ROYAN INSTITUTE

THE FIFTEENTH ROYAN INTERNATIONAL RESEARCH AWARD

Reproductive Biomedicine & Stem Cell

SEPTEMBER 2014

TEHRAN - IRAN

THE SIXTEENTH

ROYAN

INTERNATIONAL RESEARCH AWARD

Reproductive Biomedicine & Stem Cell

Deadline for Application: April, 2015

Kazemi Prize, 2015

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

SEPTEMBER, 2015

TEHRAN - IRAN

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I. R. IRAN
TEHRAN

In the name of

GOD

The Fifteenth

ROYAN

INTERNATIONAL RESEARCH AWARD

Dr Saeid Kazemi Ashtiani

The Late Founder of ROYAN Institute

Cover Legend:
Cluster of Cardiac Stem Cells After Differentation into Cardiomyocytes
Photographer: Sadaf Vahdat

ACECR
Iranian Academic Center for Education, Culture and Research (ACECR)

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FOREWORD

On behalf of the Iranian Academic Center for Education, Culture and Research (ACECR) it is my pleasure to announce that Royan Institute founded by the late Dr Saeid Kazemi Ashtiani has evolved into a source of pride for Iran. Royan international research award also as a prestigious international scientific program on reproductive biomedicine and stem cell biology and technology gets closer to the ACECR goals and thereby approaches Royan objectives in developing science and extending international collaborations as well.

Hereby, I appreciate my colleagues in Royan Institutes as well as the scientific and Jury board whose endeavors led this scientific event to a success. I firmly believe, such scientific event will remind the memory of Dr Saeid Kazemi.

Tayyebi HR, PhD
President of Academic Center for Education, Culture and Research (ACECR)

INTRODUCTION

I am so delighted for holding Royan 15th International Research Award this year. Royan award was founded by the late Dr Saeid Kazemi Ashtiani with the chief aim of encouraging young researchers from worldwide for their efforts to progress sciences and also establishing relationship between these researchers and their Iranian counterparts. This esteemed event requires the participants' trust which can be fulfilled by a fair evaluation of the submitted projects by the national and international jury board. Fortunately, during the previous awards even the participants whose projects were almost scored approximately to the winners' confirmed the fairness of the jury process and had no objection. We hope to improve this confidence every year.

This year, award secretariat has received 223 projects from about 42 countries, 216 projects of which were recognized to reach the second stage of evaluation; 109 projects in the field of stem cell biology and technology as well as regenerative medicine and 107 related to reproductive biomedicine. In reproductive biomedicine most of the projects were shared among different groups.

Evaluation of the projects was hold in two stages; one according to innovation score plus impact factor of the journals which the projects were published in, and the other getting scored by national and international juries. Finally, the results get precisely reviewed in specialist groups and reported to scientific council of the institute to make the final decision.

Despite busy schedule, 145 national and international referees acted in award jury board this year, to whom my greatest thanks goes.

Holding an accurate award requires continues efforts of award executive committee, representatives of scientific groups as well as their directors to whom I express my sincere appreciation. I also would like to thank the invited speakers for their presence in Royan 15th International Congress which is held alongside Royan prize award ceremony. I hope the scientists attending the congress will be the messenger of peace and Iranian friendship to the people in the world. Hope to hold the next award with participation of more young scientists from all the nations of the world!

Gourabi H, PhD
Award Chairman and Royan Institute President

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 nine scientific groups: female infertility, reproductive genetics, epidemiology, ethics, embryology, andrology, reproductive imaging, stem cell biology and technology 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 at most 5 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 has been discussed in the board of juries and their decisions have been 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 September every year and will 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 | September 2000 | Received Papers: 72

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 Ratein Women with Clomiphen Resistant PCOS

- **Mohammad Ebrahim Parsanezhad**
  Section of the Cervical Septum Doesn't Impair Reproductive Outcome

The Second Royan International Research Award | September 2001 | Received Papers: 78

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

The Third Royan International Research Award | September 2002 | Received Papers: 212

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-Protmine-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 Salpingoovolysis. 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

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

The Fourth Royan International Research Award | September 2003 | Received Papers: 222

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

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 | September 2004 | Received Papers: 199

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, Oogenesin: 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

The Sixth Royan International Research Award | September 2005 | Received Papers: 198

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 Testostrone Replacement Therapy

Iranian Winners:

- **Seyed Javad Mowla**
  The Profile of Gene Expression Changes During the Neural Differentiation of Bone Marrow Stormal Cells (BMSCs)

- **Jaleh Zolghadr**
  Pregnancy Outcome Following Laparoscopic Tubal Ligation of Hydrosalpinx Tube in Patients with Early Recurrent Abortion

  Finally, this year we got more papers and the jury procedure was more difficult. The papers were very close together in scientific level, so a hairsplitting jury procedure was needed to find out the best of them.

The Seventh Royan International Research Award | September 2006 | Received Papers: 221

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
  Opoptosis of Ejaculated Human Sperm Is Induced by Co-Incubation with Chlamydia Trachomatis Lipopolysaccaride

- 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

The Eighth Royan International Research Award | September 2007 | Received Papers: 248

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 genetics 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

The Ninth Royan International Research Award | September 2008 | Received Papers: 202

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 genetics 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 project in female infertility field

- **Federico Prefumo,** Italy
  Uterine Doppler Investigations and Trophoblast Biology in Early Pregnancy

Best research project in female infertility field

- **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

The Tenth Royan International Research Award | September 2009 | Received Papers: 253

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 genetics 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

The Eleventh Royan International Research Award | September 2010 | Received Papers: 358

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 genetics 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 Piryaei**
  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

The Twelfth Royan International Research Award | September 2011 | Received Papers: 280

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 fields

- **Hiromitsu 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 genetics 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

The Thirteenth Royan International Research Award | September 2012 | Received Papers: 169

International Winners:

Best research project in stem cell 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 project in female fertility field

- **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

Best research project in female fertility field

- **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 genetics field

- **Signe Atlmäe,** Sweden
  Interactorme 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 Winners:

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

The Fourteenth Royan International Research Award | September 2013 | Received Papers: 206

International Winners:

Best research project in stem cell field

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

Best research project in reproductive genetics & 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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3	**Al-Jefout,** Moamar	Australia	Diagnosis of Endometriosis by Detection of Nerve Fibres in an Endometrial Biopsy: A Double Blind Study
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6	**Anjos-Afonso,** Fernando	UK	CD34– Cells at the Apex of the Human Hematopoietic Stem Cell Hierarchy Have Distinctive Cellular and Molecular Signatures
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No	Name	Country	Title
22	**Cancedda,** Ranieri	Italy	From Tissue Engineering to Regenerative Medicine: Learning From Natural Tissue Healing Process
23	**Cao,** Tong	Singapore	Efficient Isolation of Bone Marrow Adipocyte Progenitors by Silica Microbeads incubation
24	**Capalbo,** Antonio	Italy	Sequential Comprehensive Chromosome Analysis on Polar Bodies, Blastomeres and Trophoblast: Insights into Female Meiotic Errors and Chromosomal Segregation in the Preimplantation Window of Embryo Development
25	**Carmina,** Enrico	Italy	Evolution of Cardiovascular Risk with Age in PCOS Women
26	**Chamayou,** Sandrine	Italy	The Use of Morphokinetic Parameters to Select All Embryos with Full Capacity to Implant
27	**Chaube,** Shail	India	An Abortive Increase of Cytosolic Free Ca2+ Level Through Ryr Channels Triggers POA-induced Abortive SEA in Rat
28	**Chene,** Gautier	France	Tubo-Ovarian Dysplasia in Relationship with Ovulation Induction in Rats
29	**Cheung,** Herman	USA	Isolation of Pluripotent Neural Crest-Derived Stem Cells from Adult Human Tissues by Connexin-43 Enrichment
30	**Chittoor,** Geetha	USA	Localization of a Major Susceptibility Locus Influencing Preterm Birth
31	**Chung,** Bon-Chu	Taiwan	Impaired Pregnancy and Misregulated Progesterone Secretion: Lessons Learned from Cyp11a1 Transgenic Mice
32	**Cooney,** Austin	USA	Epigenetic Reprogramming of the Germ Cell Nuclear Factor Gene Is Required for Proper Differentiation of Induced Pluripotent Cells
33	**Coskun,** Serdar	Saudi Arabia	Gene Expression Profiling of Granulosa Cells from PCOS Patients Following Varying Doses of Human Chorionic Gonadotropin
34	**Craciunas,** Laurentiu	UK	Carbon Dioxide Versus Normal Saline as Distension Medium for Diagnostic Hysteroscopy: A Systematic Review and Meta-analysis of Randomized Controlled Trials
35	**Craciunas,** Laurentiu	UK	Cervical Mucus Removal Before Embryo Transfer in Women Undergoing in vitro Fertilization/Intracytoplasmic Sperm Injection: A Systematic Review and Meta-analysis of Randomized Controlled Trials
36	**Darmochwal-Kolarz,** Dorota	Poland	The Expressions of Co-stimulatory Molecules Are Altered on Putative Antigen-Presenting Cells in Cord Blood
37	**Das,** Moushumi	India	Crude Bark Extract of Dysozylum Alliarium Induces Alteration in Histological Structures and VEGF-C Expression in Uterus During Days 4–7 of Gestation in Albino Rat
38	**Davis,** Richard	Netherlands	Modelling Congenital Cardiac Arrhythmias Using Pluripotent Stem Cells
39	**Del Sol,** Antonio	Luxembourg	A General Strategy for Cellular Reprogramming: The Importance of Transcription Factor Cross-Repression
40	**Deng,** Wenbin	USA	Generation and Characterization of Spiking and Non-spiking Oligodendroglial Progenitor Cells from Embryonic Stem Cells
41	**Deng,** Wenbin	USA	Generation of Novel Human Astroglial Transplants from Hesc-Derived Olig2+ Progenitors
42	**Deschepper,** Mickael	France	Pro-angiogenic and Pro-survival Functions of Glucose in Human Mesenchymal Stem Cells upon Transplantation in an Ischemic Environment
43	**D'hooghe,** Thomas	Kenya	Menstrual Endometrial Supernatant May Induce Stromal Endometriosis in Baboons
44	**Di Girolamo,** Nick	Australia	Human Limbal Epithelial Progenitor Cells Express Alphavbeta5-Integrin and the Interferon-Inducible Chemokine CXCL10/IP-10
45	**Di Nardo,** Paolo	Italy	Restoring an Adequate Number of Healthy Cardiomyocytes in Injured Hearts
46	**Diaz-Gimeno,** Patricia	Spain	The Accuracy and Reproducibility of the Endometrial Receptivity Array Is Superior to Histology as a Diagnostic Method for Endometrial Receptivity

