Tor Vergata University, Rome (1998-2000), Deputy Head, Laboratory of Cell Differentiation, Istituto Nazionale per la Ricerca sul Cancro, Genova (1992-1995), Group Leader in the same Institute (1986-1992), Visiting Scientist at the Department of Cell Biology, Harvard Medical School, Boston (1985), Fogarty Fellow at the National Institutes of Arthritis, Diabetes, Digestive and Kidney Diseases (NIADDK), National Institutes of Health (NIH), Bethesda (1982-1985). He graduated MD in 1980 and obtained a Specialty in Endocrinology in 1984. He is founding member of International Ocular Surface Society, member of numerous scientific societies and member of national and international committees. He is author of more than 110 scientific publications in major international journals and author of 4 international patents. He was invited lecturer in more than 120 international meetings and symposia. He is currently coordinating several ex-vivo epidermal stem cell-mediated combined cell and gene therapy clinical trials for genetic skin diseases as Epidermolysis Bullosa. During these studies, Michele De Luca and Graziella Pellegrini reported lifesaving regeneration of the entire human epidermis of a Junctional EB patient by means of transgenic epidermal stem cells. He was born in Savona, Italy, May, 17, 1956.



ROYAN INSTITUTE

www.royaninstitute.org



Royan Institute is a world-renowned center committed to multidisciplinary, campus-wide, integration and collaboration of scientific, academic, and medical personnel for understanding male/ female infertility, embryo development, stem cell biology, and biotechnology. Royan Institute provides comprehensive services for the treatment of infertility, regenerative medicine/ cell therapy and production of recombinant proteins.

Royan Institute was established in 1991 by the late Dr Saeid Kazemi Ashtiani (May he rest in peace) in Tehran, Iran. The center supports innovation, excellence and the highest ethical standards focusing on increasing the success rate of infertility treatment alongside embryo health. Furthermore, this center supports the placement of stem cell research findings into operation in cell therapy and disease treatment with the purpose of increasing the level of health.

Mission

The mission of Royan Institute, which is aligned with the country's comprehensive scientific roadmap and the Iranian Academic Center for Education, Culture and Research (ACECR) development plan, can be categorized in the following aspects:

- Research and development of science and technology in the fields of reproductive biomedicine, stem cells and biotechnology
- Education and promotion of scientific findings at national and international levels
- Commercialization of research findings to offer services and biological products for the purpose of resolving the country's specialized needs
- Treatment of infertile patients and difficult-to-treat diseases by the efficient use of research findings

Vision

Royan Institute is a center of excellence in research and technology at an international level, a pioneer in development of science, technology and innovation of biological sciences, and an internationally renowned authority on stem cells science, reproduction, biotechnology, and regenerative medicine alongside its effective role in improving the society's health.

Royan Consists of Three Research Institutes and a Core Facility

1. Royan Institute for Reproductive Biomedicine (RI-RB)
2. Royan Institute for Stem Cell Biology and Technology (RI-SCBT)
3. Royan Institute for Biotechnology (RI-B)
4. Laboratory Animal Core Facility

Royan Institute for Reproductive Biomedicine (RI-RB)

Royan Institute for Reproductive Biomedicine, founded in 1991, consists of six departments and one infertility clinic actively working on different aspects of infertility and the development of new methods for infertility treatment. Its vision is to improve the population's health through infertility treatments and giving infertile families the hope of having children.

In this regard, RI-RB's mission is to research on different aspects of infertility and its treatment in order to increase the success rate alongside improving embryo health.

