

THE THIRTEENTH  
**ROYAN**  
INTERNATIONAL  
RESEARCH AWARD

Reproductive Biomedicine & Stem Cell.....



**SEPTEMBER 2012**

TEHRAN - IRAN

THE FOURTEENTH  
**ROYAN**  
INTERNATIONAL RESEARCH AWARD

Reproductive Biomedicine & Stem Cell  
Deadline for Application: April, 2013



## Kazemi Prize, 2013

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

**SEPTEMBER, 2013**

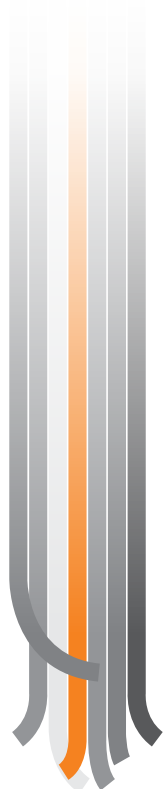
TEHRAN - IRAN

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In the name of  
**GOD**

The Thirteenth  
**ROYAN**  
INTERNATIONAL RESEARCH AWARD



*Dr Saeid Kazemi Ashtiani*  
*The Late Founder of ROYAN Institute*



**Cover Legend:**  
Immunofluorescence staining of GFAP expressing Neural Progenitors Cells derive Induced Pluripotent Stem Cells, 14 days after spontaneously differentiation.  
**Photographer:** Shiva Nemati

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# FOREWORD



On behalf of the Iranian Academic Center for Education, Culture and Research 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, the Oriental Cradle of Art and Science. This award seems to be credible in the field of Reproductive Biomedicine and Stem cell Biology and Technology both in Iran and all over the world. Moreover, according to the reports of Dr Gourabi, award chairman, valuable scientific cooperation has been established among Iranian and international scientists which is worthier than the award itself.

Hereby, I appreciate my colleagues in Royan Institutes whose endeavors led this Award to a success which certainly evolves and develops further. My thanks also go to the board of Jury and all the researchers who participate in Royan 13<sup>th</sup> Award with their invaluable papers. At last, I hope this award will be the messenger of Islamic Republic of Iran's peace and friendship to the world.

**Yadegari MH, PhD**

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

# INTRODUCTION



It is my great pleasure that Royan 13<sup>th</sup> international research award is held successfully like previous years. The key point in success of such an affair is considering it as an important and great event by the executive board. This team had unremitting effort in holding weekly meetings throughout the year and pursuing the whole process of award for the sake of establishing better relationships with all the addressees from young researchers to the prominent scientists.

In the 13<sup>th</sup> award despite the quantitative decrease in the number of articles, qualitative advancement was evident. Accordingly, along with award winners, the invitation of some other candidates was suggested by the jury board in each group for giving a speech in the congress. The suggestion that award committee also agreed upon.

This year 169 projects from 35 countries were received by award secretariat, the most of which were related to stem cell group with 77 projects and then embryology, female infertility, andrology and reproductive genetics. Regarding the geographical division, too, most of the received projects belong to United States, China, Iran, Japan, India, and Germany.

The projects having passed the primary evaluation, i.e. being reviewed in terms of IF of the published articles and innovation score, were reviewed by 115 national and 65 international referees, the outcome of which is available in the following pages. The evaluation process, regardless of being held in two phases, seems to be free from any bias such as national trend or the likes.

The present book includes annual report of the institute like previous years. And I am delighted to meet acceptable record again as an upshot of my colleagues' endless efforts. The outcome of such efforts is worth more when the tough conditions of their performance are noticed.

Hereby, I would like to express my sincere appreciation to the executive committee for their extraordinary contribution in better holding the 13<sup>th</sup> award. I, also, would like to thank all the scientists, scientific staff and board, researchers, and the personnel of the institute for their endless effort in previous year.

My great thank goes to the research, clinical and university centers plus their scientific staff along with national and international scientists who reviewed the research projects. Finally, I greatly appreciate the sponsors without whose support and assistant holding this event was not possible.

As a final point, I hope that holding Royan international research award which is held every year by the remembrance of Dr Saeid Kazemi Ashtiani, the late founder of Royan Institute, will be the messenger of peace and Iranian friendship to the people in the world. Too, it is hoped to lead to international scientific collaborations in line with human health promotion without any racism or seeking for materialistic superiority.

**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, genetics, stem cell biology and technology, and regenerative medicine.

## **Nomination and Selection Procedure of Award**

The submitted research articles are categorized according to eight scientific groups: female infertility, reproductive genetics, reproductive health (epidemiology and ethics), embryology, andrology, reproductive imaging, stem cell biology and technology and animal 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 a special ceremony in the second night of congress.

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





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**The First Royan International Research Award** | September 2000 | Received Papers: 72

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**International Winners:**

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

**Iranian Winners:**

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





#### International Winners:

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

#### Iranian Winners:

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



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

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**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-Protnine-Exchange on Male Infertility
- **Third Place: Franck Pellestor**, France  
Chromosomal Investigations in Human Gametes: Study of the Interchromosomal Effect in Sperm of Chromosomal Rearrangement Carriers and Mechanisms of Non Disjunction in Oocytes
- **Fourth Place: Ghazala S. Basir**, Hong Kong  
The Effect of High Estradiol Levels on Endometrial Development in Assisted Reproduction Technology: Evaluation of Sonographic Doppler Haemodynamic and Morphometric Parameters
- **Fifth Place: Mohamed Ali Bedaiwy**, USA  
Transplantation of Intact Frozen-Thawed Mammalian Ovary with Vascular Anastomosis: A Novel Approach

**Iranian Winners:**

- **Saeed Alborzi**  
Laparoscopic Salpingoovulysis. Is There Any Place for Second Look Laparoscopy?
- **Saeed Rahbar**  
Laser Assisted Hatching in Young Women Significantly Increases Pregnancy and Implantation Rates
- **Shir Ahmad Sarani**  
Morphological Evidence for the Implantation Window in Human Luminal Endometrium  
**Special Winner in Reproductive Health**
- **V. I. Sodestrom- Anttila**, Finland  
Embryo Donation-Outcome & Attitude Among Embryo Donors & Recipient





#### 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



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**The Fifth Royan International Research Award** | September 2004 | Received Papers: 199

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**International Winners:**

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

**Iranian Winners:**

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







**International Winners:**

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

**Iranian Winners:**

- **Seyed Javad Mowla**  
The Profile of Gene Expression Changes During the Neural Differentiation of Bone Marrow Stromal 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  
Oopoptosis of Ejaculated Human Sperm Is Induced by Co-Incubation with Chlamydia Trachomatis Lipopolysaccharide
- **Fourth Place: Lone Schmidt**, Denmark  
Does Infertility Cause Marital Benefit? An Epidemiological Study of 2250 Women and Men in Fertility Treatment
- **Fifth Place: Louis Chukwuemeka Ajonuma**, Hong Kong  
Molecular and Cellular Mechanisms Underlying Abnormal Fluid Formation in the Female Reproductive Tract: The Critical Role of Cystic Fibrosis Transmembrane Conductance Regulators

#### Iranian Winners:

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





#### 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



#### 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





#### 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 project in female infertility field (share)

- **Sherman Silber**, USA  
A Series of Monozygotic Twins Discordant for Ovarian Failure: Ovary Transplantation (Cortical versus Microvascular) and Cryopreservation

Best research project in female infertility field (share)

- **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





#### 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 Bashambo**, 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





#### International Winners:

Best research project in regenerative medicine field

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

Best research project in stem cell biology & technology field

- **Hirimitsu 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 field

- **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

# TABLE OF TITLES

## SORTED BY NAME



No	Name	Country	Title
1	<b>Abdou, Asmaa</b>	Egypt	Immunohistochemical Expression of Cyclin A in Testicular Biopsies of Fertile and Infertile Men: Correlation with the Morphometry of Seminiferous Tubules
2	<b>Abu Hashim, Hatem</b>	Egypt	Letrozole Versus Combined Metformin and Clomiphene Citrate for Ovulation Induction in Clomipheneresistant Women with Polycystic Ovary Syndrome: A Randomized Controlled Trial
3	<b>Adiga, Satish</b>	India	Ransgenerational Changes in Somatic and Germ Line Genetic Integrity of First-Generation Offspring Derived from the DNA Damaged Sperm
4	<b>Almstrup, Kristian</b>	Denmark	Screening of Subfertile Men for Testicular Carcinoma in Situ by an Automated Image Analysis-Based Cytological Test of The Ejaculate
5	<b>Ashok, Pranita</b>	India	Correlation of Fasting Blood Glucose with Menopausal Status In Middle Aged Women with Their Obesity Status
6	<b>Atlmäe, Signe</b>	Sweden	Interactorme of Human Embryo Implantation: Identification of Gene Expression Pathways, Regulation, and Integrated Regulatory Networks
7	<b>Balabanič, Damjan</b>	Slovenia	Negative Impact of Endocrine-Disrupting Compounds on Human Reproductive Health
8	<b>Baratta, Mario</b>	Italy	Characterization of Stem Cells in the Ruminant Mammary Gland and Their Use for the Production and Secretion of Transgenes in Milk
9	<b>Barroso, Gerardo</b>	Mexico	The Effect of Age on the Expression of Apoptosis Biomarkers in Human Spermatozoa
10	<b>Behr, Bjorn</b>	USA	Locally Applied VEGFA Increases the Osteogenic Healing Capacity of Human Adipose Derived Stem Cells by Promoting Osteogenic and Endothelial Differentiation
11	<b>Bhansali, Anil</b>	India	Predictors of Pilosebaceous Unit Responsiveness to Testosterone Therapy in Patients with Hypogonadotrophic Hypogonadism
12	<b>Bhat, Krishna</b>	USA	The Transcriptional Coactivator TAZ Regulates Mesenchymal Differentiation in Malignant Glioma Stem Cells
13	<b>Bhonde, Ramesh</b>	India	Development of Stem Cell Based Novel Strategies for Treating Type 2 Diabetes
14	<b>Bilodeau-Goeseels, Sylvie</b>	Canada	Activation of AMP-Activated Protein Kinase May Not Be Involved in AICAR- and Metformin-Mediated Meiotic Arrest in Bovine Denuded and Cumulus-Enclosed Oocytes in vitro.
15	<b>Boscia, Francesca</b>	Italy	Silencing or Knocking Out the Na <sup>+</sup> /Ca <sup>2+</sup> Exchanger-3 (NCX3) Impairs Oligodendrocyte Differentiation
16	<b>Calegari, Federico</b>	Germany	Expansion of Neural Stem Cells in the Adult Mammalian Brain
17	<b>Carr, Bruce</b>	USA	Gonadotropin Releasing Hormone Antagonist Supresses Aromatase and Anti-Mullerian Hormone in Human Granulosa Cells
18	<b>Chen, Yuhong</b>	China	Clinical Trial of Mesenchymal Stromal Cells
19	<b>Chiarini-Garcia, Helio</b>	Brazil	Effects of Multiple Doses of Cyclophosphamide on Mouse Testes: Accessing the Germ Cell Lost., and Functional Damage of Stem Cells
20	<b>Colledge, William</b>	UK	Dietary Phytoestrogens Can Stimulate Spermatogenesis
21	<b>Dai, Long-Jun</b>	Canada	MSC-Mediated Cancer Therapy: A Dual-Targeted Strategy of Personalized Medicine
22	<b>Decimo, Ilaria</b>	Italy	Nestin- and Doublecortin-Positive Cells Reside in Adult Spinal Cord Meninges and Participate in Injury-Induced Parenchymal Reaction
23	<b>Demirhan, Osman</b>	Turkey	The Genotoxic Effect of Nicotine on Chromosomes of Human Fetal Cells: The First Report Described As an Important Study
24	<b>Dhawan, Veena</b>	India	Role of 8-Iso-Prostaglandin F2a and 25-Hydroxycholesterol in the Pathophysiology of Endometriosis