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47	**Dirandeh,** Essa	Iran	Effect of Different Fat Supplementation on Ovarian and Uterine Responses, Metabolic Status, the Endometrial Expression of Prostaglandin Cascade Components, Growth Axis in Lactating Dairy Cows
48	**Dominguez,** Francisco	Spain	Deciphering the Human Proteomic Endometrial Signature
49	**Duailibi,** Silvio	Brazil	Tooth Tissue Engineering: The Influence of Hydrophilic Surface on Nano-Crystalline Diamonds Films for Human Dental Stem Cells
50	**Duque,** Gustavo	Australia	Pharmacological Inhibition of Ppar γ Increases Osteoblastogenesis and Bone Mass in Male C57BL/6 Mice
51	**Erceg,** Slaven	Spain	Hypoxia Increases the Yield of Photoreceptors Differentiating from Mouse Embryonic Stem Cells and Improves the Modeling of Retinogenesis in vitro
52	**Evans,** Jemma	Australia	Endometrial Alterations in IVF Cycles Are Detrimental to Pregnancy Success
53	**Fakhr Taha,** Masoumeh	Iran	Coculture with Embryonic Stem Cells Improves Neural Differentiation of Adipose Tissue-Derived Stem Cells
54	**Fan,** Zhipeng	China	Mesenchymal Stem Cells Mediated Dental Tissue Regeneration and Regulatory Mechanism
55	**Fan,** Guoping	USA	Transcriptome Dynamics of Human and Mouse Preimplantation Embryos Revealed by Single Cell RNA-Sequencing
56	**Fan,** Wufang	China	Familial Complex Chromosome Rearrangement (CCR) Involving 5 Breakpoints on Chromosomes 1, 3 and 13 in a Severe Oligozoospermic Patient
57	**Fathi,** Ali	Iran	Quantitative Proteomics Analysis Highlights the Role of Redox Hemostasis and Energy Metabolism in Human Embryonic Stem Cell Differentiation to Neural Cells
58	**Fathi,** Rouhollah	Iran	Optimal Strategy Toward Fertility Preservation: In vivo and in vitro Post-thaw Options in Gamete, Embryo and Ovarian Tissue Cryostorage
59	**Fauza,** Dario	USA	The Amniotic Fluid as a Source of Neural Stem Cells in the Setting of Experimental Neural Tube Defects
60	**Fazili,** Mujeeb	India	Pinhole Castration: A Safe, Simple & Swift Procedure to Control Stray Dog Overpopulation & Eradicate Rabies
61	**Ferreira-Dias,** Graca	Portugal	Cytokines, Ovarian Steroids and Neutrophil Extracellular Traps on Equine Endometrium: Friends or Foes?
62	**Freund,** Christian	Netherlands	Polycistronic Lentivirus induced Pluripotent Stem Cells from Skin Biopsies after Long Term Storage, Blood Outgrowth Endothelial Cells and Cells from Milk Teeth
63	**Fuentes-Mera,** Lizeth	Mexico	Characterization of Mesenchymal Stem Cell Subpopulations from Human Amniotic Membrane with Dissimilar Osteoblastic Potential
64	**Gaillard,** Afsaneh	France	Potentials of Exogenous Grafted Neurons in Synergy with Endogenous Stem Cells in Cortical Repair
65	**Gharagozloo,** Parviz	USA	Fertilixtm, a Novel Antioxidant Formulation Designed to Treat Male Infertility Emanating from Sperm Oxidative DNA Damage: Promising Preclinical Evidence from Mouse Models
66	**Ghosh,** Sourabh	India	Matrix-Embedded Cytokines to Simulate Osteoarthritis-Like Cartilage Microenvironments
67	**Gilany,** Kambiz	Iran	Metabolomics Fingerprinting of the Human Seminal Plasma of Asthenozoospermic Patients
68	**Gómez,** Ana	Spain	Gonadotropin Somatic Gene Therapy Results in Long-Lasting Circulation of Biologically Active Hormones in a Vertebrate Model System
69	**Grzmil,** Pawel	Poland	Reproductive Defects in Ube2q1 Knockout Mice
70	**Guo,** Sun-Wei	China	Overexpression of Lysine-Specific Demethylase 1 (Lsd1) in Ovarian Endometriomas and Its Inhibiton Reduces Cellular Proliferation, Cell Cycle Progression and Invasiveness
71	**Hao,** Cuifang	China	Differences in the Transcriptional Profiles of Human Cumulus Cells Isolated from MI and MII Oocytes of Patients with Polycystic Ovary Syndrome

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72	**Hashemi,** Motahare-Sadat	Iran	The Role of Fndc5 in Cellular Differentiation of Embryonic Stem Cells
73	**Hassani,** Seyedeh Nafiseh	Iran	The Augmented BMP Pluripotency Pathway via TGF-B Suppression Maintains the Ground State of Embryonic Stem Cells Self-Renewal
74	**Hatzipetros,** Ioannis	Hungary	Assessment of Cells in the Ascitic Fluid of Women with Ovarian Hyperstimulation Syndrome: The Clinical Implications for Subsequent Ovarian Malignancy
75	**Hendarto,** Hendi	Indonesia	The Effect of Bone Marrow Transplantation on Oocyte-Granulosa Cell Interaction and Follicular Development of Cisplatin-Induced Ovarian Failure in Rat
76	**Hens,** Kristien	Netherlands	Towards the Transparent Embryo? Dynamics and Ethics of Comprehensive Preimplantation Genetic Screening
77	**Ikeda,** Shuntaro	Japan	Astaxanthin as a Stress-Alleviator of Preimplantation Embryos – Its Cellular Uptake and Interaction with Mitochondria –
78	**Irez,** Tulay	Turkey	Evaluation of Sperm Selection Based on Motility in Polyvinylpyrollidone According to DNA Fragmentation, ROS Production and DNA Methylation
79	**Ito,** Hideaki	Japan	Elucidation of Proliferative Capability of Tetraploid Cells Arising from Diploid Cells Spontaneously
80	**Izadyar,** Fariborz	USA	Maturation of Spermatogenic Cells in Artificial Seminiferous Tubules
81	**Jafari,** Shahram	Iran	Improved in vitro Development of Cloned Bovine Embryos Using S-Adenosylhomocysteine, A Non-toxic Epigenetic Modifying Reagent
82	**Jahan,** Parveen	India	Do Ace I/D Gene Polymorphism Serve as a Predictive Marker for Age at Onset in PCOS?
83	**Javid,** Amaneh	Iran	Novel Biodegradable Polymer-Coated Magnetic Nanocomposite System for Targeted Drug Delivery to Human Ovarian Cancer in vitro
84	**Jin,** Fan	China	Alterations in the Frequency of Trinucleotide Repeat Dynamic Mutations in offspring Conceived Through Assisted Reproductive Technology
85	**Jones,** Rhodri	UK	Hematopoietic Stem Cell (Cd34+) Uptake of Superparamagnetic Iron Oxide Is Enhanced by but Not Dependent on a Transfection Agent
86	**Jung,** Ui-Won	Korea	Recombinant Human BMP-2 Stimulates the Osteogenic Potential of the Schneiderian Membrane: A Histometric Analysis in Rabbits
87	**Kanafi,** Mohammad	India	Transplantation of Islet-Like Cell Clusters Derived from Human Dental Pulp Stem Cells Restores Normoglycemia in Diabetic Mice
88	**Karaoz,** Erdal	Turkey	Adipose Tissue Derived Mesenchymal Stem Cells Efficiently Differentiate into Insulin-Producing Cells in Pancreatic Islet Microenvironment Both in vitro and in vivo
89	**Karimi-Zarchi,** Mojgan	Iran	Evaluation of the Effect of GnRH Agonist on Menstrual Reverse in Breast Cancer Cases Treated with Cyclophosphamide
90	**Kawano,** Yasushi	Japan	The Production of Vascular Endothelial Growth Factor, Metalloproteinase and Chemokines via Protease-Activated Receptor in Human Endometrial Stromal Cells
91	**Khan,** Khaleque	Japan	Bacterial Contamination Hypothesis: A New Concept in Endometriosis
92	**Kim,** Edward	USA	The Treatment of Hypogonadism in Men of Reproductive Age
93	**Kim,** Minyoung	Korea	Umbilical Cord Blood Therapy Potentiated with Erythropoietin for Children with Cerebral Palsy: A Double-Blind, Randomized, Placebo-Controlled Trial
94	**Klein,** Gerd	Germany	Proteolytic Activity in the Human Hematopoietic Stem Cell Niche
95	**Koh,** Eitetsu	Japan	Aberrant Methylation of the TDMR of the GTF2A1L Promoter Does Not Affect Fertilization Rates via TESE in Patients with Hypospermatogenesis
96	**Ku,** Seung-Yup	Korea	Micrornas Transfected into Granulosa Cells May Regulate Oocyte Meiotic Competence During in vitro Maturation of Mouse Follicles
97	**Kuang,** Yanping	China	Clomiphene Citrate as an Adjuvant to hMG Stimulation of the Ovaries in Mid-to-Late Follicular Phase and Subsequently Pregnancy Outcome of Frozen-Thawed Embryo Transfers