RI-RB Departments

- Endocrinology and Female Infertility
- Andrology
- Embryology
- Reproductive Genetics
- Epidemiology and Reproductive Health
- Reproductive Imaging
- Infertility Clinic

For more communication between basic sciences and clinics, there are also four subgroups:

- Polycystic Ovary Syndrome (PCOS)
- Oncofertility
- Recurrent Implantation Failure (RIF)
- Premature Ovarian Failure (POF)



- Establishment of cell therapy pre-hospital (2011)
- Establishment of Stem Cell Bank (2011)
- The first healthy child birth after Molecular PGD for beta-thalassemia in Iran (2012)
- Birth of eight cloned goats through the simplified method of SCNT in Iran (2013)
- Birth of the first cloned wild ram as an endangered species in Iran (2015)

Royan Institute for Reproductive Biomedicine (RI-RB)

Endocrinology and Female Infertility Department of RI-RB

History and Introduction

This department was established in 1995, and began to research on new strategies and advanced methods for the diagnosis and treatment of female infertility and recurrent abortion with the intent of increasing implantation rates.

Goals

- Evaluation and treatment of infertile couples
- New guidelines for improving IVF outcomes
- Achieving new strategies for diagnosing infertility causes
- Ovulation induction and COH
- Improving methods for oocyte and embryo culture
- Endometrial preparation
- The promotion of prenatal care



Articles

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Andrology Department of RI-RB

History and Introduction

This department was established in 1995 and started to research on male infertility factors. The first step in infertility management is to evaluate the couple. Male factor infertility accounts for approximately 50% of all infertility cases. Thus in order to study male factor infertility it is necessary to use appropriate diagnostic and therapeutic techniques. The intent of this research department is to develop new diagnostic methods and treatment for male factor infertility.

Goals

- Determining the etiology of spermatogenesis, sperm function and ejaculation disorders
- Determining the etiology of azoospermic, genetic, and maturation disorders
- Determining the etiology of dry and retrograde ejaculation

Main Activities

- Improving diagnostic and therapeutic methods
- Determining the etiology of spermatogenesis, as well as functional and ejaculation disorders



Articles

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Embryology Department of RI-RB

History and Introduction

The Department of Embryology, founded in 1995, is a part of Royan Institute's Reproductive Biomedicine. During the preceding decade, a fundamental description of human and animal experimental studies has emerged in the field of embryology.

The Main Focuses

- Increasing the quality of gametes and embryos
- Studying molecular aspects of gamete maturation and embryo development
- Performing embryo co-culture with various types of somatic cells
- Studying molecular aspects of gamete and embryo freezing
- In vitro maturation of animal and human gametes
- Evaluating molecular and cellular events of embryo implantation
- Three-dimensional culture of cells to design an endometrial biomodel



- Three-dimensional culture of follicles in order to acquire good quality oocytes
- Performing nuclear transfers
- Performing animal cloning and transgenesis
- Finding the best method for preserving gametes, ovarian, and testicular tissues

Goals

- Increasing the number of high quality human embryos
- Producing transgenic animals with selected genes
- Establishing in vitro human follicle culture following ovarian tissue cryopreservation



The mission of the RI-RB Embryology Department is to perform multiple research activities regarding different aspects of fertility preservation and different treatments of infertility in order to improve embryo health and increase the pregnancy success rate.

Its aim is to make the wish of having children for infertile couples come true, and to give them a promising future.

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Reproductive Genetic Department of RI-RB

History and Introduction

Department of Genetics was established in 2001. Some routine activities of this department include: genetic counseling, lymphocyte karyotyping, preimplantation genetic diagnosis (PGD), as well as molecular diagnostic tests which involve the diagnosis of Y chromosomal deletions and certain mutations in candidate genes that may be related to the causes of abortions or failed ART.

The major research interests in this department are genetic causes of male and female infertility, recurrent spontaneous abortion (RSA), genetic factors leading to azoospermia, mutations leading to congenital agenesis of the vas deferens, preimplantation genetic diagnosis, pharmacogenetics plus epigenetic and gene expression profiles of early embryogenesis.

The production of recombinant proteins by genetic manipulation in different host cells in addition to the joint production of transgenic animals in a mutual project with Embryology Group is another main activity of this department. Activities carried out in collaboration with Royan Institute for Stem Cell Research are karyotyping of stem cell lines following various manipulations, epigenetic and genetic studies of stem cells and iPS cells, in addition to other common research interests.