No	Name	Country	Title
25	<b>D'Hooghe</b> , Thomas	Belgium	Advances in Understanding Endometriosis: Pathogenesis, Biomarkers, Surgery, and Cost
26	<b>Di Pietro</b> , Cinzia	Italy	Tap73 Is Down Regulated in Human Mature Oocytes from Women of Advanced Reproductive Age
27	<b>Donchin</b> , Anne	USA	In Whose Interest? Policy and Politics in Assisted Reproduction
28	<b>Dundar</b> , Munis	Turkey	Idiopathic Hirsutism: Local and Peripheral Expression of Aromatase (CYP19A) and 5 $\alpha$ -Reductase Genes (SRD5A1 and SRD5A2)
29	<b>Edalatmanesh</b> , Mohammad	Iran	Bone Marrow Derived Mesenchymal Stem Cell Transplantation in Cerebellar Degeneration Model
30	<b>Elgindy</b> , Eman	Egypt	Progesterone Level and Progesterone/Estradiol Ratio on the Day of hCG Administration: Detrimental Cutoff Levels and New Treatment Strategy
31	<b>Elgindy</b> , Eman	Egypt	Blastocyst-Stage Versus Cleavage-Stage Embryo Transfer in Women with High Oestradiol Concentrations: Randomized Controlled Trial
32	<b>El-Mazny</b> , Akmal	Egypt	A Double-Blind Randomized Controlled Trial of Vaginal Misoprostol for Cervical Priming Before Outpatient Hysteroscopy
33	<b>Enciso</b> , Maria	Spain	The Ability of Sperm Selection Techniques to Remove Single- or Double-Strand DNA Damage
34	<b>Erhabor</b> , Osaro	UK	Reproductive Health Options Among HIV-Infected Persons in the Low Income Niger Delta of Nigeria
35	<b>Fan</b> , Guoping	USA	Promoter CPG Methylation Contributes to ES Cell Gene Regulation in Parallel with Oct4/Nanog, PCG Complex, and Histone H3 K4/K27 Trimethylation
36	<b>Fauza</b> , Dario	USA	Amniotic Mesenchymal Stem Cells Enhance Normal Fetal Wound Healing
37	<b>Figueiredo</b> , Marxa	USA	Adipose-Derived Stromal/Mesenchymal Stem Cells Are Efficient in Treating Prostate Cancer by Delivering Novel Cytokine Therapies
38	<b>Frith</b> , Lucy	UK	Ethical Boundary Work in the Infertility Clinic
39	<b>Galvez</b> , Beatriz	Spain	Mitochondria Determine the Differentiation Potential of Cardiac Mesoangioblasts
40	<b>Gao</b> , Shaorong	China	Reprogramming of Trophoblast Stem Cells into Pluripotent Stem Cells by Oct4
41	<b>Gao</b> , Shaorong	China	iPS Cell Can Support Full-Term Development of Tetraploid Blastocyst-Complemented Embryos
42	<b>Ghaedi</b> , Kamran	Iran	Influences of Ppar $\gamma$ and PEP on Proliferation and Differentiation of Mouse Embryonic Stem Cells
43	<b>Gharagozloo</b> , Parviz	USA	Diagnosis and Treatment of Sperm Oxidative DNA Damage in Male Infertility
44	<b>Ghorbani</b> , Masood	Iran	Determination and Comparison Specifics Nucleous Pulposus Cells of Intervertebral Disc of Human in Alginate and Chitosan-Gelatin Scaffolds
45	<b>Giojalas</b> , Laura	Argentina	Sperm Chemotaxis Towards Progesterone, A Guiding Mechanism That May Be Used to Select the Best Spermatozoa for Assisted Reproduction
46	<b>Golestaneh</b> , Nady	USA	Human Induced Pluripotent Stem-Derived Retinal Pigment Epithelium (RPE) Cells Exhibition Transport, Membrane Potential, Polarized Vascular Endothelial Growth Factor Secretion, and Gene Expression Pattern Similar to Native RPE
47	<b>Gritti</b> , Angela	Italy	Neural Stem Cell Gene Therapy Ameliorates Pathology and Function in a Mouse Model of Globoid Cell Leukodystrophy
48	<b>Gulum</b> , Mehmet	Turkey	Sperm DNA Damage and Seminal Oxidative Status after Shock-Wave Lithotripsy for Distal Ureteral Stones
49	<b>Gupta</b> , Mukesh	USA	Combinatorial Electrospun Matrices Promote Physiologically-Relevant Cardiomyogenic Stem Cell Differentiation
50	<b>Hammadeh</b> , Mohamad	Germany	Protamine Contents and P1/P2 Ratio in Human Spermatozoa from Smokers and Non-smokers
51	<b>Hari</b> , Danielle	USA	Isolation of Live Label-Retaining Cells and Cells Undergoing Asymmetric Cell Division via Nonrandom Chromosomal Cosegregation from Human Cancers
52	<b>Harvey</b> , Richard	Australia	Definition and Embryonic Origins of MSC-Like Stem Cells in the Adult Mammalian Heart
53	<b>Hashemi</b> , Seyed Mahmoud	Iran	The Promotion of Stemness and Pluripotency Following Feeder-Free Culture of Embryonic Stem Cells on Collagen-Graf Ted 3-Dimensional Nano Fibrous Scaffold
54	<b>Hay</b> , David	UK	Unbiased Screening of Polymer Libraries to Define Novel Substrates for Functional Hepatocytes with Inducible Drug Metabolism

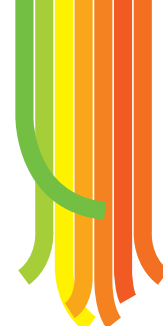


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55	<b>Heeschen</b> , Christopher	Spain	Embryogenesis Meets Tumorigenesis – Nodal/Activin Signaling Drives Self-Renewal and Tumorigenicity of Pancreatic Cancer Stem Cells
56	<b>Hekal</b> , Ihab	Egypt	Penile Haemodynamic Changes in Post-Radical Cystectomy Patients
57	<b>Huang</b> , He-Feng	China	Attenuated Oocyte Fertilization and Embryo Development Associated with Altered Growth Factor/Signal Transduction Induced by Endometriotic Peritoneal Fluid
58	<b>Huang</b> , Jian	China	Oxaliplatin-Incorporating Micelles Eliminate both Cancer Stem-Like and Bulk Cell Populations in Colorectal Cancer
59	<b>Hugues</b> , Jean-Noel	France	Assessment of Theca Cell Function Prior to Controlled Ovarian Stimulation: The Predictive Value of Serum Basal/Stimulated Steroid Levels
60	<b>Huszar</b> , Gabor	USA	Double Probing Individual Human Spermatozoa: Aniline Blue Staining for Persistent Histones and Fluorescence in Situ Hybridization for Aneuploidies
61	<b>Ibañez</b> , Elena	Spain	A Novel Embryo Identification System by Direct Tagging Using Silicon-Based Barcodes
62	<b>Ishijima</b> , Sumio	Japan	Dynamics of Flagellar Force Generated by a Hyperactivated Spermatozoon
63	<b>Jäger</b> , Kersti	Estonia	Human Dermal Fibroblasts Exhibit Delayed Adipogenic Differentiation Compared with Mesenchymal Stem Cells
64	<b>Jaganathan</b> , Anbalagan	India	Mechanism Underlying Transient Gestational-Onset Hypothyroidism-Induced Impairment of Posttesticular Sperm Maturation in Adult Rats.
65	<b>Javan</b> , Mohammad	Iran	Analysis of Structural, Molecular and Functional Consequences Associated with Adult Rat Optic Chiasm and Nerves Demyelination and Remyelination; Possible Role for 3 <sup>rd</sup> Ventricle Proliferating Cells
66	<b>Jin</b> , Guohua	China	Ectopic Neurogenesis in Forebrain Cholinergic System-Related Areas of Rat Dementia Model
67	<b>Karimi</b> , Mohammad	Canada	DNA Methylation and SETDB1/H3k9me3 Regulate Predominantly Distinct Sets of Genes, Retroelements, and Chimeric Transcripts in Mescs
68	<b>Karimi Zarchi</b> , Mojgan	Iran	Fertility Sparing Treatments in Young Patients with Gynecological Cancers: A Large Iranian Experience and a Literature Review
69	<b>Karimi Zarchi</b> , Mojgan	Iran	Conservative Treatment in Young Patients with Cervical Cancer: A Review
70	<b>Karimi Zarchi</b> , Mojgan	Iran	Good Pregnancy Outcome after Prenatal Exposure to Bleomycin, Etoposide and Cisplatin for Ovarian Immature Teratoma: A Case Report and Literature Review
71	<b>Kaur</b> , Pritinder	Australia	Functional Characterization of Quiescent Keratinocyte Stem Cells and Their Progeny Reveals a Hierarchical Organization in Human Skin Epidermis
72	<b>Khan</b> , Khaleque	Japan	Multifunctional Role of GnRH Agonist Therapy in Endometriosis, Adenomyosis and Uterine Myoma
73	<b>Khlusov</b> , Igor	Russian Federation	"Niche-Energy" Concept for Stem Cells and Microenvironment Cooperation
74	<b>Kobayashi</b> , Hideyuki	Japan	Reprogramming of Adult Human Testicular Cells by Four Transcription Factors (OCT4, SOX2, KLF4, and C-MYC)
75	<b>Kobayashi</b> , Masayuki	Japan	Positive and Negative Regulators Synthesized by Rat Hepatoma Cells for the Development of Murine and Bovine Embryos Cultured in vitro
76	<b>Koh</b> , Eitetsu	Japan	Features of Constitutive Gr/Gr Deletion in a Japanese Population
77	<b>Koh</b> , Kian Peng	USA	Tet1 and Tet2 Regulate 5-Hydroxymethylcytosine Production and Cell Lineage Specification in Mouse Embryonic Stem Cells
78	<b>Kumar</b> , Ashok	India	Latent Celiac Disease in Reproductive Performance of Women
79	<b>Kunej</b> , Tanja	Slovenia	Comparative Integratomics Approach to Identify Candidate Genetic Loci for Male Fertility
80	<b>Kuo</b> , Calvin	USA	Bmi1 and Lgr5 Mark Functionally Distinct Intestinal Stem Cells
81	<b>Kypta</b> , Robert	Spain	Distinct Roles for Wnt-4 and Wnt-11 During Retinoic Acid-Induced Neuronal Differentiation
82	<b>Laird</b> , Diana	USA	Ror2 Enhances Polarity and Directional Migration of Primordial Germ Cells
83	<b>Lauterbach</b> , Edward	USA	Psychiatric Drug Effects on Neurodegenerative Diseases, Stem Cells, Neurogenesis, and Embryogenesis
84	<b>Li</b> , Yuan	China	The Evaluation of the Immature Human Oocytes from Unstimulated Cycles in Polycystic Ovarian Syndrome Patients Using a Novel Scoring System