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98	**Kumar,** Dharmendra	Germany	Generation of Porcine Induced Pluripotent Stem Cells from Mcherry Expressing Fibroblasts Mediated Through Piggybac Transposon
99	**Kumar,** Sanjay	India	Human Wharton's Jelly Mesenchymal Stem Cells Plasticity Augments Scar-Free Skin Wound Healing with Hair Growth
100	**Kuo,** Yur-Ren	Taiwan	Long-Term Existence of Donor Adipose-Derived Stem Cells in the Recipient May Modulate the Vascularized Composite Tissue Allotransplantation Survival in a Rodent Model
101	**Kuo,** Yur-Ren	Taiwan	Bone Marrow-Derived Mesenchymal Stem Cells Enhanced Diabetic Wound Healing via Recruitment of Tissue Regeneration in a Rat Model of STZ-Induced Diabetes
102	**Kuo,** Yur-Ren	Taiwan	Serum Proteomic Analysis of Extracorporeal Shock-Wave Therapy Enhanced Diabetic Wound Healing in a STZ-Induced Diabetes Model
103	**Laterza,** Cecilia	Italy	Ipsc-Derived Neural Precursors Exert a Neuroprotective Role in Immune-Mediated Demyelination via the Secretion of LIF
104	**Lee,** Bonghee	Korea	Heat Shock Instructs Hescs to Exit from the Self Renewal Program Through Negative Regulation of OCT4 By Sapk/Jnk and HSF1 Pathway
105	**Lee,** Kyung-Ah	Korea	Gas6 Downregulation Impaired Cytoplasmic Maturation and Pronuclear Formation Independent to the MPF Activity
106	**Leung,** Peter	Canada	Theca-Derived BMP4 and BMP7 Down-Regulate Connexin43 Expression and Decrease Gap Junction Intercellular Communication Activity in Immortalized Human Granulosa Cells
107	**Levine,** Fred	USA	Efficient Beta-Cell Regeneration by a Combination of Neogenesis and Replication Following Beta-Cell Ablation and Reversal of Pancreatic Duct Ligation
108	**Li,** Tao-Sheng	Japan	Ex vivo Expansion of Stem Cells in Physiological Low Oxygen
109	**Li,** Ziyi	China	Effects of TET1 Knockdown on Gene Expression and DNA Methylation in Porcine Induced Pluripotent Stem Cells
110	**Li,** Gang	Hong Kong	Immortalized Human Fetal Bone Marrow-Derived Mesenchymal Stem Cell Expressing Anti-Tumor Suicide Gene for Anti-Tumor Therapy in vitro and in vivo
111	**Li,** Gang	Hong Kong	Circulating Stem Cells and Its Clinical Implications
112	**Li,** Kun	China	Inhibition of Sperm Capacitation and Fertilizing Capacity by Adjudin Is Mediated by Chloride and Its Channels in Humans
113	**Licciardi,** Frederick	USA	Using the Oocyte Donation Model to Identify Early Trophoblast Pregnenolone Production
114	**Liehr,** Thomas	Germany	Molecular Cytogenetic Aspects of Infertility with a Special Focus on Small Supernumerary Marker Chromosomes
115	**Liu,** Guei-Sheung	Australia	Differentiation of Human Adipose-Derived Stem Cells into Fat Involves Reactive Oxygen Species
116	**Luño,** Victoria	Spain	Boar Sperm Tyrosine Phosphorylation Patterns in the Presence of Oviductal Epithelial Cells: In vitro, ex vivo, and in vivo Models
117	**Mamoulakis,** Charalampos	Greece	The (TAAAA)N Polymorphism of Sex Hormone-Binding Globulin Gene Is Not Associated with Testicular Maldescent
118	**Manassero,** Mathieu	France	Bone Regeneration in Sheep Using Acropora Coral, a Natural Resorbable Scaffold, and Autologous Mesenchymal Stem Cells
119	**Markoff,** Arseni	Germany	The M2/ANXA5 Haplotype as Recurrent Pregnancy Loss Factor, Assessing Timing of Miscarriage and Partner Risk
120	**Maruyama,** Tetsuo	Japan	Identification, Isolation and Functional Analysis of Stem/Progenitor Cells in the Human Uterus
121	**Mfopou,** Josué	Belgium	Role of BMP Signaling in Pancreatic Progenitor Differentiation from Human Embryonic Stem Cells
122	**Miao,** Xiangyang	China	Genome-Wide Transcriptome Analysis Between Different Sheep Using RNA-Seq

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123	**Michaut,** Marcela	Argentina	Molecular Mechanisms of Membrane Fusion Involved in Fertilization
124	**Minguell,** Jose	USA	Combination Stem Cell Therapy for the Treatment of Severe Limb Ischemia: Results After Phase I and II FDA-Clinical Trials
125	**Moawad,** Adel	UK	Production of Good-Quality Blastocyst Embryos Following IVF of Ovine Oocytes Vitrified at the Germinal Vesicle Stage Using a Cryoloop
126	**Moeini,** Aida	Iran	The Effects of Orlistat on Insulin Resistance of Obese Women with Polycystic Ovary Syndrome
127	**Moll,** Guido	Sweden	Do Cryopreserved Mesenchymal Stromal Cells Display Impaired Immunomodulatory and Therapeutic Properties?
128	**Mondal,** Mohan	USA	Deciphering the Luteal Transcriptome: Potential Mechanisms Mediating Stage-Specific Luteolytic Response of the Bovine Corpus Luteum
129	**Monti,** Manuela	Italy	Identification of the Molecular and Cellular Mechanisms Behind the Formation of Poor Quality Immature Oocytes
130	**Motran,** Claudia	Argentina	The Role of Pregnancy-Specific Glycoprotein 1a (PSG1a) in Regulating the Innate and Adaptive Immune Response
131	**Mukherjee,** Srabani	India	Integrated Omics Approach to Understand Pathophysiology of Polycystic Ovary Syndrome
132	**Nagamatsu,** Go	Japan	Induction of Pluripotent Stem Cells Based on the Characteristics of Primordial Germ Cells
133	**Nagyova,** Eva	Czech	Lapatinib Inhibits Meiotic Maturation of Porcine Oocyte-Cumulus Complexes Cultured in vitro in Gonadotropins-Supplemented Medium
134	**Nair,** Lakshmi	USA	Biological Activity of Lactoferrin and Injectable Lactoferrin Gels
135	**Nakajima,** Hideaki	Japan	Impaired Hematopoietic Differentiation of RUNX1-Mutated Induced Pluripotent Stem Cells Derived from FPD/AML Patients
136	**Naziroğlu,** Mustafa	Turkey	Intracellular Ca21 and Antioxidant Values Induced Positive Effect on Fertilization Ratio and Oocyte Quality of Granulosa Cells in Patients Undergoing in vitro Fertilization
137	**Naziroğlu,** Mustafa	Turkey	N-Acetylcysteine Reduces Oxidative Toxicity, Apoptosis and Calcium Entry Through TRPV1 but Not TRPM2 Channels in the Neutrophils of Patients with Polycystic Ovary Syndrome
138	**Nestor,** Michael	USA	Differentiation of Serum-Free Embryoid Bodies from Human Induced Pluripotent Stem Cells into Networks
139	**Nikukar,** Habib	UK	Osteogenesis of Mesenchymal Stem Cells by Nanoscale Mechanotransduction
140	**Nixon,** Brett	Australia	Investigation of the Mechanisms by Which the Molecular Chaperone Hspa2 Regulates the Expression of Sperm Surface Receptors Involved in Human Sperm–Oocyte Recognition
141	**Nomikos,** Michail	UK	A Novel Therapy for the Treatment of Certain Forms of Male Infertility
142	**O'brien,** Fergal	Ireland	Orchestrating Osteogenic Differentiation of Mesenchymal Stem Cells – Identification of Placental Growth Factor as a Mechanosensitive Gene with a Pro-osteogenic Role
143	**O'flaherty,** Cristian	Canada	Novel Players in the Antioxidant Protection in Human Spermatozoa
144	**Ohnishi,** Yu-Ichiro	Japan	Olfactory Stem Cell Therapy for Central and Peripheral Nervous Injury
145	**Oktay,** Kutluk	USA	Safety and Feasibility of Performing Two Consecutive Ovarian Stimulation Cycles with the Use of Letrozole-Gonadotropin Protocol for Fertility Preservation in Breast Cancer Patients
146	**Omidi,** Marjan	Iran	Does Women's Age Influence Zona Pellucida Birefringence of Metaphase I I Oocytes in in vitro Maturation Program?
147	**Orihuela,** Pedro	Chile	New Biological Role of TNF-Alpha as Modulator of the Action of Estrogens and Their Metabolites in the Mammalian Oviduct