Goals

- To improve implantation rates along with health of embryos by preimplantation genetic screening and diagnosis
- To assist physicians with prescribing medicine for controlled ovarian stimulation via pharmacogenetics
- Genetic follow up of newborns conceived by ART
- Evaluation of candidate genes related to recurrent abortion in the Iranian population
- Epigenetic studies of oocytes, sperm and embryos

The mission of the Genetic Department is basic research on genetic and epigenetic factors that may influence fertility, embryo development, and implantation, bringing these research results to the clinical setting with the purpose of improving the health of patients and newborns, as well as the production of pharmaceutical proteins through transgenic animals.

The vision of this department is to perfect diagnosis and treatment of infertility based on reproductive genetic knowledge, which will lead to healthy newborns in a short period of time.

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Epidemiology and Reproductive Health Department of RI-RB

History and Introduction

The Epidemiology and Reproductive Health Department was established in 1999 with the aim of doing extensive researches on epidemiological aspects of infertility and reproduction in addition to reproductive and sexual health. This department cooperates with five other research groups in Royan as research methodologist or statistical analyzer. One section has been recently established in this department called Royan Center of professional services for quantitative and qualitative studies, its job is to offer the professional services for methodology and research analysis to local groups and other researchers beyond Royan Institute as a commercial sector. This department undertakes multicenter research between Iran and other countries in the following areas:

- Frequency, incidence and influencing factors for all subfertility and infertility types
- Environmental and occupational factors affecting fertility and reproduction
- Psychosocial issues affecting infertile couples, their treatment and coping mechanisms
- Experiences, quality of life, marital and sexual satisfaction of infertile couples, even after IVF failure
- Ethical issues, legislation and guidelines in assisted reproduction
- Statistical models and methods for research in reproduction, genetics and the cellular and molecular fields
- Animal ethics

The mission of this department is the promotion of reproductive health in Iran which is an important aspect of general health and involves people of all ages within the society, from an embryo to the elderly. Focusing on sexual and reproductive health guarantees the future health of society by ensuring healthy children and healthy adults. Finally, its job involves research into all reproduction related areas including social, medical, psychological and ethical issues, and therefore its vision is to ensure the health of the society.

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Reproductive Imaging Department of RI-RB

History and Introduction

Reproductive Imaging Department was established in 2008 to focus on infertility assessment as well as evaluation of pregnancies in both clinic and research fields.

During the last two decades, dynamic advances have been made in the evaluation and treatment of infertility. Imaging technique has been a significant breakthrough in the diagnosis and management of infertility. A broad range of imaging techniques, from the old and proven - such as hysterosalpingography- to the latest and cutting edge - such as three-dimensional hysonostero-graphy, has been employed.

After applying these advanced techniques in this department, we are able to upgrade the management of infertility and obstetric care, and thereby, positively provide better services for infertile couples.

The main goal of imaging department is to provide comprehensive evaluation of infertility using the latest knowledge and innovative research in order to provide the highest quality of infertility management and to monitor emergency obstetric care.



The mission of this research department is to expand clinical and fundamental research in reproductive imaging in order to provide modern strategies and improve clinical services for infertile couples.

The main aim of these projects classified as:

- Diagnostic accuracy investigation of imaging modalities (hysterosalpingography, hysterosonography and three-dimensional ultrasound)
- Role of imaging in (male & female) infertility management
- Fetal screening
- Measurement standards/ultrasound measurement charts appropriate for Iranian fetuses

The vision of this department is performing national and international multicentral researches and having collaboration with universities and other infertility centers to provide educational courses in diagnostic ultrasound including transvaginal, color

Doppler, power Doppler, 3D/4D imaging and radiology for radiologist, gynecologist and fellowships.