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85	<b>Li, Tao-Sheng</b>	Japan	Mechanical Stress and Stem Cell-Based Myocardial Regeneration
86	<b>Liu, Yang</b>	USA	Targeting HIF1alpha Eliminates Cancer Stem Cells in Hematological Malignancies
87	<b>Liu, Kaiyan</b>	China	Co-infusion of Mesenchymal Stromal Cells Facilitates Platelet Recovery Without Increasing the Leukemia Recurrence in Haploidentical Hematopoietic Stem Cell Transplantation: A Randomized, Controlled Clinical Study
88	<b>Lourenço, Mário</b>	Portugal	The Psychological Impact of the Infertility in the Couple
89	<b>Malakar, Dhruva</b>	India	Germ Cells Production from Established Goat Embryonic Stem Cells and iPSCs
90	<b>Mangoli, Esmat</b>	Iran	Effect of Diabetes on Sperm Parameters and Chromatin Quality in Mice
91	<b>Martensen, Pia</b>	Denmark	Virus Infection and Type 1 Interferon in Endometriosis
92	<b>Mccloskey, Kara</b>	USA	Endothelial Cells from Embryonic Stem Cells in Chemically Defined Medium
93	<b>Mellembakken, Jan</b>	Norway	Sustained Fertility from 22 to 41 Years of Age in Women with Polycystic Ovarian Syndrome
94	<b>Mesut, Nursen</b>	Turkey	Cryopreservation of Blastocysts Is the Most Feasible Strategy in Good Responder Patients
95	<b>Michetti, Fabrizio</b>	Italy	The Use of Mesenchymal Stem Cells for Regenerative Medicine in Brain Injury
96	<b>Moreb, Jan</b>	USA	Long-Term Outcome After Autologous Stem Cell Transplantation with Adequate Peripheral Blood Stem Cell Mobilization Using Plerixafor and G-CSF in Poor Mobilizer Lymphoma and Myeloma Patients
97	<b>Nasu, Kaei</b>	Japan	Role of Mevalonate-Ras Homology (Rho)/Rho-Associated Coiled-Coil-Forming Protein Kinase-Mediated Signaling Pathway in the Pathogenesis of Endometriosis-Associated Fibrosis
98	<b>Nishihara, Shoko</b>	Japan	Lacdinac Carbohydrate Structure Regulates LIF/STAT3 Signaling and Is Required for Self-Renewal of Naive State Pluripotent Stem Cells
99	<b>Oliveira, André</b>	Brazil	Involvement of Hormonal Imbalance and Disruption of the Transepithelial Calcium Transport in the Formation of Epididymal Stones in Roosters
100	<b>Oluwagbemiga, Oyinlola</b>	Nigeria	Sexual Behavior, Knowledge and Attitude of Young Adolescent in Nigeria
101	<b>Pang, Myung-Geol</b>	Korea	Numerical Chromosome Abnormalities are Associated with Sperm Tail Swelling Patterns
102	<b>Pavlik, Roman</b>	Germany	Divergent Effects of the 677C>T Mutation of the 5,10-Methylenetetrahydrofolate Reductase (MTHFR) Gene on Ovarian Responsiveness and Anti-Müllerian Hormone Concentrations
103	<b>Peister, Alexandra</b>	USA	Cell Sourcing for Bone Tissue Engineering: Amniotic Fluid Stem Cells Have a Delayed, Robust Differentiation Compared to Mesenchymal Stem Cells
104	<b>Petanovski, Zoranco</b>	Macedonia	Recombinant FSH Versus HP-HMG for Controlled Ovarian Stimulation in Intracitoplasmic Sperm Injection Cycles
105	<b>Polanco, Carlos</b>	Spain	Willingness to Pay and Conjoint Analysis to Determine Women's Preferences for Ovarian Stimulating Hormones in the Treatment of Infertility in Spain
106	<b>Pouya, Alireza</b>	Iran	Human Induced Pluripotent Stem Cells Differentiation into Oligodendrocyte Progenitors and Transplantation in a Rat Model of Optic Chiasm Demyelination
107	<b>Prabha, Vijay</b>	India	Molecular Mimicry Between Spermatozoa and Bacteria
108	<b>Prigione, Alessandro</b>	Germany	Human Induced Pluripotent Stem Cells Harbor Homoplasmic and Heteroplasmic Mitochondrial DNA Mutations While Maintaining Human Embryonic Stem Cell-Like Metabolic Reprogramming
109	<b>Quarto, Natalina</b>	USA	Unique Skeletogenic Phenotype of Human Marfan Embryonic Stem Cells Faithfully Phenocopied by Patient-Specific Induced-Pluripotent Stem Cells
110	<b>Rajamannan, Nalini</b>	USA	Oxidative-Mechanical Stress Signals Stem Cell Niche Mediated Lrp5 Osteogenesis in Enos(-/-) Null Mice
111	<b>Ramsay, Robert</b>	Australia	C-Myb Is a Key Regulator of Stem Cell Function in Multiple Epithelial Compartments
112	<b>Rasmussen, Mikkel</b>	Denmark	Directed Differentiation of Porcine Epiblast-Derived Neural Progenitor Cells into Neurons and Glia
113	<b>Rehen, Stevens</b>	Brazil	Agathisflavone Enhances Retinoic Acid-Induced Neurogenesis and Its Receptors Alpha and Beta in Pluripotent Stem Cells
114	<b>Remboutsika, Eumorphia</b>	Greece	Sox1 Maintains the Undifferentiated State of Cortical Neural Progenitor Cells via the Suppression of Prox1-Mediated Cell Cycle Exit and Neurogenesis



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115	<b>Riazuddin</b> , Sheikh	Pakistan	Growth Factor Preconditioning Increases the Function of Diabetes-Impaired Mesenchymal Stem Cells
116	<b>Rivero</b> , Virginia	Argentina	Innate Immunity in the Male Genital Tract: Keratinocyte-Derived Chemokine Production in Response to TLR Ligands and Chlamydia Trachomatis. Chemokine Response Induced by Chlamydia Trachomatis in Prostate Derived CD45+ and CD45- Cells
117	<b>Rodriguez</b> , Annabelle	USA	Clinical Impact of Scavenger Receptor Class B Type I Gene Polymorphisms on Human Female Fertility
118	<b>Romeo</b> , Paul-Henri	France	Adult Hematopoiesis Is Regulated by TIF1 $\gamma$ , a Repressor of TAL1 and PU.1 Transcriptional Activity
119	<b>Rucker</b> , Edmund	USA	The Role of Autophagy in Murine Ovarian Development and Infertility
120	<b>Ryu</b> , Hyun Mee	Korea	Non-invasive Prenatal Detection of Achondroplasia Using Circulating Fetal DNA in Maternal Plasma
121	<b>Safarinejad</b> , Mohammad Reza	Iran	The Influence of Genetic Polymorphism on Idiopathic Male Infertility
122	<b>Saffery</b> , Richard	Australia	Wide-Ranging DNA Methylation Differences of Primary Trophoblast Cell Populations and Derived Cell Lines: Implications and Opportunities for Understanding Trophoblast Function
123	<b>Sakata</b> , Naoaki	Japan	Utility of Co-transplanting Mesenchymal Stem Cells in Islet Transplantation
124	<b>Sala</b> , Arturo	UK	Frizzled Receptor 6 Marks Rare, Highly Tumourigenic Stem-Like Cells in Mouse and Human Neuroblastomas
125	<b>Savaris</b> , Ricardo	Brazil	Prospective, Randomized Comparison Between Raloxifene and Clomiphene Citrate for Ovulation Induction in Polycystic Ovary Syndrome
126	<b>Schwamborn</b> , Jens	Germany	Fate Specification in Adult Neural Stem Cells
127	<b>Seiler</b> , Katharina	Germany	Efficiencies of Hematopoietic Differentiation from iPS Cells of Different Origins
128	<b>Senosy</b> , Waleed	Japan	Impact of Ovarian and Uterine Conditions on Some Diagnostic Tests Output of Endometritis in Postpartum High-Yielding Dairy Cows
129	<b>Shahhoseini</b> , Maryam	Iran	Epigenetic Analysis of Human Embryonal Stem Cells During Neural Differentiation
130	<b>Shahzadeh Fazeli</b> , Abolhassan	Iran	Proteomic Profiling of the Central Nervous System in Murine Experimental Autoimmune Encephalomyelitis Before and After Treatment with Mouse Embryonic Stem Cell-Driven Neural Precursor Cells
131	<b>Sharina</b> , Iraida	USA	Nitric Oxide Receptor Soluble Guanylyl Cyclase Undergoes Splicing Regulation in Differentiating Human Embryonic Cells
132	<b>Sills</b> , E Scott	USA	Ovarian Dysgenesis Associated with an Unbalanced X;6 Translocation: First Characterisation of Reproductive Anatomy and Cytogenetic Evaluation in Partial Trisomy 6 with Breakpoints at Xq22 and 6p23
133	<b>Sousa</b> , Marlos	Brazil	Cardiac Function in Dogs with Chronic Chagas Cardiomyopathy Undergoing Autologous Stem Cell Transplantation into the Coronary Arteries
134	<b>Speck</b> , Nancy	USA	Erythroid/Myeloid Progenitors and Hematopoietic Stem Cells Originate from Distinct Populations of Endothelial Cells
135	<b>Sudoma</b> , Iryna	Ukraine	Optimization of Cryocycles by Using Pinopode Detection in Patients with Multiple Implantation Failure: Preliminary Report
136	<b>Sugimoto</b> , Kouhei	Japan	Cancellation of in vitro Fertilization Treatment Cycles Predict Treatment Outcome in Female Infertility Patients Aged 40 Years or Older
137	<b>Tada</b> , Takashi	Japan	Effects of Sox2 Expression Level on Direct Reprogramming Efficiency by Alternative Somatic Cell Fate
138	<b>Taguchi</b> , Y-H	Japan	Inference of Gene Regulation via Mirnas During ES Cell Differentiation Using Mirage Method
139	<b>Talebi</b> , Ali Reza	Iran	Cytochemical Evaluation of Sperm Chromatin and DNA Integrity in Couples with 3 Unexplained Recurrent Spontaneous Abortion
140	<b>Tang</b> , Chad	USA	An Antibody Against SSEA-5 Glycan on Human Pluripotent Stem Cells Enables Removal of Teratoma-Forming Cells
141	<b>Tang</b> , Liping	USA	Transplantation of Mesenchymal Stem Cells from Young Donors Delays Aging in Mice

