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148	**Osuga,** Yutaka	Japan	Interleukin-4 and Prostaglandin E2 Synergistically Upregulate 3beta-Hydroxysteroid Dehydrogenase Type 2 in Endometrioma Stromal Cells: Cooperation of Th2 Immune Response and Inflammation in the Development of Endometriosis
149	**Palini,** Simone	Italy	Genomic DNA in Human Blastocoele Fluid
150	**Pande,** Gopal	India	Hematopoietic Niches in Bone Marrow Stroma and During Liver Regeneration
151	**Pant,** Aditya	India	Functional Neuronal Differentiation of Human Cord Blood Stem Cells: Tool to Study the Chemical Induced Developmental Neurotoxicity
152	**Park,** Bong-Wook	Canada	Deleted in Azoospermia-Like (DAZL) Enhances in vitro-Derived Porcine Germ Cell Formation and Meiosis
153	**Parolini,** Ornella	Italy	Placenta Derived Mesenchymal Stromal Cells: From Their in vitro Characterization and Preclinical Studies Towards Perspectives in the Regenerative Medicine
154	**Pereira,** Carlos-Filipe	USA	Induction of Hemogenesis in Fibroblasts
155	**Peymani,** Maryam	Iran	Tracing Ppar γ Influence on Mouse and Human Embryonic Stem Cells Biology
156	**Pierantoni,** Riccardo	Italy	Kisspeptin Receptor, GPR54, as a Candidate for the Regulation of Testicular Activity in the Frog, Rana Esculenta
157	**Porteu,** Francoise	France	Decreased Radiotherapy-Induced Hematopoietic Stem Cell Injury and Mutagenesis by Thrombopoietin
158	**Prat,** Maria	Italy	Isolation, Characterization and Use of a Spontaneously Immortalized Multipotent Mesenchymal Cell Line Derived from Mouse Subcutaneous Adipose Tissue
159	**Price,** David	UK	Foxg1 Is Required to Limit the Formation of Ciliary Margin Tissue and Wnt/B-Catenin Signalling in the Developing Nasal Retina of the Mouse
160	**Puri,** Pawan	USA	Regulation of Spermatogenesis by the Tyrosine Phosphatase Shp2
161	**Rahimipour,** Marzieh	Iran	Effects of Different Doses of Ethanol on Sperm Parameters, Chromatin Structure and Apoptosis in Adult Mice
162	**Ramalho-Santos,** Joao	Portugal	In vitro Effects of Cationic Compounds on Functional Human Sperm Parameters
163	**Ramaswamy,** Sharan	USA	Periodontal Ligament Progenitor Cell Mechano-Biology Promoting Engineered Heart Valves
164	**Reis,** Rui	Portugal	Vascular Endothelial Growth Factor and Fibroblast Growth Factor-2 Incorporation in Starch-Based Bone Tissue-Engineered Constructs Promote the in vivo Expression of Neovascularization Mediators
165	**Relloso,** Miguel	Spain	Estradiol Impairs the Sperm Th17 Induction
166	**Richards,** Peter	Switzerland	Therapeutic Potential of Adipose-Derived Stromal Cells in Age-Related Osteoporosis
167	**Ringdén,** Olle	Sweden	Fetal Membrane Cells for Treatment of Steroid-Refractory Acute Graft-Versus-Host Disease
168	**Ringe,** Jochen	Germany	Transdifferentiation of Mesenchymal Stem Cells-Derived Adipogenic-Differentiated Cells into Osteogenic- or Chondrogenic-Differentiated Cells Proceeds via Dedifferentiation and Have a Correlation with Cell Cycle Arresting and Driving Genes
169	**Rizzoti,** Karine	UK	Mobilized Adult Pituitary Stem Cells Contribute to Endocrine Regeneration in Response to Physiological Demand
170	**Rogers,** Ian	Canada	Donor Blood Cells Can Obtain Recipient Mhc-Class 1 Through Trogocytosis and Are Protected from NK Cell Mediated Killing
171	**Rousseaux,** Sophie	France	Male Genome Programming, Infertility and Cancer
172	**Ruan,** Yechun	Hong Kong	Activation of The Epithelial NA+ Channel Triggers Prostaglandin E2 Release and Production Required for Embryo Implantation
173	**Sadeghi,** Behnam	Sweden	Early-Phase GVHD Gene Expression Profile in Target Versus Non-Target Tissues: Kidney, a Possible Target?

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174	**Sakellari,** Ioanna	Greece	Chronic Graft-Versus-Host-Disease as a Major Cause of Morbidity and Mortality in Allogeneic Haematopoietic Cell Transplantation
175	**Salehpour,** Saghar	Iran	A Two Purpose Use of Orlistat in Obese Women with Polycystic Ovary Syndrome: Weight Loss and Androgen Reduction
176	**Salgado,** Antonio	Portugal	Stem Cells Secretome and Tunable Hydrogel Based Biomaterials in Spinal Cord Injury Repair
177	**Sánchez Pozo,** Maria	Spain	Proposal of Guidelines for the Appraisal of Semen Quality Studies (SEMQUA)
178	**Sanchez-Ramon,** Silvia	Spain	New Decision-Tree Model for Defining the Risk of Reproductive Failure
179	**Sawada,** Kenjiro	Japan	Targeting Interleukin-6 Receptor Inhibits Preterm Delivery Induced by Inflammation
180	**Sazonova,** Antonina	Sweden	Neonatal and Maternal Outcomes Comparing Women Undergoing Two in vitro Fertilization (IVF) Singleton Pregnancies and Women Undergoing one IVF Twin Pregnancy
181	**Scaruffi,** Paola	Italy	Mitochondrial DNA Content in Embryo Culture Medium Is Significantly Associated with Human Embryo Quality
182	**Schatten,** Gerald	USA	Elongating and Elongated Spermatids Manufactured in vitro from Non-human Primate Pluripotent Stem Cells
183	**Schrepfer,** Sonja	Germany	Immunological Properties of Extraembryonic Human Mesenchymal Stromal Cells Derived from Gestational Tissue
184	**Schwarz,** Carolin	Germany	Mechanical Load Modulates the Stimulatory Effect of BMP2 in a Rat Nonunion Model
185	**Shahrokhi,** Somayeh	Iran	Tumor Necrosis Factor-A/CD40 Ligand Engineered Mesenchymal Stem Cells Greatly Enhanced the Anti-tumor Immune Response and Lifespan in Mice
186	**Shahryari,** Alireza	Iran	Two Novel Splice Variants of SOX2OT, SOX2OT-S1, and SOX2OT-S2 Are Coupregulated with SOX2 and OCT4 in Esophageal Squamous Cell Carcinoma
187	**Shi,** Zhendan	China	Immunoneutralization of Inhibin Alpha Subunit as a Tool for Improving Farm Animal Fertility
188	**Singh,** Ajeet	USA	SOX8 Regulates Permeability of the Blood-Testes Barrier That Affects Adult Male Fertility in the Mouse
189	**Singh,** Sheila	Canada	Foxg1 Interacts with Bmi1 to Regulate Self-Renewal and Tumorigenicity of Medulloblastoma Stem Cells
190	**Souza-Fabjan,** Joanna Maria	Brazil	Optimization of in vitro Embryo Production (IVP) on Goat Species
191	**Spits,** Claudia	Belgium	Microarray Analysis in Normally Developing Day-3 and Day-4 Human Embryos
192	**Srivastava,** Neeraj	India	Studies on Sequestration of PDC-109 Protein on Cryodamage and in vitro Fertility of Crossbred Bull Spermatozoa
193	**St. John,** Justin	Australia	Mitochondrial DNA Haplotypes Define Gene Expression Patterns in Pluripotent and Differentiating Embryonic Stem Cells
194	**Steyn,** Leah	USA	Oxytocin Stimulated Release of PGF2 and Its Inhibition by a Cyclooxygenase Inhibitor and an Oxytocin Receptor Antagonist from Equine Endometrial Cultures
195	**Sun,** Woong	Korea	Function of Ezrin-Radixin-Moesin Proteins in Migration of Subventricular Zone-Derived Neuroblasts Following Traumatic Brain Injury
196	**Sung,** Hak-Joon	USA	Peptide-Functionalized Injectable Polymers Regulating Angiogenesis and Inflammation in Peripheral Artery Disease
197	**Talebi,** Ali Reza	Iran	The Effect of Zinc Oxide Nanoparticles on Mouse Spermatogenesis
198	**Tao,** Feng	USA	A Novel Stem Cell Therapy for Spinal Cord Injury-Induced Chronic Neuropathic Pain
199	**Tata,** Laila	UK	Occurrence of Fertility Problems Presenting to Primary Care: Population-Level Estimates of Clinical Burden and Socioeconomic Inequalities Across the UK
200	**Teoh,** Swee-Hin	Singapore	Evaluation of Polycaprolactone-Based Scaffolds Designed for Cranial Reconstruction with Brain Tissue Following Traumatic Brain Injury

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201	**Verma,** Paul	Australia	Cryopreservation and Long-Term Maintenance of Bovine Embryo-Derived Cell Lines
202	**Vicini,** Elena	Italy	Novel Stage Classification of Human Spermatogenesis Based on Acrosome Development
203	**Viville,** Stéphane	France	Assisted Oocyte Activation Overcomes Fertilization Failure in Globozoospermic Patients Regardless of the DPY19L2 Status
204	**Walczak-Jedrzejowska,** Renata	Poland	Semen Analysis Standardization in Polish Laboratories
205	**Wang,** Yongxiang	USA	Foxo3a Contributes to the Reprogramming Process and the Differentiation of Induced Pluripotent Stem Cells
206	**Wang,** Ronald	Hong Kong	Anti-angiogenesis of Green Tea and Potentials of Prodrug of Epigallocatchin-3-Gallate (Pro-Egcg) as a Novel Anti-angiogenesis Agent for Endometriosis
207	**Wang,** Xiao Qi	Hong Kong	Hematopoietic Chimerism in Liver Transplantation Patients and Hematopoietic Stem/Progenitor Cells in Adult Human Liver
208	**Weitzer,** Georg	Austria	In vitro Maintenance of Cardiac Stem Cells, Their Characterization, and Their Application in the Characterization of New Cardiogenic Drugs
209	**Wilhelm,** Dagmar	Australia	Micrornas-140-5p/140-3p Modulate Leydig Cell Numbers in the Developing Mouse Testis
210	**Woodward,** Elizabeth	USA	Endometrial Inflammatory Markers of the Early Immune Response in Mares Susceptible or Resistant to Persistent Breeding Induced Endometritis (Pbie)
211	**Wu,** Zhenfang	China	Effects of Donor Fibroblast Cell Type and Transferred Cloned Embryo Number on the Efficiency of Pig Cloning
212	**Yamada,** Yoichi	Japan	Clinical Application Outcome and the Long-Term Prognosis by Stem Cell Therapy, and the Prospective View
213	**Yang,** Xuebin	UK	Bone Tissue Engineering Using a Combination of Polymer/Bioglass® Composites with Human Adipose Derived Stem Cells
214	**Yang,** Li-Guo	China	Improved Sperm Injection Outcomes by Combining Sperm Capacitation with Removal of the Sperm Acrosome and Plasma Membrane
215	**Yang,** Zheng-Wei	China	Long-Term Effect of Vasectomy on Spermatogenesis in Men: A Morphometric Study
216	**Ye,** Zhaoyang	China	Mesenchymal Stem Cells Downregulate Articular Chondrocyte Differentiation in Noncontact Coculture Systems: Implications in Cartilage Tissue Regeneration
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WINNERS

INTERNATIONAL WINNER

Reproductive Genetics & Andrology

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Research Director at INSERM (French National Institute of Health and Medical Research). Director of the EpiMed translational research – Bio-informatic activity at INSERM-UJF Unit 823, IAB Institute, Grenoble University in France. Education, degrees and curriculum: MD in 1990, internship and specialty (Medical Biology) in Grenoble University Hospital (1990-1995). PhD degree in 1995 (meiotic segregation in male chromosomal translocation carriers). Post Doc in Human Genetic lab of Sue Povey (UCL, London; 1995-1996). Assistant professor (1997-2006), then full professor (2006-2007) at Grenoble Medical School. Recruited at INSERM in 2007 as a full-time senior researcher (Research Director).
Main research interests: 1/ co-direction of the fundamental research project in S. Khochbin's team aiming to understand the molecular mechanisms of male genome programming. 2/ Translational research activity in 2 areas i/ male infertility (genetic and epigenetic abnormalities associated with male infertility) and ii/ cancer biology (male germ-cells genes ectopically expressed in somatic cancers).