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Royan Institute for Stem Cell Biology and Technology

History and Introduction

Royan Institute for Stem Cell Biology and Technology (RI-SCBT), formerly known as the Department of Stem Cells was first established in 2002 to promote research on general stem cell biology in Iran. Thereafter, Department of Stem Cells expanded to sixteen main research groups that conduct studies on stem cells and developmental biology and molecular systems' biology. Moreover Department of Regenerative Medicine consists of five main research groups which conduct research focused on translational and clinical studies using cell therapy. Throughout, the vision of RI-SCBT has been to make stem cell research findings applicable in disease treatment to improve public health. Therefore, today, RI-SCBT is providing a comprehensive and coordinated "bench to bedside" approach to regenerative medicine, as well as a greater understanding of fundamental biology of stem cells, developmental biology, development of translational research of stem cell therapeutics and administration of new cell-therapy approaches that can restore tissue function to patients.





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Royan Institute for Biotechnology

History and Introduction

In 2004, the late Dr Kazemi Ashtiani, the founder of Royan Institute, along with Dr Nasr- Esfahani established Royan Institute for Biotechnology, as the first research branch of Royan Institute, in Isfahan Province. Their goal were advancing research in reproduction, development, cell and molecular biology, in addition to the fields of bioengineering and reproductive technology.

At present, this branch homes around 100 researcher and students working in 5 groups to expand the science over their areas. Therefore over the time the below subgroups and laboratory were established.

- Cellular Biotechnology- Laboratory of Genetics
- Cellular Biotechnology- Laboratory of Stem Cell Biology and Tissue Engineering
- Molecular Biotechnology- Laboratory of Recombinant Protein and Nano-Biotechnology
- Reproductive Biotechnology- Laboratory of Andrology
- Reproductive Biotechnology- Laboratory of Embryology

This Institute has focused on somatic cell nuclear technology (SCNT) of farm animal, interspecies-SCNT, transgenesis, novel sperm selection methods for assisted reproductive technology, male infertility, production of recombinant proteins, neuro-degenerative disease, RNA biology, cancer and stem cell biology, tissue engineering and nano-biotechnology. The endeavors of Royan Institute for Biotechnology have made us the pioneer of animal cloning in Iran and the Middle East. Therefore, this Institute is well known for its cloned animals, Royana and Hanna, the first cloned sheep and goat in Iran. It is of note that SCNT in goat has reached an efficacy that it is commercialized.

The intensive seminar schedule in each group has encouraged interactivity and opportunity for scientific discussion between students and the scientists to facilitate the progress of science in their filed. Therefore, in 2010 through this interactive science, this department has achieved a number of important goals, including establishment of zona free somatic cell nuclear transfer (SCNT) in goat, evaluation of epigenetic modifier on outcome of SCNT and vitrified embryos, introducing novel approach for selection of intact sperm for ICSI based on sperm functional characteristics, understanding the role of embryonic structure in neurogenesis and cardiogenesis, assessment of the role of PEP (a peroxisomal protein) and PPAR γ in neurogenesis and finally role of biotechnology in production of biological products. Royan Institute for Biotechnology also offers PhD and MSc post graduate courses with university of Isfahan and ACECR



Institute of Higher Education (Isfahan Branch) in the fields of developmental biology and cell and molecular biology, respectively.

The institute's vision is to attain new heights in biotechnology research, shaping biotechnology into a premier precision tools of the future, for creation of wealth, ensuring social justice and efficiently bridging science with daily life.



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Animal Core Facility

Introduction

The Laboratory Animal Science Core Facility of Royan Institute plays a national role in education of scholars performing ground researches on experimental animals, by organizing proficient gadget in all categories within the animal research fields. Each center has three major activities:

- Maintenance and breeding the animals
- Creating animal models with surgical manipulations or chemical interactions
- Research and develop animal modeling

Scientists of this service unit facility who are responsible for the design of animal experiments have to be graduated in Veterinary Medicine or one of biomedical science fields and must have taken a course on laboratory animal science which concentrates on humane and gentle handling of animals. They also should be aware of knowledge of alternative routes and ethical aspects of animal experimentation.