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142	<b>Taraviras</b> , Stavros	Greece	Investigating Mechanisms Regulating Stem Cells Self-Renewal and Differentiation Decisions
143	<b>Tesar</b> , Paul	USA	Rapid and Robust Generation of Functional Oligodendrocyte Progenitor Cells from Pluripotent Stem Cells
144	<b>Thakur</b> , Mayank	Germany	Pharmacological and Molecular Evaluation of Herbal Drugs in the Treatment of Sexual Dysfunction and As Stimulating Agents
145	<b>Thanoi</b> , Samur	Thailand	Methamphetamine Induces Abnormal Sperm Production
146	<b>Thornhill</b> , Alan	UK	Polar Body Analysis by Array CGH Identifies Women with Varying Susceptibility to Aneuploidy and Suggests That Non-disjunction Is Not the Predominant Mechanism Leading to Aneuploidy in Humans
147	<b>Tong</b> , Guoqing	China	Vitrified-Warmed Blastocyst Transfer Cycles Yield Higher Pregnancy and Implantation Rates 148Compared with Fresh Blastocyst Transfer Cycles--Time for a New Embryo Transfer Strategy?
148	<b>Toushah</b> , Mohammad	Iran	The Effect of Ginger Essence and Cyclophosphamid on Ovarian Follicles Growth
149	<b>Turan</b> , Ramazan Gökmen	Germany	Enhanced Mobilisation and Functional Activity of the Bone Marrow Derived Circulating Progenitor Cells by Intracoronary Freshly Isolated Bone Marrow Cells Transplantation in Patients with Acute Myocardial Infarction
150	<b>Turan</b> , Ramazan Gökmen	Germany	Improved Mobilisation and Functional Activity of Bone Marrow Derived Circulating Progenitor Cells by Freshly Isolated Intracoronary Bone Marrow Cells Transplantation in Patients with Ischemic Heart Disease
151	<b>Wang</b> , Lei	China	Genetics of Intermediate Phenotype of PCOS
152	<b>Wang</b> , Paulus	Taiwan	Effects of Polybrominated Diphenyl Ethers on Steroidogenesis in Rat Leydig Cells
153	<b>Wang</b> , Wei	China	The Time Interval Between hCG Priming and Oocyte Retrieval in ART Program: A Meta-analysis
154	<b>Wang</b> , Feng	China	Effect of Different Levels of Short-Term Feed Intake on Folliculogenesis and Intrafollicular Microenvironment
155	<b>Weng</b> , Qiang	China	Expression of Steroidogenic Enzymes and Inhibin/Activin Subunits in the Scented Gland of Muskrat
156	<b>Wetthasinghe</b> , Tithila	Sri Lanka	Y Chromosome Microdeletions Are Not Associated with Spontaneous Recurrent Pregnancy Loss in a Sinhalese Population in Sri Lanka
157	<b>Xiao</b> , Yin	Australia	The Ratio of VEGF/PEDF Expression in Bone Marrow Mesenchymal Stem Cells Regulates Neovascularization
158	<b>Xiaoke</b> , Wu	China	Polycystic Ovary Syndrome Is Associated with Negatively Variable Impacts on Domains of Health-Related Quality of Life: Evidence from a Meta-analysis
159	<b>Yadav</b> , Prem	India	Culture, Characterization and Differentiation of Fetal Derived Stem Cells in Buffalo
160	<b>Yildizhan</b> , Recep	Turkey	Serum Retinol-Binding Protein 4, Leptin, and Plasma Asymmetric Dimethylarginine Levels in Obese and Nonobese Young Women with Polycystic Ovary Syndrome
161	<b>Yotova</b> , Iveta	Austria	Testosterone Dependent Androgen Receptor Stabilization and Activation of Cell Proliferation in Primary Human Myometrial Microvascular Endothelial Cells
162	<b>Yu</b> , John	Taiwan	Harnessing Human Embryonic Stem Cell Biomarkers for Cancer Therapeutics
163	<b>Zamani Esteki</b> , Masoud	Belgium	Genome Haplotyping and Detection of Meiotic Homologous Recombination Sites in Single Cells, A Generic Method for Preimplantation Genetic Diagnosis
164	<b>Zara</b> , Vincenzo	Italy	Evaluation of Mitochondrial Respiratory Efficiency During in vitro Capacitation of Human Spermatozoa
165	<b>Zhang</b> , Chengcheng	USA	Ex vivo Expanded Hematopoietic Stem Cells Overcome the MHC Barrier in Allogeneic Transplantation
166	<b>Zhou</b> , Rongjia	China	Characterization of Androgen Receptor Structure and Nucleocytoplasmic Shuttling of the Rice Field Eel
167	<b>Zhu</b> , Wenjie	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

# NOMINEES



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<b>Abdou, asmaa</b>	 Egypt	Immunohistochemical Expression of Cyclin A in Testicular Biopsies of Fertile and Infertile Men: Correlation with the Morphometry of Seminiferous Tubules
<b>Adiga, Satish</b>	 India	Ransgenerational Changes in Somatic and Germ Line Genetic Integrity of First-Generation Offspring Derived from the DNA Damaged Sperm
<b>Almstrup, Kristian</b>	 Denmark	Screening of Subfertile Men for Testicular Carcinoma in Situ by an Automated Image Analysis-Based Cytological Test of the Ejaculate
<b>Barroso, Gerardo</b>	 Mexico	The Effect of Age on the Expression of Apoptosis Biomarkers in Human Spermatozoa
<b>Bhansali, Anil</b>	 India	Predictors of Pilosebaceous Unit Responsiveness to Testosterone Therapy in Patients with Hypogonadotropic Hypogonadism
<b>Colledge, William</b>	 UK	Dietary Phytoestrogens Can Stimulate Spermatogenesis
<b>Enciso, Maria</b>	 Spain	The Ability of Sperm Selection Techniques to Remove Single- or Double-Strand DNA Damage
<b>Gharagozloo, Parviz</b>	 USA	Diagnosis and Treatment of Sperm Oxidative DNA Damage in Male Infertility
<b>Hammadeh, Mohamad</b>	 Germany	Protamine Contents and P <sub>1</sub> /P <sub>r</sub> Ratio in Human Spermatozoa from Smokers and Non-smokers
<b>Kunej, Tanja</b>	 Slovenia	Comparative Integratomics Approach to Identify Candidate Genetic Loci for Male Fertility
<b>Pang, Myung-Geol</b>	 Korea	Numerical Chromosome Abnormalities Are Associated with Sperm Tail Swelling Patterns
<b>Safarinejad, Mohammad Reza</b>	 Iran	The Influence of Genetic Polymorphism on Idiopathic Male Infertility
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<b>Wetthasinghe, Tithila</b>	 Sri Lanka	Y Chromosome Microdeletions Are Not Associated with Spontaneous Recurrent Pregnancy Loss in a Sinhalese Population in Sri Lanka

## EMBRYOLOGY
















<b>Atlmäe, Signe</b>	 Sweden	Interactome of Human Embryo Implantation: Identification of Gene Expression Pathways, Regulation, and Integrated Regulatory Networks
<b>Colledge, William</b>	 UK	Dietary Phytoestrogens Can Stimulate Spermatogenesis
<b>Giojalas, Laura</b>	 Argentina	Sperm Chemotaxis Towards Progesterone, a Guiding Mechanism That May Be Used to Select the Best Spermatozoa for Assisted Reproduction
<b>Huszar, Gabor</b>	 USA	Double Probing Individual Human Spermatozoa: Aniline Blue Staining for Persistent Histones and Fluorescence in Situ Hybridization for Aneuploidies
<b>Ishijima, Sumio</b>	 Japan	Dynamics of Flagellar Force Generated by a Hyperactivated Spermatozoon
<b>Kobayashi, Masayuki</b>	 Japan	Positive and Negative Regulators Synthesized by Rat Hepatoma Cells for the Development of Murine and Bovine Embryos Cultured in vitro
<b>Laird, Diana</b>	 USA	Ror $\gamma$ Enhances Polarity and Directional Migration of Primordial Germ Cells
<b>Sudoma, Iryna</b>	 Ukraine	Optimization of Cryocycles by Using Pinopode Detection in Patients with Multiple Implantation Failure: Preliminary Report
<b>Yotova, Iveta</b>	 Austria	Testosterone Dependent Androgen Receptor Stabilization and Activation of Cell Proliferation in Primary Human Myometrial Microvascular Endothelial Cells
<b>Zara, Vincenzo</b>	 Italy	Evaluation of Mitochondrial Respiratory Efficiency During in vitro Capacitation of Human Spermatozoa

## EPIDEMIOLOGY & ETHICS

<b>Ashok, Pranita</b>	 India	Correlation of Fasting Blood Glucose with Menopausal Status in Middle Aged Women with Their Obesity Status
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# WINNERS

## INTERNATIONAL WINNER



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### ANDROLOGY



#### Kristian Almstrup, PhD

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Dr Almstrup earned his PhD degree from Rigshospitalet, Copenhagen University Hospital, Denmark by studying gene expression profiles of normal and neoplastic germ cells. During these studies he defined the tight link between normal fetal germ cells and the precursor cells of testicular cancer. Dr Almstrup conducted his post-doctoral training at the Danish pharmaceutical Novo Nordisk but returned to the Department of Growth and Reproduction at Rigshospitalet. He is working in the field of molecular andrology as senior scientist and has special interests in epigenetics, testicular cancer and semen analysis.

### Screening of Subfertile Men for Testicular Carcinoma in Situ by an Automated Image Analysis-Based Cytological Test of the Ejaculate

**Objective:** Testicular cancer (TC) is usually diagnosed after manifestation of an overt tumour. Tumour formation is preceded by a pre-invasive and asymptomatic stage, carcinoma in situ (CIS) testis, except for very rare subtypes. The CIS cells are located within seminiferous tubules but can be exfoliated and detected in ejaculates with specific CIS markers.

**Materials and Methods:** We have built a high throughput framework involving automated immunocytochemical staining, scanning microscopy and in silico image analysis allowing automated detection and grading of CIS-like stained objects in semen samples. In this study, 1175 ejaculates from 765 subfertile men were tested using this framework.

**Results:** In 5/765 (0.65%) cases, CIS-like cells were identified in the ejaculate. Four of these had bilateral testicular biopsies performed and CIS was histologically confirmed in three. In total, 63 bilateral testicular biopsy were performed in conjunction with analysis of the ejaculates because of infertility work-up. Histological analysis of the biopsies for the presence of CIS yielded a test sensitivity of 0.67 and a specificity of 0.98. In addition, ejaculates from 45 patients with clinical signs of an overt TC were investigated and yielded a slightly lower sensitivity (0.51), possibly because of obstruction.

**Conclusion:** We conclude that this novel non-invasive test combining automated immunocytochemistry and advanced image analysis allows identification of TC at the CIS stage with a high specificity, but a negative test does not completely exclude CIS. On the basis of the results, we propose that the assay could be offered to subfertile men and other patients who are at increased risk of TC.

**Keywords:** carcinoma in situ testis, semen analysis, diagnostic test, image analysis

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### EMBRYOLOGY

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## Sperm Chemotaxis Towards Progesterone, a Guiding Mechanism That May Be Used to Select the Best Spermatozoa for Assisted Reproduction

**Objective:** The aim of the project was to characterize the sperm chemotactic response and its potential applications for assisted reproduction. Spermatozoa are able to sense an attractant molecule gradient and as a consequence, orient their movement towards the source of the attractant. This mechanism is known as sperm chemotaxis (1). In recent years, our laboratory contributed to the knowledge of several features of mammalian sperm chemotaxis. These include the size and physiological state of the chemotactic sperm population, the biological sources of attractants, the identity of a physiological attractant candidate, the species specificity of the phenomenon, some signal transduction pathways by which chemotaxis is induced, the chemotactic pattern of movement, and the verification of sperm chemotaxis under vivo conditions.

**Materials and Methods:** In order to study mammalian sperm chemotaxis we first developed a method to objectively assess sperm directionality and additional kinetic parameters. This method consists on a device (a chemotaxis chamber) and a videomicroscopy and image analysis system. The chamber has two wells (W1 and W2) that are connected by a bridge over which a capillary space filled with culture medium is formed by adding a coverslip. The cells are loaded in W1, while the attractant in W2, which immediately diffused from W1 to W2 forming a unidirectional long-lasting gradient across the bridge. Cells freely swimming over the bridge are digitally recorded and the tracks evaluated by computer image analysis which includes a software developed in our lab (2-3).