Male Genome Programming, Infertility and Cancer

Objective: During male germ cells differentiation, genome-wide re-organizations and highly specific programming of the male genome occur. These changes not only include the large-scale meiotic shuffling of genes, taking place in spermatocytes, but also a complete "re-packaging" of the male genome in post meiotic cells, leading to a highly compacted nucleo-protamine structure in the mature sperm cells. This process is essential to protect the male genome for its journey out of the male body through the hostile environment of the female organism, as well as to prepare its rapid activation after fertilization. Although it is a critical step for successful reproduction in most species, nearly nothing is known on the molecular basis of this process. Our objective is to identify molecular actors driving male genome programming and functionally characterize their roles.

Results: Early post-meiotic cells, round spermatids, inherit a haploid genome associated with histones, in a somatic-like nucleosome based chromatin, which then undergoes a genome-wide reorganization associated with the replacement of histones by protamines. Our work during the last 12 years has unravelled several key molecular mechanisms involved in this formidable remodelling of the genome. Our initial investigations were based on two observations. First, several specific histone variants are expressed and incorporated into the chromatin of male germ cells. Second, a genome-wide histone hyperacetylation wave occurs in elongating spermatids (HazzouriEJCB2000_pmid11152286; FaureMHR2003_pmid14614037), which precedes their removal and replacement by transition proteins and protamines. Combining proteomic and bioinformatics screens (RousseauxSBiRM2012_pmid22788531), we identified several candidate factors. In depth characterization of these factors involved structural and molecular approaches, as well as the use of genetically modified mouse models. One of our major findings regarding the role of histone acetylation is that Brdt, a double bromodomain containing testis specific member of the BET family, guided by acetylated chromatin, is playing essential roles in the stage-specific programming of the male genome (PivotPajotMCB2003_pmid12861021; MoriniereNature09_pmid19794495; GaucherEMBOJ12_pmid22922464). Recently, our investigation of the role of the histone acetyl transferases (HAT) p300 and CBP in post-meiotic cells, using a double conditional KO mouse model, highlighted their role in the control of a late post-meiotic gene expression program involved in the metabolic remodelling of male germ cells (Boussouar_Andrology14_pmid24522976). We also unravelled the role of testis-specific variants in the programming of pericentric regions, as well as in specifically preparing chromatin for post-meiotic packaging, and for post-fertilization events (GovinJCB07_pmid17261847; WuJRD08_pmid18703863; MontellierGenesDev2013_pmid23884607). Our lab is also involved in collaborative studies with Pr Y.M. Zhao's lab, leading to the discovery of a large panel of new histone modifications, hugely enlarging the so-called "histone code", and increasing our understanding of their role in male genome programming (TanCell11_pmid21925322; DaiNCB14_pmid24681537).

Conclusion: We are now in a position to propose the first molecular models explaining male genome programming (Goudarzi_JMB2014_pmid24613302). Medical applications are described below in "Project application and usage".

Keywords: Male genome; Epigenetics; Infertility; Chromatin; Spermiogenesis

WINNERS

INTERNATIONAL WINNER

Ethics

Towards the Transparent Embryo? Dynamics and Ethics of Comprehensive Pre-implantation Genetic Screening

Objective: To study the ethical aspects of comprehensive preimplantation genetic screening (PGS) through microarrays and whole genome sequencing.

Results: The increasing complexity and amount of information yielded by comprehensive testing techniques will lead to challenges to the principle of reproductive autonomy and the right of the child to an open future. Furthermore, it may complicate the responsibility of the clinician regarding the welfare of the future child, and may lead to conflicts with prospective parents. Moreover, the analytic and clinical validity and the clinical utility of whole genome sequencing as a tool for embryo selection is unproven. An alternative testing approach is preconception carrier screening for a number of disorders, combined with targeted PGD for couples at high risk. This may avoid some of the ethical problems of comprehensive embryo screening. Obviously, the ethics of this alternative needs further ethical scrutiny as well. Moreover, there is a need for studies querying the opinions of infertile couples undergoing IVF/PGS regarding the desirability of embryo screening beyond aneuploidy.

Conclusion: The introduction of comprehensive screening techniques for embryo selection is premature at best and calls for further ethical reflection that is grounded in empirical work.

Keywords: PGS, Embryo Screening, Whole Genome Sequencing, Micro-arrays, Embryo Selection

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Dr Hens is a bioethicist working at Maastricht University, The Netherlands. Her research focus is on genetics and reproductive medicine. She has obtained her PhD in 2010 at the University of Louvain, Belgium, on the subject of pediatric biobanks. This PhD was the basis for guidelines for best practice of the European Society of Human Genetics (ESHG), published in their journal European Journal of Human Genetics. As a postdoctoral researcher, she focuses on the ethical issues of comprehensive embryo screening using microarrays and whole genome sequencing in the context of Preimplantation Genetic Screening (PGS) and Preimplantation Genetic Diagnosis (PGD). She particularly focuses on issues surrounding reproductive autonomy and professional responsibility and is also interested in disability studies. She lives in Leuven, Belgium.

WINNERS

INTERNATIONAL WINNER

Female Infertility

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Christiani Andrade Amorim is a veterinarian who has been working on preantral follicles for almost 20 years now. Initially, she focused on domestic animals, developing strategies to safeguard native breeds from Italy, where she worked as an associate researcher at Florence University, before moving back to Brazil, where she was appointed professor at Brasilia University. In 2007, she joined the research team of Professor Jacques Donnez at the Catholic University of Louvain, Belgium. Since then, she has been working with human preantral follicles, developing projects on cryopreservation of ovarian tissue and assembly of an artificial ovary.

New Steps Towards the Artificial Ovary

Objective: In recent years, transplantation of cryopreserved ovarian tissue has proved to be a promising approach to restore fertility in cancer patients. However, such a procedure cannot be carried out in women at risk of ovarian involvement due to the threat of reintroducing malignant cells. The aim of this study was therefore to create an artificial ovary as an alternative to restore fertility in these patients.

Results: After one week, the follicle recovery rate ranged between 30.8% (F25/T4) and 31.8% (F12.5/T1). With both fibrin formulations, all follicles were found to be alive or minimally damaged, as demonstrated by TUNEL assay, and at the growing stage (primary, secondary and antral follicles), confirmed by Ki67 immunostaining. Isolated OCs also survived and proliferated after grafting, as evidenced by less than 1% of apoptotic cells and a high proportion of Ki67-positive cells. Vessels were found in both fibrin formulations and the global vascular surface area varied from 1.35% (F25/T4) to 1.88% (F12.5/T1). Numerous CD45-positive cells were also observed in F25/T4 and F12.5/T1 combinations.

Conclusion: Our results indicate that fibrin is a promising candidate as a matrix for the construction of an artificial ovary. Xenotransplantation of isolated human follicles and OCs is the necessary next step to validate these findings.

Keywords: Fibrin, Artificial Ovary, Isolated Follicles, Cancer, Fertility Preservation, Ovarian Tissue

WINNERS

INTERNATIONAL WINNER

Regenerative Medicine

Role of Endogenous Neural Precursor Cells in Multiple Sclerosis

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Head of research at INSERM, Anne Baron-Van Evercooren is coordinator of "Development, Glial pathology and Repair" research axe (Centre de Recherche de l'Institut du Cerveau et de la Moëlle épinière, Pitié-Salpêtrière Hospital) and group leader of the team "Molecular and cellular approaches of CNS myelin repair". She studies myelin repair of de- or dysmyelinating diseases in different animal models (rodent and primate) in order to develop therapeutical strategies to promote the endogenous or exogenous repair of central myelin for patients suffering from multiple sclerosis, and some leucodystrophies. Since 1988, her major focus is on stem cell plasticity and their role in myelin repair. She was awarded with the Charles Ketelear Prize of the Belgian Society of Multiple Sclerosis in 1984, Prize of the Institut Electricité-Santé in 1996, and the NRJ Prize from the Institut de France in 2008. Knight of the Legion of Honour, Anne Baron-Van Evercooren is also teaching at Paris 6, Paris-Sud 11 and Paris 12 Universities.

Objective: In the adult brain, microenvironments that maintain a source of neural stem cells and NPCs are the SVZ of the lateral ventricle and the DG of the hippocampus. Experimental demyelination and MS, reactivate the SVZ, leading to increased proliferation, oligodendrogenesis and ectopic migration to periventricular white matter. The goal of this paper is to review the importance of specialized cellular niches showing plasticity regarding cell number, fate decision, migration and differentiation in the context of demyelinating pathologies such as multiple sclerosis (MS).