Modern laboratory animal science builds on the three Rs of Russell & Burch:

- Replacement: Replace animal experiments with alternatives whenever possible
- Reduction: Reduce the number of experiments and number of animals in each experiment to an absolute minimum
- Refinement: Refine experiments so that the animals undergo a minimum of discomfort

The primary aim of the Laboratory Animal Facility is to ensure that the three Rs are followed in practice.



Goals

- Providing quality care for all animals used at Royan Institute
- Assisting researchers in their mission of quality research with respect to humane use of laboratory animals
- Providing researchers with a relevant education to enable them achieve scientific eminences in selected areas
- Producing, supporting and maintaining laboratory animals required for research
- Managing the animal care and having commitment to them
- Managing a preventive medicine program for disease control
- Advising research departments on all aspects of experimental use of animals, including experimental design, surgical, pre and post-operative care, oocyte and embryo harvesting, and experimental animal modeling establishment

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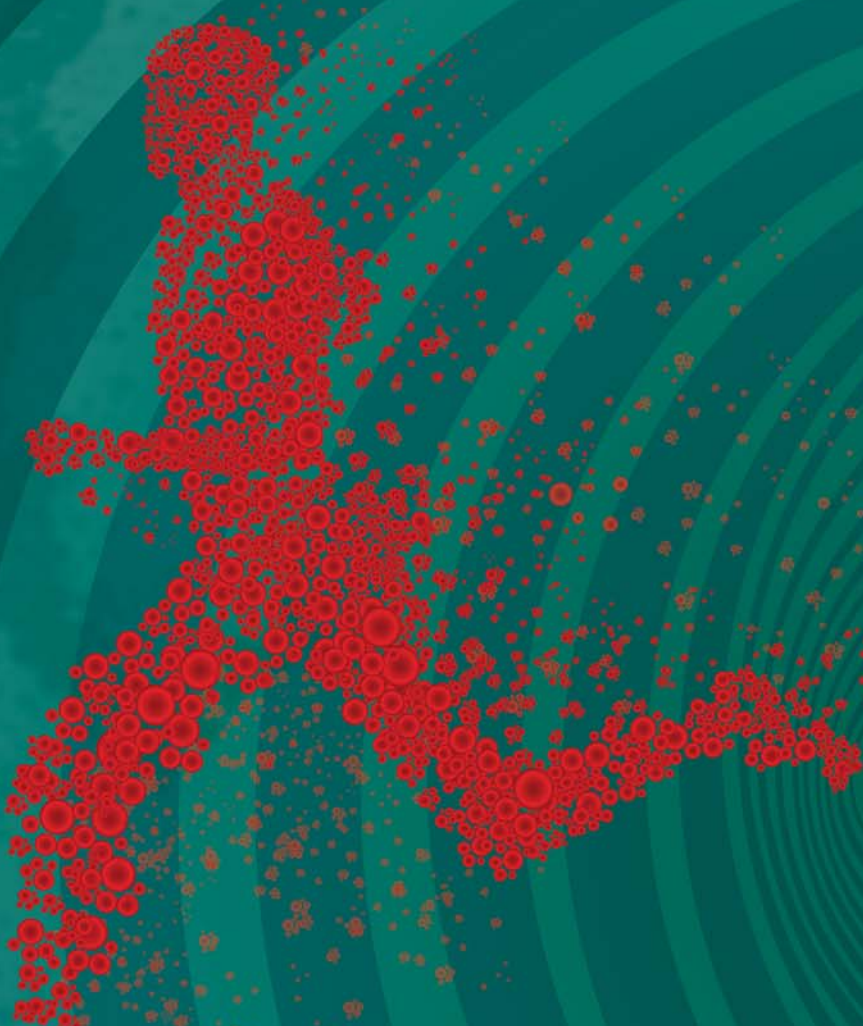


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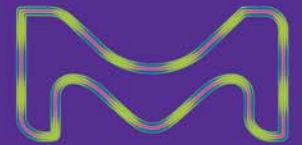
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2. Loumaye E, et al. *Hum Reprod* 1996;11(Suppl 1):95-107.
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