**Results:** We first characterized the sperm chemotactic response under in vitro conditions. We described for the first time the chemotactic response in animal sperm from mouse, rabbit and bovine. In addition, spermatozoa respond to several biological sources of chemoattractants like follicular fluid, oviductal fluid and conditioned medium of the egg-cumulus complex (2,5-6). To elicit a chemotactic response spermatozoa must have accomplished capacitation, whereas only a small subpopulation of spermatozoa (~10% of the cells) are chemotactic at any given time (2,4). Follicular fluid that has been obtained from one species may attract spermatozoa of other species, suggesting that chemotaxis may not be a species-specific phenomenon (7). Several sperm attractants have been reported, however, we observed that progesterone seems to be of physiological importance (3). Thus, a small quantity of progesterone, which is secreted by the cells surrounding the egg, is able to attract spermatozoa (8). Moreover, the chemotactic response was suppressed when either egg conditioned medium was depleted of progesterone or the sperm progesterone receptor was blocked (3). We next investigated the molecular mechanisms that lead to the sperm chemotactic response towards progesterone. Thus, the transmembrane adenylyl cyclase-cAMP-protein kinase A pathway and soluble guanylate cyclase-cGMP-protein kinase G pathway, calcium mobilization and protein tyrosine phosphorylation appear to be involved (9). Chemotactic spermatozoa swimming towards an attractant source are indistinguishable from non chemotactic sperm, but we observed that they showed a unique pattern of movement when they returned towards the source of a chemotactic concentration of progesterone (10). Next we observed under in vivo conditions that the chemotactic mechanism helps to transport sperm to the fertilization site (11), thus validating the in vitro observations. As whole, the results obtained along years lead us to design a new sperm selection assay based on sperm chemotaxis towards progesterone.



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Laura Giojalas is a Full Professor of Cell Biology at the University of Cordoba, and an Independent Researcher of the National Council of Research in Argentina. She is the Director of the Centre for Cell and Molecular Biology of the same University. In the last 15 years, her laboratory has been focused on understanding the chemical interaction between mammalian gametes before fertilization, with particular interest in sperm guiding navigation and its potential application for Assisted Reproduction.

**Conclusion:** Human spermatozoa are able of chemotactic response to very low levels of progesterone. This steroid has been considered a physiological attractant since by the time of ovulation it is secreted by the cells surrounding the egg. Only capacitated spermatozoa (those ready to fertilize the egg) may show chemotactic behavior. Therefore, a sperm population enriched with capacitated spermatozoa by means of chemotaxis may be considered a physiological selection procedure that may be useful for assisted reproduction technologies.

**Keywords:** sperm chemotaxis – progesterone

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# WINNERS

## INTERNATIONAL WINNER



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### FEMALE INFERTILITY



**Wenjie Zhu, MD**

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Wenjie Zhu was graduated from Medical Department of Jiang-Su Province Xu-Zhou Medical College in 1982. In 1987, he engaged the post-graduated study in Department of Gynecology and Obstetrics of Zhong-Shen Medical University and graduated in 1990. Then he engaged in gynecology and infertility work in Affiliated Shen-Zhen Maternity and Child Healthcare Hospital of Southern Medical University. In 1999, he built the Reproductive Medical Center in the hospital and became the centre's head and performed in vitro fertilization and embryo transfer. He became the head of Department of Reproductive Health in 2002, the professor of Southern Medical University in 2007. He has been the commissioner of Shen-Zhen City Reproductive Medical Society from 2000, the Reproductive Brand member of Guang-Dong Province Maternity and Child Healthcare Commission from 2008, and the commissioner of Guang-Dong Province Reproductive Medical Society from 2010.

## 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

**Objective:** In 2005, we designed and evaluated the effectiveness of the transvaginal ultrasound-guided ovarian interstitial laser treatment in twenty-three anovulatory women with clomifene citrate (CC)-resistant polycystic ovary syndrome (PCOS) as a new method of ovulation induction in infertile PCOS women, with a more than 80% ovulation rate and 36% pregnancy rate during six postoperative months. Objective of this study was to explore an optimal laser dose for this new treatment protocol.

**Materials and Methods:** Eighty infertile PCOS patients with CC-resistant were enrolled between January 2006 and June 2008. All women presented with oligo-/amenorrhea and anovulation for at least 2 years and were seeking pregnancy. The mean ( $\pm$  SD) age was  $29.1 \pm 3.1$  years and the mean duration of infertility  $3.3 \pm 2.0$  years. The mean body mass index (BMI) was  $22.9 \pm 3.5$  kg/m<sup>2</sup>. PCOS was diagnosed referring The Rotterdam criteria. Serum concentrations of FSH ( $6.5 \pm 1.4$  IU/L), LH ( $13.7 \pm 4.6$  IU/L) and T ( $2.9 \pm 0.75$  nmol/L) were assessed at the third day of progesterone-induced bleeding. TVS examination revealed 10-30 subcapsular follicles of 2-8 mm in diameter in unilateral ovary. Any contraindications to surgery, previous treatment with LOD and the presence of tubal or male factors for infertility were considered as exclusion criteria. All subjects were randomly divided into group A, B, C, D and laser coagulation points were as follows: group A, one coagulation point per ovary; group B, two points; group C, three points; group D, four to five points. The procedure of laser treatment has been detailed previously. Briefly, it was location and puncture, laser coagulation and the fibre-optic withdrawal and relocation. Postoperative Monitoring include the serum hormone concentrations, follicle development and ovulation, pregnancy and miscarriage and adverse effects. Statistical significance was set at  $P < 0.05$ .

**Results:** The ovulation rates of group C (75.00%, 15/20) and D (80.00%, 16/20) were significantly higher than of group A (5.00%, 1/20) ( $P < 0.001$ ;  $P < 0.001$ ) and B (15.00%, 3/20) ( $P < 0.001$ ;  $P < 0.001$ ). The conception rates were significantly higher in group C (45.00%, 9/20) and D (40.00%, 8/20) than in group A (5.00%, 1/20) and B (15.00%, 3/20) ( $P < 0.05$ ;  $P < 0.05$ ). The mean postoperative serum testosterone levels were significantly lower in group C ( $2.08 \pm 0.62$  nmol/l) and D ( $2.07 \pm 0.42$  nmol/l) compared with group A ( $3.10 \pm 0.63$  nmol/l) ( $P < 0.001$ ;  $P < 0.001$ ) and B ( $2.98 \pm 0.63$  nmol/l) ( $P < 0.001$ ;  $P < 0.001$ ). The mean LH value and LH/FSH ratio in group C and D were also significantly lower than in group A and group B. Each increase of dose with one point, would decrease the mean LH level  $2.238$  IU/l ( $y = 14.175 - 2.238x$ , R square = 0.918), the mean serum T level  $0.671$  nmol/l ( $y = 4.55 - 0.671x$ , R square = 0.925) and LH/FSH ratio value  $0.411$  ( $y = 2.585 - 0.411x$ , R square = 0.834). There were no adverse events.

**Conclusion:** Three coagulation points per ovary seems to be the plateau dose sufficient to produce an optimal outcome for ovarian interstitial laser treatment in anovulatory PCOS women. Reducing the laser dose below that level is associated with poorer results and increasing the dose above it does not improve the outcome.

**Keywords:** Anovulation, dose laser, ovarian interstitial, Polycystic ovary syndrome, transvaginal, ultrasound-guided

# WINNERS

## INTERNATIONAL WINNER



### FEMALE INFERTILITY

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## Role of Mevalonate-Ras Homology (Rho)/Rho-Associated Coiled-Coil-Forming Protein Kinase-Mediated Signaling Pathway in the Pathogenesis of Endometriosis-Associated Fibrosis

**Objective:** Endometriosis, a disease affecting 3-10% of women of reproductive age, is characterized by the ectopic growth of endometrial glands and stroma surrounded by dense fibrous tissue. Whereas, normal eutopic endometrium shows scarless tissue repair during menstrual cycles, which suggests that the endometriotic tissues have distinct mechanisms of fibrogenesis. During the development of endometriotic lesions, excess fibrosis may lead to scarring and to alteration of tissue function. It has been suggested that type I collagen is a major contributor to endometriosis-associated fibrosis. Alpha-smooth muscle actin (SMA)-positive myofibroblastic cells were frequently detected in the fibrotic areas of endometriosis lesions. We have previously demonstrated that endometriotic stromal cells can differentiate to alpha-SMA-positive myofibroblasts. One approach to understanding the pathogenesis of endometriosis is to investigate the mechanisms underlying the fibrogenesis associated with this disease. Using 3-dimensional collagen gel culture model, we have evaluated the extracellular matrix contractility and myofibroblastic differentiation of endometriotic stromal cells. Endometriotic stromal cells showed enhanced extracellular matrix contractility in comparison with normal endometrial stromal cells. Activation of the mevalonate-Ras homology (Rho)/Rho-associated coiled-coil-forming protein kinase (ROCK)-mediated signaling pathway with simultaneously enhanced myofibroblastic differentiation is involved in this mechanism. In the present study, we investigated the effect of various agents that target mevalonate-Rho/ROCK mediated signaling pathway for the treatment of endometriosis-associated fibrosis using the 3-dimensional collagen gel culture system.

**Materials and Methods:** Primary cultures of endometriotic cyst stromal cells were utilized for the experiments. The effects of simvastatin, Y-27632, fasudil, heparin and Decidualization on the contractile profile, morphology, cell density, and contraction-related molecule expression of these cells in the 3-dimensional collagen gel culture were investigated using laser scanning microscopy, collagen gel contraction assay, and Western blot analysis. The effects of these mevalonate-Rho/ROCK pathway-targeting agents on the cell proliferation, apoptosis, and cell cycle of endometriotic cyst stromal cells in 2-dimensional culture were also evaluated by methylthiazolotetrazolium (MTT) assay, 5-bromo-2'-deoxyuridine (BrdU) incorporation assay, and terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL) assay.

**Results:** Mevalonate-Rho/ROCK pathway-targeting agents examined in this study attenuated the contractility of endometriotic stromal cells by inhibiting mevalonate-Rho/ROCK pathway activation, cell proliferation, attachment to surrounding extracellular matrices, and the differentiation into the alpha-smooth muscle actin-positive myofibroblastic phenotype. These agents also induced the apoptosis and cell cycle arrest of cultured endometriotic stromal cells.

**Conclusion:** Research on endometriotic stromal cell biology using 3-dimensional collagen matrices offers new opportunities to understand the reciprocal and adaptive interactions that occur between cells and surrounding matrix in a tissue-like environment. Such interactions are integrated with the regulation of endometriotic tissue morphogenesis and dynamics that characterizes endometriosis-associated fibrosis. It is suggested that



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Dr Nasu earned his MD degree in 1990 and his PhD in pathology in 1995 at Oita Medical University, Yufu-shi, Japan. From 1996 to 2001 he was an instructor at department of Obstetrics and Gynecology in Oita University, and took his post-doctoral training at Department of Stomatology, School of Dentistry, University of California, San Francisco from 1997 to 1998. He is a professor at department of Obstetrics and Gynecology, faculty of Medicine, Oita University. He is also a visiting professor at Hubei University and an associate editor of *Obstetrics and Gynecology Research Journal*.

the enhanced extracellular matrix contractility of endometriotic stromal cells in the 3-dimensional collagen gel culture is associated with myofibroblastic differentiation and the activation of mevalonate-Rho/ROCK-mediated signaling pathways, and that modulation of mevalonate-Rho/ROCK pathways seems to be a novel therapeutic target for the treatment and prevention of endometriosis-associated fibrosis.

**Keywords:** endometriosis, contractility, mevalonate-Rho/ROCK pathway, fibrosis, myofibroblast



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## INTERNATIONAL WINNER



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### REPRODUCTIVE GENETICS



**Signe Altmäe, PhD**

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Signe Altmäe is currently a post-doc fellow at the University of Granada, Spain. She received her PhD in gene technology at the Department of Biotechnology, University of Tartu, Estonia on 'Genomics and Transcriptomics of human induced ovarian folliculogenesis'. She continued her research in female reproduction at the Division of Obstetrics and Gynaecology, Karolinska Institutet, Sweden, where she defended her second thesis, in medical sciences, on topic 'Human endometrial receptivity and embryo-endometrium interactions'. She has authored several scientific publications on female infertility and endometrial receptivity, and her current research also includes female reproduction, and embryo-endometrium networks.