Results: Tracing studies indicate that while -B cells are the SVZ source of newly formed oligodendrocytes in normal conditions, -A and -C cells undergo a functional switch in response to demyelination to increase oligodendrogenesis. Specialized cell-cell interactions occur within the niche, suggesting ongoing communication within the different cell types and namely specialized interactions between ependymal cells and B cells. Gaining more insights in the modulation of these interactions in animal models, could help to understand how the niche is reactivated in response to inflammatory demyelination. Maintaining the balance between neural stem cells and NPCs in the SVZ niche is critical to supply the brain with specific neural populations, both under normal or demyelinating conditions. Several factors influencing SVZ homeostasis were elucidated and found to play a crucial role in regulating the balance between neural stem cells and NPCs as well as neurogenic and oligodendrogenic NPCs. Some of these mechanisms are perturbed in response to chronic inflammation leading to enhanced SVZ thickness, increased oligodendrogenesis at the expense of neurogenesis. Furthermore, -A and -B cells are vulnerable to chronic inflammation, further contributing to a diminished neuronal renewal in the OBs and resulting in olfactory deficits. A major question concerns the nature of the molecular cues involved in the correct targeting of the migrating NPCs to the OBs. These include growth factors, cell adhesion molecules, integrins, chemokines and repellents. While, growth factors and chemokines were identified as major players in ectopic recruitment of SVZ cells to lesion sites, little is known on the role of other molecular cues in directing NPCs and derivatives to the lesion site.

Conclusion: In spite of the demonstration of the adult SVZ reactivation in experimental models and MS, mobilization, differentiation and oligodendrocyte recruitment remain limited. Therefore, understanding the mechanisms regulating the biology of the stem cell niches in normal and pathological conditions could help in designing therapeutic strategies preventing the loss of NPCs and promoting their proliferation, migration and differentiation for myelin diseases such as MS.

Keywords: Adult Neural Stem Cells, Oligodendrogenesis, Myelin, Demyelination, Remyelination

WINNERS

INTERNATIONAL WINNER

Stem Cell Biology and Technology

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Milena Bellin obtained a BSc in Biological Sciences and a PhD in Genetics and Molecular Biology of the Development at the University of Padua, Italy. From 2008 to 2010, as a post-doc at the Technical University of Munich, Germany, she significantly contributed to the characterisation of isl1-positive cardiovascular progenitors both from mouse and human pluripotent stem cells. Furthermore, she actively studied the use of patient-specific human induced pluripotent stem cells to model the congenital cardiac disease type-1 long-QT syndrome. From 2011 she has joined the Leiden University Medical Centre (LUMC), the Netherlands, to derive the first cardiac isogenic pluripotent stem cell pairs for unravelling the molecular mechanisms underlying the type-2 long-QT syndrome. Since May 2014 she is a research fellow at the LUMC, using human pluripotent stem cells to study and treat congenital arrhythmias. Milena Bellin is the author of several peer-reviewed scientific papers.

Human Pluripotent Stem Cells for Modelling and Correcting Long-QT Syndrome

Objective: Long-QT syndrome (LQTS) is an electrical disease of the heart characterized by delayed cardiac repolarization, which causes prolongation of the QT interval (the distance between the Q and T peaks) on the surface electrocardiogram. Its clinical manifestations are often dramatic, with ventricular tachycardia and syncope resulting in cardiac arrest and sudden death. The LQTS variants LQT1, LQT2, and LQT3 comprise the majority documented to date. The objectives of our studies were 1) to demonstrate that human induced pluripotent stem cells (hiPSCs) are a suitable tool to recapitulate the LQT1 phenotype by studying the R190Q-KCNQ1 mutation; 2) to investigate whether elevation of the intact repolarising current IKr could effectively restore normal QT duration if KCNQ1 is mutated; 3) to study the LQT2-associated N996I-KCNH2 mutation under genetically defined conditions, by generating two genetically distinct isogenic pairs of LQT and control lines.

Results: We generated patient-specific hiPSCs from members of a family affected by LQT1 and differentiated into functional CMs. These cells recapitulated the electrophysiological features of the disorder, including prolongation of the action potential duration (APD), as compared with cells from healthy controls. Further characterization of the role of the R190Q-KCNQ1 mutation in the disease pathogenesis revealed a dominant negative trafficking defect associated with a 70% to 80% reduction in the KCNQ1-conducted IKs current and altered channel activation and deactivation properties. Furthermore, mutated CMs had an increased susceptibility to catecholamine-induced tachyarrhythmia and beta-blockade attenuated this phenotype. Next, a unique specific chemical activator for IKr that reduced voltage sensitivity of inactivation, caused a dose-dependent shortening of the APD and was able to normalize action potentials of CMs of patients with LQT1. Finally, we derived hiPSCs from a patient carrying the LQT2-associated N996I-KCNH2 mutation and corrected it. Furthermore, we introduced the same mutation in hESCs, generating two genetically distinct isogenic pairs of LQTS and control lines. Correction of the mutation normalized the IKr current conducted by the KCNH2 channel and the APD in hiPSC-derived CMs. Introduction of the same mutation reduced IKr and prolonged the APD in hESC-derived CMs. Further characterization of N996I-KCNH2 pathogenesis revealed a trafficking defect.

Conclusion: Our results demonstrate that hiPSC models recapitulate aspects of genetic cardiac diseases, including APD prolongation, altered IKs, and an abnormal response to catecholamine stimulation, with a protective effect of beta-blockade. Furthermore our studies provide both the theoretical basis and experimental support for compensatory normalization of APD by a pharmacological agent. Finally we have demonstrated that the N996I-KCNH2 mutation is the primary cause of the LQTS phenotype. Precise genetic modification of pluripotent stem cells provided a physiologically and functionally relevant human cellular context to reveal the pathogenic mechanism underlying this specific disease phenotype.

Keywords: Long-QT Syndrome; Human Pluripotent Stem Cells; KCNQ1; KCNH2; Gene Targeting

WINNERS

INTERNATIONAL WINNER

Embryology & Biotechnology

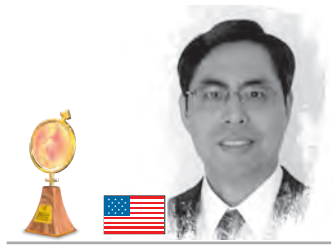
Transcriptome Dynamics of Human and Mouse Pre-implantation Embryos Revealed by Single Cell RNA-sequencing

Objective: Mammalian preimplantation development is a complex process involving dramatic changes in the transcriptional architecture. However, it is still unclear about the crucial transcriptional network and key hub genes that regulate the proceeding of preimplantation embryos.

Results: We found that each developmental stage can be concisely delineated by a small number of functional modules of co-expressed genes that are involved in the pathways of cell cycle, gene regulation, protein translation, and metabolism and mitochondrial function, respectively. Cross-species comparisons reveal that the majority of human stage-specific modules (7 out of 9) are remarkably preserved, only to diverge in developmental specificity and timing in mice. Our results shed light on the gene regulatory mechanism underlying progressive development of mammalian early embryos.

Conclusion: We have identified conserved key genes in human and mouse embryos that drive mammalian preimplantation development. When compared to exome or genomic sequencing of individual blastomeres, RNA-seq has the advantage of quantifying gene expression defects due to either genetic or epigenetic alterations. We suggest that single cell RNA-seq of a blastomere would be a valuable approach in parallel with other well established preimplantation genetic diagnosis methods

Keywords: Gene Transcription, RNA-Seq, Preimplantation Embryos, Network Analysis



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Dr. Fan has been a professor in the Department of Human Genetics at the University California Los Angeles (UCLA) since 2001. He earned his bachelor's degree in Biochemistry from Nanjing University in China and his doctorate degree in Neuroscience from Case Western Reserve University. Before joining UCLA to set up his own research lab, Dr. Fan pursued his postdoctoral training in mouse genetics and stem cell biology at the Whitehead Institute for Biomedical Research, Massachusetts Institute of Technology. Dr. Fan's laboratory focuses on addressing the molecular and cellular mechanisms underlying mammalian embryonic development and neurological diseases. He has published original papers in the prestigious journals including Nature, Science, Cell Stem Cell, Nature Neuroscience and PNAS. Among the many professional activities, Dr. Fan has served as grant reviewer for National Institute of Health, Maryland Stem Cell Research Program, Connecticut State Stem Cell Program, etc.

WINNERS

NATIONAL WINNER

Embryology

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Rouhollah Fathi was graduated from Tarbiat Modares University and finished his PhD in September 2013 in the field of anatomical sciences under supervision of professor Valojerdi with the thesis entitled "Study of ultrastructural and maturation, angiogenetic and apoptotic genes expression of rat ovarian tissue after vitrification and autotransplantation". Cryobiology of gamete, embryo and gonadal tissue was the main scientific research base during Fathi's advanced courses (MSc & PhD). Rouhollah now is working in embryology department (oocyte biology subgroup) of Royan institute and hopes to obtain a mature oocyte ready for fertilization after ovarian/follicular culture and transplantation.

Optimal Strategy Toward Fertility Preservation: In vivo and in vitro Post-thaw Options in Gamete, Embryo and Ovarian Tissue Cryostorage

Objective: Oocyte, embryo and ovarian tissue cryopreservation are proposed for fertility preservation to cancer patients who hope to be a mother after getting rid of the disease.

Results: In seven years' experience, vitrification mostly could help us to reach our scientific aims in fertility preservation. To obtain enough healthy vitrified-warmed embryos, 93.89% were considered as surviving embryos. Re-vitrifying 4-cell mouse embryos using closed pulled straw (CPS) was not discernibly detrimental to embryos. In the case of blastomere damage after vitrification, both laser assisted hatching (LAH) and necrotic blastomere removal (NBR) techniques could reduce the incidence of embryo cell death but have no significant effect on development and cell number. In comparison of different ovarian vitrification methods, because of the better primordial follicular preservation and more survivability, it appears that the combination of EG + DMSO with sucrose is better suited for vitrification of human, sheep, monkey and rat ovarian tissues, particularly at the initial stage could relatively restore ovarian function after vitrification and autotransplantation. Additionally, fewer cell death incidences occurred after 2-step dehydration procedure as compared to the 4-step vitrification method and using of therapeutic ultrasound may accelerate and increase re-angiogenesis and can help to promote ovarian follicular growth. Ultrastructural changes of the vitrified ovaries using EG + DMSO with sucrose, were considerable compared to the control but this result did not differ compared to the sucrose-free group. Both of the vitrified and nonvitrified ovarian autotransplantation caused restoration of the hormone cycle and ovarian function; these results approximated the controls after gonadectomy. In the last groups the percentage of follicular maturation and ultrastructure of transplanted ovaries were in better condition. Also the rate of expression of angiogenic factors in all of the transplanted ovaries, were comparable with the control ones (non-published data).

Conclusion: Although vitrification is a reliable method for cryostorage of gamete, embryo and ovarian tissue, now this is a challenge that: can vitrified oocyte, embryo or ovarian tissue lead to a completely health delivery? And this is the main future vision in the field of fertility preservation.

Keyword: Fertility Preservation, Cancer Patient, Vitrification, Transplantation, Culture

WINNERS

NATIONAL WINNER

Stem Cell Biology and Technology

The Augmented BMP Pluripotency Pathway via TGF-β Suppression Maintains the Ground State of Embryonic Stem Cells Self-Renewal

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Seyedeh Nafiseh Hassani (born on March 21, 1981) received her PhD degree from Royan Institute in 2012 in the field of Developmental Biology under the supervision of Prof. Baharvand. Her major research interest is signaling pathways in mouse embryonic stem (ES) cells. She and her colleagues introduced a novel, efficient method for establishing ground state ES cells from refractory strains using chemical inhibitors of the MEK and TGFβ signaling pathways. Currently, she is the chief researcher of "Biology of Pluripotent Stem Cells" group in department of stem cells and developmental biology at RI-SCBT.

Objective : Embryonic stem cells (ESCs) are pluripotent cells with capacity for differentiation into all cell types that are most frequently established from the inner cell mass (ICM) of blastocysts. However, the efficiency of ESC generation is influenced by genetic background in mice; as some strains are recalcitrance to mESC line derivation. Recently, we identified the suppression of mitogen-activated protein kinase (MAPK) kinase (also known as MEK) and transforming growth factor β (TGFβ) type I receptors by PD0325901 and SB431542, respectively-the combination named as Royan 2 inhibitors or R2i- enables the highly efficient derivation of pluripotent mouse embryonic stem cells (mESCs) from different strains. The cellular and molecular analysis indicated that R2i supports the ground state of pluripotency in a different route from well-known 2i condition which the latter inhibits MEK and glycogen synthase kinase 3 (GSK3) by PD0325901 and CHIR99021, respectively.

Results: We observed no significant changes in the morphology of ES cells and Oct4 expression in 2i-grown cells in the presence of the BMP4 signaling inhibitors, even after several passages. However, the self-renewal capability of R2i-grown cells was strongly and adversely affected over a brief time period

Conclusion: Our analysis highlighted BMP signaling as a pathway markedly induced by TGFβ inhibition in R2i-grown cells. Since several studies have indicated that BMP4 signaling through Smad1/5/8 suppresses developmental regulators such as neuroectodermal-associated genes and FGF signaling, we here demonstrated that R2i via activation of the 'differentiation-inhibiting' BMP4 signaling enhanced pluripotent state in mESCs even though this pathway seems to be dispensable in 2i culture condition.

Keyword: Embryonic Stem Cell, Pluripotency, Signaling Pathway, Small Molecule

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Dadkhah, Farid, MD	Iran
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Deng, HongKui, PhD	China
Ebner, Thomas, PhD	Austria
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Eshrati, Babak, PhD	Iran
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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

Royan Institute for Stem Cell Biology and Technology (RI-SCBT)

Royan Institute for Stem Cell Biology and Technology (RISCBT) was established in 2002 to promote research on general stem cell biology in Iran. Since early 2010, it has continued its activities in:

- Stem Cells and Developmental Biology: 16 Research Programs, 10 Core Facilities
- Regenerative Medicine : 6 Research Programs, 5 Core Facilities

RI-SCBT's vision is to efficiently put stem cell research findings into operation in disease treatment with the aim of improving health. RI-SCBT's mission is to generate insights into the biology of stem cells through basic research and to provide the foundation needed for novel therapies from regenerative medicine.

Royan Institute for Biotechnology (RI-B)

Royan Institute for Biotechnology was initially established in 2004 as the first research branch of Royan Institute. It is located in Isfahan Province, which is famous for its architecture, rivers and handcrafts, and is known as the city of "blue tiles".
Royan Institute for Biotechnology was established with the purpose of advancing research in reproduction, development, cell and molecular biology, in addition to the fields of bioengineering and reproductive technology. In this regard, this institute has focused on somatic cell nuclear technology (SCNT), interspecies-SCNT, transgenesis, establishment of novel sperm selection methods for assisted reproductive technology, cell differentiation, production of recombinant proteins and cell biology of peroxisomes. 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, and Bovana; the first calf born with IVF. Areas of interest at this institute are: gene reprogramming during SCNT, transgenesis, sperm cell biology, the role of sub-cellular organelles in differentiation and recombinant protein technology. In addition, Royan is providing a comprehensive and coordinated "bench to production" approach in recombinant protein technology, animal farming and establishing methods to increase the efficiency of assisted reproductive techniques.

RI-B Groups:

- Cellular Biotechnology- Genetic Laboratory
- Cellular Biotechnology- Stem Cell Laboratory
- Molecular Biotechnology- Recombinant Protein Laboratory
- Reproductive Biotechnology- Andrology Laboratory
- Reproductive Biotechnology- Embryology Laboratory

The institute's vision is to attain new heights in biotechnology research, shaping biotechnology into a premier

precision tool of the future for creation of wealth, ensuring social justice and efficiently bridging science with daily life.

Overview of the Institute

- The first IVF child born in Tehran (1993)
- The first ICSI child born in Tehran (1995)
- Iran's second success in open testicular biopsy to treat severe male infertility (1996)
- The first frozen embryo child born in Iran (1996)
- The first ICSI birth by frozen sperm of a gonadectomized man in Iran (1999)
- The first human embryonic stem cell line established in Iran and the region (2003)
- The first PGD child born in Iran (2004)
- First time use of adult stem cells in the treatment of MI during CABG in Iran (2004)
- Production of insulin producing cells from human embryonic stem cells (2004)
- Culture of human limbal stem cells on chorionic membrane (2004)
- Establishment of the first Private Cord Blood Bank in Iran (2005)
- The first IVM-IVF sheep born in Iran (2006)
- The first cloned sheep born in Iran (2006)
- Establishment of mouse and human induced pluripotent stem cells (iPS) (2008)
- The first cloned goat born in Iran (2009)
- A new method for treatment of Vitiligo by cell transplantation (2009)
- The first transgenic goats born in Iran (2010)
- The first calves born from vitrified in vitro developed embryos in Iran (2011)
- 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)

Royan Institute for Reproductive Biomedicine (RI-RB)

Endocrinology and Female Infertility Department of RI-RB

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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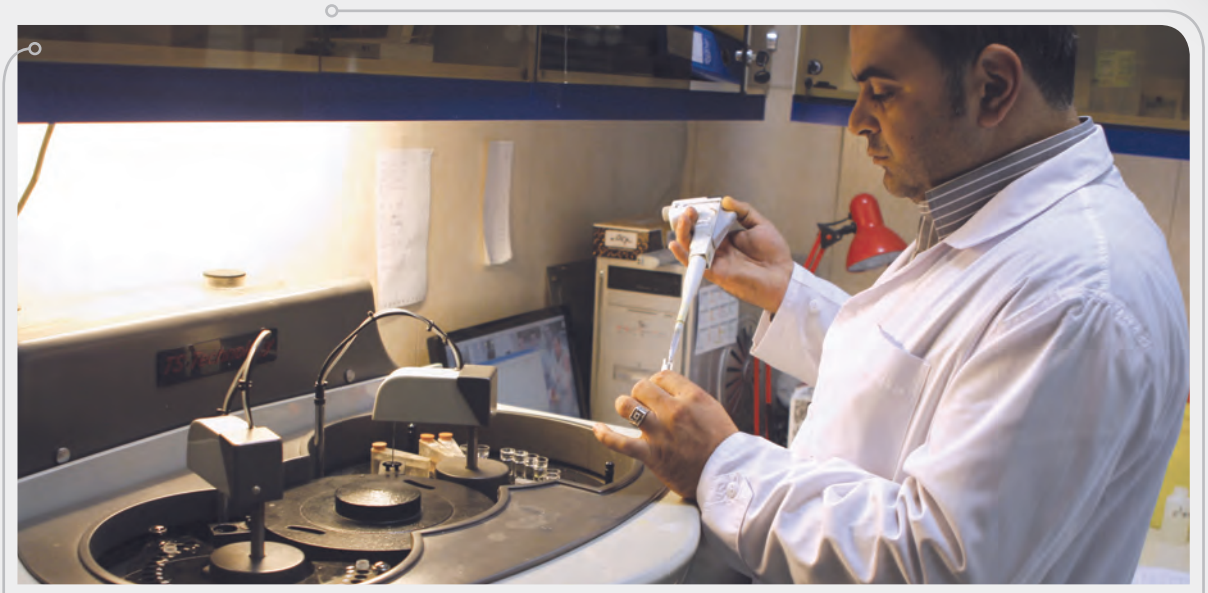
Andrology Department of RI-RB

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



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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.