### Interactome of Human Embryo Implantation: Identification of Gene Expression Pathways, Regulation, and Integrated Regulatory Networks

**Objective:** A prerequisite for successful embryo implantation is adequate preparation of receptive endometrium and the establishment and maintenance of a viable embryo. The success of implantation further relies upon a two-way dialogue between the embryo and uterus. However, molecular bases of these preimplantation and implantation processes in humans are not well known.

**Materials and Methods:** We performed genome expression analyses of human embryos ( $n = 128$ ) and human endometria ( $n=8$ ). We integrated these data with protein-protein interactions in order to identify molecular networks within the endometrium and the embryo, and potential embryo–endometrium interactions at the time of implantation. For that we applied a novel network profiling algorithm HyperModules, which combines topological module identification and functional enrichment analysis.

**Results:** We found a major wave of transcriptional down-regulation in preimplantation embryos. In receptive-stage endometrium, several genes and signalling pathways were identified, including JAK-STAT signalling and inflammatory pathways. The main curated embryo–endometrium interaction network highlighted the importance of cell adhesion molecules in the implantation process. We also identified cytokine–cytokine receptor interactions involved in implantation, where osteopontin, LIF and LEP pathways were intertwining. Further, we identified a number of novel players in human embryo–endometrium interactions, such as APOD, EDN1, FGF7, GAST, KREMEN1, NRP1, SERPINA3, VCAN, and others.

**Conclusion:** Our findings provide a fundamental resource for better understanding of the genetic network that leads to successful embryo implantation. We demonstrate the first systems biology approach into the complex molecular network of the implantation process in humans.

**Keywords:** Implantation, embryo-endometrium interactions, receptive endometrium

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## INTERNATIONAL WINNER



### REGENERATIVE MEDICINE

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## Ex vivo Expanded Hematopoietic Stem Cells Overcome the MHC Barrier in Allogeneic Transplantation

**Objective:** The lack of understanding of the interplay between hematopoietic stem cells (HSCs) and the immune system has severely hampered the stem cell research and practice of transplantation. Major problems for allogeneic transplantation include low levels of donor engraftment and high risks of graft-versus-host disease (GVHD). Transplantation of purified allogeneic HSCs diminishes the risk of GVHD, but results in decreased engraftment. Here we show that ex vivo expanded mouse HSCs efficiently overcame the major histocompatibility complex barrier and repopulated allogeneic recipient mice.

**Materials and Methods:** An 8-day expansion culture led to a 40-fold increase of the allograft ability of HSCs.

**Results:** Both increased numbers of HSCs and culture-induced elevation of expression of the immune inhibitor CD274 (B7-H1 or PD-L1) on the surface of HSCs contributed to the enhancement.

**Conclusion:** Our study indicates the great potential of utilizing ex vivo expanded HSCs for allogeneic transplantation, and suggests that the immune privilege of HSCs can be modulated.

**Keywords:** hematopoietic stem cells, allogeneic transplantation, ex vivo expansion, immunology



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Dr Chengcheng (Alec) Zhang earned his BS degree in Molecular Biology from the University of Science and Technology of China in 1992 and his PhD in Biochemistry from the University of Illinois at Urbana-Champaign in 1999. He received his postdoctoral training under the mentorship of Dr Harvey Lodish at Whitehead Institute/MIT, where he started a project on growing hematopoietic stem cells. Dr Zhang established his independent lab at UT Southwestern Medical Center in 2007. He is studying the function of immune surface molecules such as CD274 and Angptl receptors on stem cells and cancer, focusing on how stem cells gain immune privilege and regulate their cell fates and metabolism through interaction with the immune system. His research aims to develop novel therapies for regenerative medicine and cancer treatment.

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### STEM CELL BIOLOGY & TECHNOLOGY



**Alireza Pouya, MSc**

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Alireza Pouya received his BA in Biology from University of Tehran and his MSc in Human Genetic from University of Social Welfare and Rehabilitation Science of Tehran in Iran. Then he started his collaboration as a research assistant with Royan institute for Stem Cell Biology and Technology in neural stem cell division. The main part of his work has been on generating of neural and glial cells from mouse and human pluripotent stem cells (ES and iPS) and study the potential role of differentiated cells to recover the myelin defect in animal models. He is currently working on direct reprogramming of fibroblasts to glial cells by overexpression of transcription factors using viral transduction delivery method.

### Human Induced Pluripotent Stem Cells Differentiation into Oligodendrocyte Progenitors and Transplantation in a Rat Model of Optic Chiasm Demyelination

**Objective:** This study aims to differentiate human induced pluripotent stem cells (hiPSCs) into oligodendrocyte precursors and assess their recovery potential in a demyelinated optic chiasm model in rats.

**Materials and Methods:** We generated a cell population of oligodendrocyte progenitors from hiPSCs by using embryoid body formation in a defined medium supplemented with a combination of factors, positive selection and mechanical enrichment. Real-time polymerase chain reaction and immunofluorescence analyses showed that stage-specific markers, Olig2, Sox10, NG2, PDGFR $\alpha$ , O4, A2B5, GalC, and MBP were expressed following the differentiation procedure, and enrichment of the oligodendrocyte lineage.

**Results:** These results are comparable with the expression of stage-specific markers in human embryonic stem cell-derived oligodendrocyte lineage cells. Transplantation of hiPSC-derived oligodendrocyte progenitors into the lysolecithin-induced demyelinated optic chiasm of the rat model resulted in recovery from symptoms, and integration and differentiation into oligodendrocytes were detected by immunohistochemistry staining against PLP and MBP, and measurements of the visual evoked potentials.

**Conclusion:** These results showed that oligodendrocyte progenitors generated efficiently from hiPSCs can be used in future biomedical studies once safety issues have been overcome.

**Keywords:** Human Induced Pluripotent Stem Cells, Oligodendrocyte Progenitors, Transplantation

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<b>Amirarjmand</b> , Mohammad Hossein, MSc	Iran	<b>Hamidieh</b> , Amir Ali, MD	Iran
<b>Aramesh</b> , Kiarash, MD	Iran	<b>Hartshorne</b> , Geraldine, PhD	UK
<b>Arefi</b> , Soheila, MD	Iran	<b>Henkel</b> , Ralf, BEd, PhD	South Africa
<b>Asghari</b> , Fariba, MD	Iran	<b>Hoseini far</b> , Hani, MSc	Iran
<b>Ashrafi</b> , Mahnaz, MD	Iran	<b>Hosseini</b> , Roya, MD	Iran
<b>Azadbakht</b> , Mehri, PhD	Iran	<b>Hosseini</b> , Seyed Jalil, MD	Iran
<b>Azin</b> , Seyed Ali, MD, PhD	Iran	<b>Hosseinkhani</b> , Hossein, PhD	Taiwan
<b>Azin</b> , Seyed Mohammad, PhD Student	Iran	<b>Jalali</b> , Mohsen, PhD	Iran
<b>Baghaban Eslaminejad</b> , Mohamadreza, PhD	Iran	<b>Jalalshokouhi</b> , Jalal, MD	Iran
<b>Bahadori</b> , Mohammad Hadi, PhD	Iran	<b>Kabir-Salmani</b> , Maryam, PhD	Iran
<b>Baharvand</b> , Hossein, PhD	Iran	<b>Kalantar</b> , Seyed Mehdi, PhD	Iran
<b>Bakhtiari</b> , Mitra, PhD	Iran	<b>Kalantary</b> , Mojgan, MD	Iran
<b>Balasinor</b> , Nafisa, PhD	India	<b>Kallen</b> , Bengt, MD, PhD	Sweden
<b>Baylis</b> , Françoise, PhD	Canada	<b>Kamali</b> , Koorosh, MD, PhD	Iran
<b>Behnam Manesh</b> , Shima, MA	Iran	<b>Kamali</b> , Mohammad, PhD	Iran
<b>Benagiano</b> , Giuseppe, MD, PhD	Switzerland	<b>Karimian</b> , Leila, MSc	Iran
<b>Chian</b> , Ri-Cheng, PhD	Canada	<b>Khalili</b> , Mohammad Ali, PhD	Iran
<b>Chieffi</b> , Paolo, MD, PhD	Italy	<b>Kiani</b> , Sahar, PhD	Iran
<b>Crosignani</b> , Pier Giorgio, MD	Italy	<b>Küpker</b> , Wolfgang, MD, PhD	Germany
<b>D'Hooghe</b> , Thomas, MD, PhD	Belgium	<b>Larijani</b> , Tahereh, MD	Iran
<b>Dadkhah</b> , Farid, MD	Iran	<b>Lutolf</b> , Matthias P., PhD	Switzerland
<b>De Geyter</b> , Christian, MD	Switzerland	<b>Maccarrone</b> , Mauro, PhD	Italy
<b>De Rooij</b> , Dirk G., PhD	Netherlands	<b>Mackay-Sim</b> , Alan, PhD	Australia
<b>Ebrahimi</b> , Marzieh, PhD	Iran	<b>Ma'dani</b> , Tahereh, MD	Iran

<b>Mahfouz</b> , Reda Z, MD	USA	<b>Rostami</b> , Sirous, MD	Iran
<b>Malekafzali</b> , Hossein, PhD	Iran	<b>Sabbaghian</b> , Marjan, PhD	Iran
<b>Martin</b> , Ivan, PhD	Switzerland	<b>Sabeti</b> , Shokofeh, MD	Iran
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<b>Mohammadi Roushandeh</b> , Amaneh, PhD	Iran	<b>Saric</b> , Tomo, MD, PhD	Germany
<b>Mohseni Meybodi</b> , Anahita, PhD	Iran	<b>Sato</b> , Eimei, PhD	Japan
<b>Moini</b> , Ashraf, MD	Iran	<b>Schlegel</b> , Peter, MD	USA
<b>Monsees</b> , T.K., PhD	South Africa	<b>Shahhoseini</b> , Maryam, PhD	Iran
<b>Moreno-Manzano</b> , Victoria, MD	Spain	<b>Shahverdi</b> , Abdolhossein, PhD	Iran
<b>Movaghar</b> , Bahar, PhD	Iran	<b>Shahzadeh Fazeli</b> , S. Abolhassan, MD, PhD	Iran
<b>Movahedin</b> , Mansoureh, PhD	Iran	<b>Shamsi pour</b> , Mansur, PhD Student	Iran
<b>Movassagh</b> , Hooman, PhD	Iran	<b>Shariatinasab</b> , Sadegh, PhD Student	Iran
<b>Mowla</b> , Seyed Javad, PhD	Iran	<b>Sheikhha</b> , Mohammad Hasan, MD, PhD	Iran
<b>Mukhopadhyay</b> , Asok, PhD	India	<b>Shiva</b> , Marzieh, MD	Iran
<b>Nasr-Esfahani</b> , Mohammad Hossein, PhD	Iran	<b>Sills</b> , Eric Scott, MD	USA
<b>Nielsen</b> , Hans Ingolf, PhD	Denmark	<b>Simpson</b> , Joe Leigh, MD	USA
<b>Niknejadi</b> , Maryam, MD	Iran	<b>Sofikitis</b> , Nikolaos, MD, PhD	Greece
<b>Noruzinia</b> , Mehrdad, MD, PhD	Iran	<b>Soleimani</b> , Masoud, PhD	Iran
<b>Nowroozi</b> , Mohammad Reza, MD	Iran	<b>Stamm</b> , Christof, MD	Germany
<b>Nussler</b> , Andreas, PhD	Germany	<b>Stewart</b> , Elizabeth, MD	USA
<b>Olsen</b> , Jorn, MD, PhD	Denmark	<b>Strauer</b> , Bodo, MD	Germany
<b>Omani Samani</b> , Reza, MD	Iran	<b>Strom</b> , Stephen C., PhD	Sweden
<b>Ory</b> , Steven, MD	USA	<b>Svoboda</b> , Petr, PhD	Czech Republic
<b>Ott</b> , Michael, MD	Germany	<b>Taheri Panah</b> , Robabeh, MD	Iran
<b>Pacey</b> , Allan, PhD	UK	<b>Tahmasebpour</b> , Ahmad Reza, MD	Iran
<b>Parsanezhad</b> , Mohammad Ebrahim, MD	Iran	<b>Tardif</b> , Steve, PhD	USA
<b>Piemonti</b> , Lorenzo, MD	Italy	<b>Tarzamni</b> , Mohammad Kazem, MD	Iran
<b>Piryaee</b> , Abbas, PhD	Iran	<b>Tehranejad</b> , Ensieh, MD	Iran
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<b>Poureisa</b> , Masoud, MD	Iran	<b>Vermeesch</b> , Joris, PhD	Belgium
<b>Pourmand</b> , Gholamreza, MD	Iran	<b>Xia</b> , Enlan, MD	China
<b>Ramezanzadeh</b> , Fatemeh, MD	Iran	<b>Zahedi</b> , Farzaneh, MD	Iran
<b>Rashidi</b> , Batool, MD	Iran	<b>Zamani</b> , Mahdi, PhD	Iran
<b>Redi</b> , CarloAlberto, PhD	Italy	<b>Ziaee</b> , Seyed Amir Mohsen, MD	Iran
<b>Rezazadeh</b> , Mojtaba, PhD	Iran		