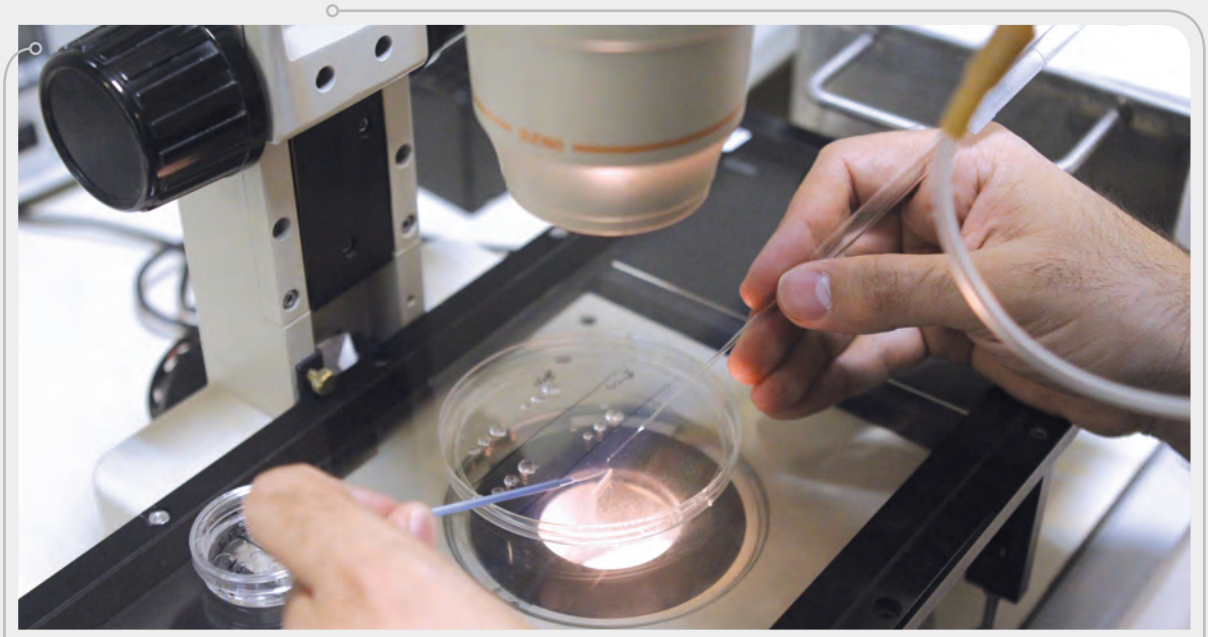
Main Focuses

- 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 the performance of multiple research 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 a promising future to them.

Articles

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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 micro 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.

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.

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

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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 is responsible to check all research proposals in Royan three research institutes and gives both methodological and statistical consultation.

This department undertakes multicentre 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.
Reproductive health 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 hysonosterography, 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 (RI-SCBT)

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 (RI-B)

History and Introduction

In 1983, the late Dr Kazemi Ashtiani, the founder of Royan Institute, along with Dr Nasr- Esfahani established Royan Institute for Biotechnology, as the third branch of Royan Research Institutes. At present, this branch homes around 100 researcher and students working in 5 departments to expand the science over their areas. The intensive seminar schedule in each department 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 results, 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, assessment of the role of PEP (a peroxisomal protein) and PPAR γ in neurogenesis and finally role of biotechnology in production of biological products.

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Laboratory 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

Articles

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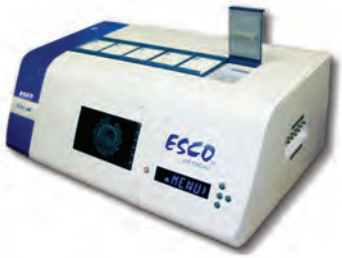

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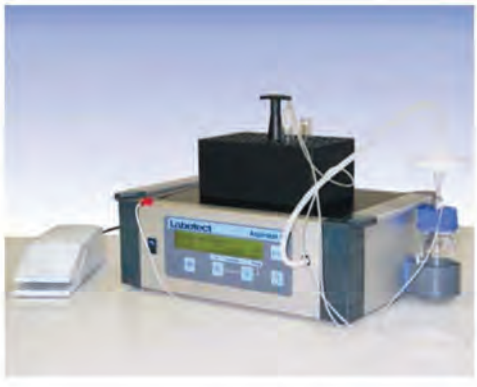

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2. Christen et al. Expert Opinion on Drug Delivery 2011.

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Each cartridge delivers either 300 IU (equivalent to 22 micrograms) in 0.5 ml. , 450 IU (equivalent to 33 micrograms) in 0.75 ml or 900 IU (equivalent to 66 microgram) in 1.5 ml **Indications:** • GONAL-f can be used to cause ovulation in women who are not ovulating and who have not responded to treatment with clomiphene citrate. • GONAL-f is used to bring about the development of several follicles (and therefore several eggs) for women undergoing assisted reproductive technologies such as in vitro fertilisation, gamete intra-fallopian transfer or zygote intra-fallopian transfer. • GONAL-f is used together with another hormone called lutropin alfa (recombinant human luteinising hormone) to cause ovulation in women who are not ovulating due to very low production of the fertility hormones (FSH and LH) by their pituitary gland. • GONAL-f is used in combination with another medicine, human chorionic gonadotrophin (hCG), to produce sperm in men who are infertile due to hormonal deficiency. **Contraindication:** • hypersensitivity to follicle stimulating hormone or to any of the other ingredients of GONAL-f • tumours of the hypothalamus and pituitary gland • ovarian enlargement or cyst not due to polycystic ovarian disease • gynaecological bleeding of unknown cause • ovarian, uterine or breast cancer • if you have irreversible testicular damage. The medicine should not be used when a condition exists which would make a normal pregnancy impossible, such as premature menopause, malformation of sexual organs or specific tumours of the womb. **Dosage & administration:** GONAL-f is administered by injection just under the skin (subcutaneous use). Women who are not ovulating and are having irregular periods or no periods at all. GONAL-f is usually given every day. The treatment should start within the first 7 days of the menstrual cycle. A commonly used dose starts at 75-150 IU FSH every day (0.12-0.24 ml). This may be increased by 37.5-75 IU at 7 or preferably 14 day intervals if necessary to obtain an adequate, but not excessive, response. The maximal daily dose is usually lower than 225 IU FSH (0.36 ml). If your doctor cannot see a response after 4 weeks of treatment, that treatment cycle should be abandoned. For the following cycle, your doctor will prescribe a treatment at a higher starting dose than in the abandoned cycle. When an optimal response is obtained, a single injection of another medicine (hCG) is administered 24-48 hours after the last GONAL-f injection. You are recommended to have sexual intercourse on the day of the administration of this second medicine and the following day. If an excessive response is obtained, treatment should be stopped and hCG withheld (see Possible side effects). For the following cycle, your doctor will prescribe a dosage lower than that of the previous cycle. Women undergoing ovarian stimulation for multiple follicular development prior to in vitro fertilisation or other assisted reproductive technologies. A commonly used dose for superovulation involves the administration of 150-225 IU (0.24-0.36 ml) of GONAL-f daily, commencing on days 2 or 3 of the treatment cycle. Treatment is continued until adequate follicular development has been achieved (as assessed by blood monitoring and/or ultrasound examination), with the dose adjusted according to your response, to usually not higher than 450 IU (0.72 ml) daily. Adequate follicular development is usually achieved on average by the tenth day of treatment (range 5 to 20 days). Then a single injection of a medicine used to induce final follicular maturation and containing 250 micrograms r-hCG or 5000 IU up to 10 000 IU human chorionic gonadotrophin (hCG) is administered 24-48 hours after the last GONAL-f injection. Women who are not ovulating, having no periods at all and have been diagnosed as FSH and LH deficient. GONAL-f is usually taken every day for up to five weeks simultaneously with injections of lutropin alfa. A commonly used dose starts with 75-150 IU (0.12-0.24 ml) of GONAL-f together with 75 IU of lutropin alfa. According to your response, your doctor may increase your dose of GONAL-f by preferably 37.5-75 IU at 7 to 14-day intervals. If your doctor does not observe a response of your ovaries after 5 weeks of treatment, that cycle should be abandoned. For the following cycle, your doctor may prescribe treatment at a higher starting dose of GONAL-f than in the abandoned cycle. When the desired response has been obtained, a single injection of 250 micrograms r-hCG or 5000 IU up to 10 000 IU hCG is given 24-48 hours after the last injections of GONAL-f and lutropin alfa. Infertile men with hormonal deficiency GONAL-f is usually prescribed at a dose of 150 IU (0.24 ml) three times a week in combination with another medicine (hCG) for at least 4 months. If you have not responded to treatment after this period, your treatment may carry on for at least 18 months. **Possible side effects:** The most commonly reported side effects are ovarian cysts, headache and local reactions at the injection site (pain, redness, bruising, swelling and/or irritation). Following treatment with GONAL-f when human chorionic gonadotrophin is administered, a condition called ovarian hyperstimulation syndrome This syndrome is characterised by large ovarian cysts. First symptoms of ovarian hyperstimulation are pain in the lower abdominal region, possibly in combination with nausea, vomiting and weight gain. Isolated cases of non-serious allergic reactions to GONAL-f have been reported. This occurs in less than 1 patient for each 10000 treated. Ectopic pregnancy (embryo implanted outside the womb) may occur especially in women with a history of prior tubal disease. Men may experience some breast development, acne or weight gain due to treatment with hCG (between 1 and 10% of the patients). **Stability and storage:** Store at 2°C - 8°C (in a refrigerator). Do not freeze. Within its shelf-life, the product may be stored at or below 25°C for up to 28 days and must be discarded if not used. **Packaging:** GONAL-f is presented as a clear, colourless solution for injection in a pre-filled pen. - Gonal-f 300 IU pen: Each cartridge delivers 300 IU (equivalent 22 micrograms) in 0.5 ml , it is supplied in packs of 1 pre-filled pen and 5 needles for administration - Gonal-f 450 IU pen: Each cartridge delivers 450 IU (equivalent 33 micrograms) in 0.75 ml. It is supplied in packs of 1 pre-filled pen and 7 needles for administration. - Gonal-f 900 IU pen: Each cartridge delivers 900 IU (equivalent 66 micrograms) in 1.5 ml. It is supplied in packs of 1 pre-filled pen and 14 needles for administration. 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