# BOARD

## EXECUTIVE COMMITTEE



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**Abdollahian**, Enayatollah, BSc

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**Alizadeh**, Seyyed Kamal, BSc

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**Behnam-manesh**, Shima, MA

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**Daliri**, Leila, MSc

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**Ebrahimi**, Marziyeh, PhD

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**Ezabadi**, Zahra, MSc

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**Gourabi**, Hamid, PhD

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**Hadi**, Mahdi, BSc

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**Jafarpour**, Farnoush, PhD

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**Kashfi**, Fahimeh, MSc

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**Mirshekar**, Zeynab, BSc

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**Niknejhadi**, Maryam, MD

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**Niknejhad**, Fatemeh, BSc

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**Ommani Samani**, Reza, MD

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**Sabbaghiyan**, Marjan, PhD

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**Shajarepour**, Laleh, BSc

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**Shahverdi**, Abdolhossein, PhD

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**Shahzadeh Fazeli**, Abolhassan, MD, PhD

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**Tavakkolifar**, Farnak, MSc

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**Tavassolian**, Rahim, BSc

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**Vosough**, Ahmad, MD

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**Zarei Moradi**, Shabnam, MSc

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**Zarrabi**, Morteza, MD





# ROYAN INSTITUTE ANNUAL REPORT

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# ANNUAL REPORT



## Royan Institute

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, 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 and also is effective 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 Animal Biotechnology (RI-AB)
4. Laboratory Animal Core Facility

## Research Institutes

### Royan Institute for Reproductive Biomedicine

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

### Royan Institute for Stem Cell Biology and Technology

- 15 Research Programs
- 9 Core Facilities

### Royan Institute for Animal Biotechnology

- Reproduction and Development
- Molecular Biotechnology
- Cell and Molecular Biology
- Dairy Assist Center

## Overview of the Institute's Developments

- 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)

## Royan Institute for Reproductive Biomedicine (RI-RB)

Royan Institute for Reproductive Biomedicine, founded in 1991, consists of six departments and one 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 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 (RI-SCBT) was established in 2002 to promote research on general stem cell biology in Iran. Since early 2010, it has continued its activities in:

- 15 Research Programs
- 9 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 Animal Biotechnology (RI-AB)

Royan Institute for Animal 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 handicrafts, and is known as the city of "blue tiles".

Royan Institute for Animal 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, the establishment of novel sperm selection methods for assisted reproductive technology, cell differentiation, production of recombinant proteins and the cell biology of peroxisomes. The endeavors of Royan Institute for Animal 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 our Institute are: gene reprogramming during SCNT, transgenesis, sperm cell biology, the role of sub-cellular organelles in differentiation and recombinant protein technology. In addition, the Institute is providing a comprehensive and coordinated "bench to production" approach in recombinant protein technology, animal farming and the establishment of methods to increase the efficiency of assisted reproductive techniques.

### RI-AB Projects and Facilities:

- Embryology
- Andrology
- Stem Cell
- Genetics
- Recombinant Protein

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.

# ANNUAL REPORT

## Endocrinology and Female Infertility Department of RI-RB

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### Message from the Department Director

The goal of our department is the performance of applied research in order to achieve the best and easiest strategies for diagnosis and improvement of ART outcomes. Our department focuses on the treatment and research of PCOS, recurrent abortion, endometriosis, poor responders and recurrent implantation failure. In addition, we investigate various ovulation induction, COH and ART/ ET methods. The goals of our group include: the 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, and endometrial preparation; and the promotion of prenatal care.

### Introduction and Department History

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

### Research Scientists:

- **Madani**, Tahereh, MD (Gynecologist)
- **Moini**, Ashraf, MD (Gynecologist)
- **Shahrokh Tehrani Nejad**, Ensieh, MD (Gynecologist)
- **Ghaffari**, Firoozeh, MD (Gynecologist)
- **Shiva**, Marzieh, MD (Gynecologist)
- **Hafezi**, Maryam, MD (Gynecologist)
- **Ramezanali**, Fariba, MD (Gynecologist)
- **Hemat**, Mandana, MD (Gynecologist)
- **Mashayekhy**, Mehri, MD (Gynecologist)
- **Hoseyni**, Roya, MD (Endocrinologist)
- **Zangene**, Mehrangiz, MD (Physician infectionist)

### Research Assistants:

- **Amirchaghmaghi**, Elham, MD, PhD (Candidate)
- **Kiani**, Kianokht, PhD (Candidate)
- **Jahangiri**, Nadia, MSc (Midwifery)
- **Mohamadi Yeganeh**, Ladan, MSc (Midwifery)
- **Malekzadeh**, Farideh, MSc (Nursing)
- **Jahanian**, Shahideh, PhD (Candidate)
- **Arabipour**, Arezou, Msc (Midwifery)

### Other Members:

- **Shajarehpour Salavati**, Laleh, BSc (Midwifery)
- **Joudmardi**, Masoumeh, BSc (Social Science)
- **Jalali**, Samaneh, BSc (Social Science)
- **Zolfaghari**, Zahra, BSc (Statistic)
- **Sanati**, Azam, BSc (Statistic)
- **Keshvarian**, Maryam, AA (Graphist)

### Students' Theses:

- 3 PhD theses
- 16 MSc theses (8 completed this year)

### Publications

*The effect of adding oral oestradiol to progesterone as luteal phase support in ART cycles: a randomized controlled study.* Moini A ,Zadeh Modarress Sh, Amirchaghmaghi E, Mirghavam N, Khafri S, Akhoond MR, Salman Yazdi R. Arch Med Sci. 2011 Feb; 7(1): 112-6.



### Department Head: Mahnaz Ashrafi, MD

■ Gynecologist

[ashrafim@royaninstitute.org](mailto:ashrafim@royaninstitute.org)

### Biography

General Physician, Tehran University of Medical Science (1977-1984)  
Obstetrics & Gynecology, Iran University of Medical Science, Tehran, Iran (1985-1989)  
Assistant Professor, Faculty of Medicine, Iran University of Medical Science (1989-2005)  
Associate Professor, Faculty of Medicine, Iran University of Medical Science (2005-Present)  
Head of Endocrinology and Female Infertility Department, Royan Institute (1989-present)

*The effect of low dose human chorionic gonadotropin on follicular response and oocyte maturation in PCOS patients undergoing IVF cycle: a randomized clinical trial of efficacy safety.* Ashrafi M, Kiani K, Ghasemi A, Rastegar F, Nabavi M. Arch Gynecol Obstet. 2011 Dec; 284(6):1431-8.

*The factors affecting the outcome of frozen thawed embryo transfer cycle.* Ashrafi M, Jahangiri N, Hassani F, Akhoond MR, Madani T. Taiwanese journal of obstetrics & gynecology. 2011 Jun; 50(2): 159-64.

*Comparing intramuscular progesterone, vaginal progesterone and 17  $\alpha$ -hydroxy progesterone caproate in IVF and ICSI cycle.* Moini A, Zafarani F, Eslami B, Sadeghi M, kamyabi Z, Jahangiri N. Iranian journal of reproductive medicine. 2011; 9(2): 119-124.

*Survival of a 580 g infant conceived by in vitro fertilization.* Shiva M, Mohammadi Yeganeh L. International Journal of Fertility & Sterility. 2011; 5(2): 116-118.

*Heterotopic pregnancy after assisted reproductive techniques: Case reports.* Moini A, Hoseini R, Mohmmadi Yeganeh L. International Journal of Fertility & Sterility. 2010; 3(4): 195-198.

*A case report of bilateral tubal ectopic pregnancy following day 5 embryo transfer (Letter to Editor).* Ghaffari F, Eftekhari P, Yazdi R, Kiani K. Arch Med Sci. 2011 Dec 31; 7(6): 1087-8.

*Comparison of different stimulation protocols efficacy in poor responders undergoing IVF: A retrospective study.* Madani T, Ashrafi M, Mohmmadi Yeganeh L. Gynecological endocrinology. 2012 Feb; 28(2): 102-5.

*Comparison of serum uric acid Iron and total Iron binding capacity (JIBC) level in preclamptic and normal pregnant women.* Eslami B, Moini A, Hosseini R, Sedaghat M. Journal of Family and Reproductive Health. 2010; 4(4):161-4.

*Improvement in pregnancy rate by removal of cervical discharge prior to embryo transfer in ICSI cycles: A randomized clinical trial.* Moini A, Kiani K, Bahmanabadi A, Akhoond M, Akhlaghi A. Australian and New Zealand Journal of Obstetrics and Gynecology. 2011 Aug; 51(4): 315-20.

## Core Facility:

### Female Infertility Research Laboratory



#### Introduction

The Female Infertility Research Laboratory is a cell and molecular research facility established in 2010 to undertake research in the field of reproduction.

#### Core Facility Head:

**Aflatoonian, Reza, MD, PhD (Molecular Reproductive Medicine)**

Dr Aflatoonian obtained a PhD in Reproductive Medicine in addition to a post-doctorate in Molecular Medicine at the University of Sheffield. He has published at least 20 international articles and more than 50 international abstracts.

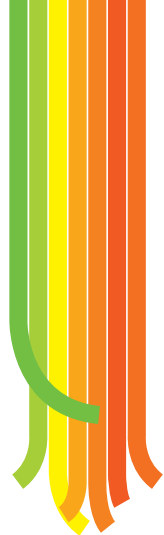
#### Staffs:

**Janan, Arghavan, MSc (Developmental Biology)**

**Aghajanpour, Samaneh, MSc (Cellular and Molecular Biology)**

#### Journal Clubs:

No	Organizer	Date	Title
1	Dr Reza Aflatoonian	May, 17, 2011	Innate immunity in reproduction
2	Dr Fariba Ramezani	November 22, 2011	Premature ovarian failure (POF)
3	Dr Fereshteh Sabeti	February 28, 2012	Psychological effects of infertility on infertile couples



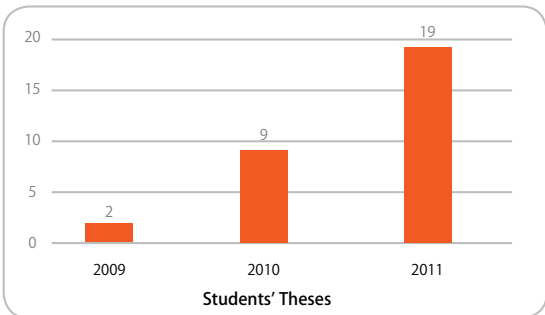
### News and Events

- OHSS Symposium, September 29, 2011**  
 This symposium covered subjects such as the epidemiology of OHSS, clinical manifestation and classification of OHSS, prevention and adjuvant therapy, imaging radiology and ultrasonography in OHSS, in addition to out patient and in patient clinical management among others.
- Pre-congress Workshop on Office Hysteroscopy: September 5, 2011**  
 This pre-congress covered subjects such as Introduction to diagnosis and operative procedures of office hysteroscopy.



- Pre-congress course of Implantation, September 6, 2011**  
 This pre-congress course covered subjects such as introduction to physiology, aspects of implantation, introduction to effects of COH on implantation, and uterine preparation protocols for ET, among others.
- CME Program of Infertility 1 & 2, February 1-2, 2012**  
 This program was held to introduce infertility issues and modern procedures of assisted reproductive techniques. It covered subjects such as recurrent implantation failure and recurrent abortion, poor ovarian response, OHSS, male and female reproductive surgery, and GIFT – ZIFT, among others.

### Staff, Publication, Budget, and Citation Charts





# ANNUAL REPORT

## Andrology Department of RI-RB



### Department Head: Dr Mohamad Ali Sadighi Gilani, MD

- Specialist in Urology, Faculty of Medicine, Iran University of Medical Science, Tehran, Iran
- MD, Faculty of Medicine, Iran University of Medical Science, Tehran, Iran

[ali.sadighi@royaninstitute.org](mailto:ali.sadighi@royaninstitute.org)

#### Biography

Dr Sadighi Gilani was born in 1954 and studied geology at Shiraz University in 1970. He continued his studies and earned his MSc degree at the School of Mines & Technology, South Dakota, USA in 1977. Afterwards he began his study of medicine at the University of Medical Science of Iran in 1980. Dr Sadighi Gilani completed his residency training at the Urology Department of Hashemi-Nejad Hospital-University of Medical Science of Iran in 1992. From 1992 to 1993 he was trained as an observer in the Institute of Urology and Nephrology in London – England. In 1995 he completed his master training for No Scalpel Vasectomy (WK) with Professor Li in Tehran, Iran By P.C.L and the training For Vasectomy By Professor Li, Tehran-Iran By P.C.I.

#### Message from the Department Director

The department of Andrology provides the most scientific protocols in the diagnosis and treatment of male fertility. This new male infertility management depends on specialized proper evaluation of the male factor by clinical examination for testicular size and checking for the presence of varicocele, hormonal profile, scrotal Doppler, and semen analysis, according to the standards of the World Health Organization. Different modalities are available in this unit to manage low sperm count, low sperm motility and increased sperm abnormality.

Andrology department includes clinic and education and research.

The mission of this department is to improve diagnostic and therapeutic methods by using and applying the results of investigative projects, in addition to using stem cells to treat patients with incomplete spermatogenesis. Providing quality health care for infertile males, educating the lay and professional communities on the latest treatments for male fertility and enhancing the understanding of male infertility issues by developing research projects are the vision of this department.

#### Department History and Introduction

The first step in infertility management is couple's evaluation. 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 of the Department

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

#### Main Activities of Andrology Department

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

## Clinic

### Introduction

Andrology Clinic of Royan Institute is the major referral centre for male infertility problems in Iran. A part of our activities in this center for diagnosis of male factor infertility includes patients' history and clinical examinations such as scrotal sonography, hormone and semen analysis, and DNA damage analysis. This Clinic is set up for the evaluation and treatment of male infertility, male sexual problems, varicocele and vasectomy reversal.

### Research Scientists:

- **Hosseini**, Seyyed Jalil, MD (Urologist)
- **Farrahi**, Faramarz, MD (Urologist)
- **Dadkhah**, Farid, MD (Urologist)
- **Salman Yazd**, Reza, MD
- **Zarrabi**, Morteza, MD (General Physician)
- **Azizi**, Mohammad, MD
- **Nour Mohammadi**, Ahmad, MD

### Publications

*The relationship between occupation and semen quality.* Vaziri MH, Sadighi Gilani MA, Kavousi A, Firoozeh M, Khani Jazani R, Vousough Tagi Dizaj A, Mohseni H, Bagery Lankarani N, Azizi M, Salman Yazdi R, IJFS 2011, 66-71.

*Conservation cloning of vulnerable esfahan mouflon (Ovis Orientals isphahanica) in vitro and in vivo studies,* Hajian M, Hosseini M, Forouzanfar M, Abedi P, Ostadhosseini S, Hosseini L, Moulavi F, Gourabi H, Shahverdi AH, Vousough Taqi Dizaj A, Kalantari SA, Fotouhi Z, Iranpour R, Mahyar H, Amiri Yekta A, Nasr-Esfahani MH, Journal of Assisted Reproduction and Genetics 2011, 1119-1127.

*The effect of adding oral estradiol to progesterone as luteal phase support in ART cycles – a randomized controlled study,* moini A, Zade Modareess Sh, Amirchaghmaghi ghghavami N, Khafri S, Akhoond MR, Salman Yazdi R, Clinical Research 2011 112-116.

*Improved in vitro development of cloned bovine embryos using S-adenosylhomocysteine, a non-toxic epigenetic modifying reagent,* Jafari S, Hosseini MS, Hajian M, Forouzanfar M, Jafarpour F, Abedi P, Ostadhosseini S, Abbasi H, Gourabi H, , Shahverdi AH, Vousough Taqi Dizaj A, Anjomshoa M, Horan W, Noorshiriza n, YAkub H, Nasr- Esfahani MH, Molecular reproduction and development 2012, 576-584.

**Group Leader:**  
**Mohamad Ali Sadighi Gilani, MD**



**Group Leader:**  
**Marjan Sabbaghian, PhD**

m.sabbaghian@royaninstitute.org

**Biography**

Marjan Sabbaghian obtained an MSc in Biochemistry in 2002 and a PhD in Biochemistry in 2009 from the Institute of Biochemistry and Biophysics, University of Tehran. She joined Royan Institute in May 2009. Dr Sabbaghian is the head of the Andrology Laboratory at Royan Institute. Her research interests focus on characterization of the molecular mechanisms underlying spermatogenesis and male infertility.

**Education & Research**

**Introduction**

The mission of this group is to improve diagnostic and therapeutic methods by focusing on the characterization of the molecular mechanisms underlying spermatogenesis and male infertility and using the results of investigative projects to treat the patients.

**Research Assistants:**

- **Hosseinfar**, Hani, MSc (Cellular Molecular Biology)
- **Modarresi**, Tahereh, MSc (Developmental Biology)

**Student Trainees:**

- **Ghasemzadeh**, Mohammad
- **Raeisi**, Asieh

**MSc Students:**

- **Yazdanikhah**, Samaneh
- **Ahmadian**, Zahra

**Publications**

*Homology modeling, docking, molecular dynamics simulation, and structural analyses of coxsievirus B3 2A proteas: An Eenzyme involved in the pathogenesis of inflammatory myocaditi.* Maghsoudi AM, Khodaghohi F, Aljavand H, Esfandiarei M, Sabbaghian M, Zakerie Z, Shaerzadeh F, Albtahi S, Maghsoudi N, International journal of biological macromolecules 2011, 487-492.

*Occurrence of 47,X,i(X)(q10),Y Klinefelter variant with hypogonadotropic hypogonadism* Sabbaghian M, Mohseni Meybodi A, Rahimian M, Sadighi Gilani MA, Fertility and Sterility 2011, 115-117.

*Prevention of thermal aggregation of an allosteric protein by small molecules: some mechanistic insights.* Sabbaghian M, Ebrahim-Habibi A, Hosseinkhani S, Ghasemi A, Nemat-Grgani M, International journal of biological macromolecules 2011, 806-813

*Benzofuranone derivatives as effective small molecules related to insulin amyloid fibrillation: a structure-function study.* Rabiee A, Ebrahim-Habibi A, Navidpour L, Morshedi D, Ghasemi A, Sabbaghian M, Nemat-Lay M, Nemat-Gorgani M, Chemical Biology & Drug Design October 2011, 659-666.

**News and Events**

**Workshops**

- **Assessment of Sperm DNA Fragmentation in Male Infertility, August 2011**

In this workshop, participants were trained the following methods of chromatin damage assessment: AOT (Acridine Orange Test), SCSA (Sperm Chromatin Structure Assay), SCD (Sperm Chromatin Dispersion Test) and CMA3 (Chromomycin A3). Their clinical applications were also discussed. It was useful for physicians and biologists to learn more about the clinical aspects of DNA fragmentation assessment.



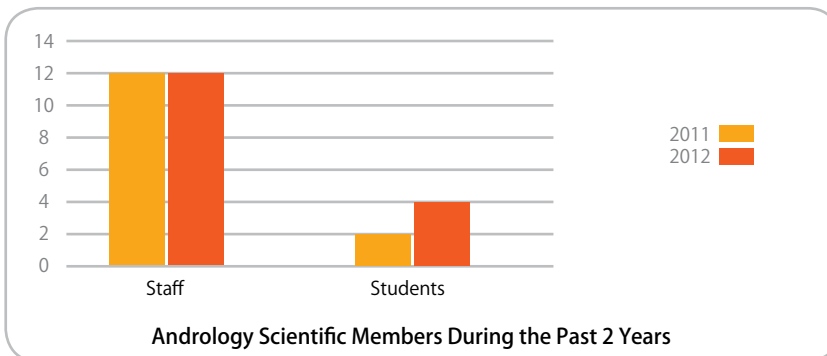
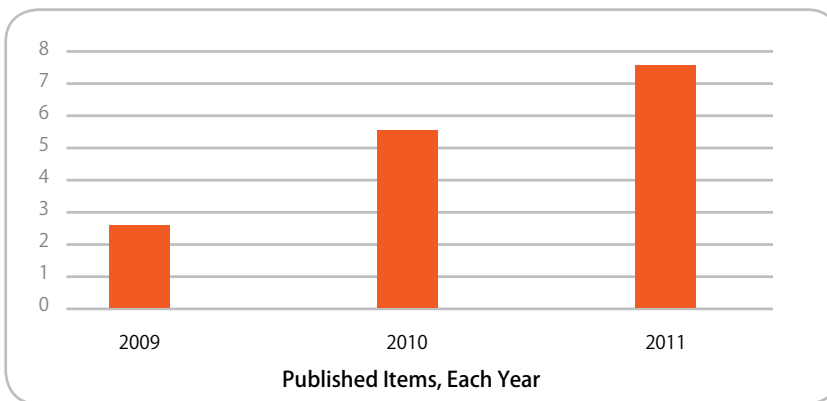
- First Aid, 2011**  
 It is important to know First Aid to be able to help one and others. The basic First Aid program is taught by the Andrology Department, and is beneficial for Royan staffs members.
- Semen Analysis, 2011**  
 This workshop detailed all the steps necessary to ensure an accurate sperm count. Many illustrations and descriptions were provided to acquaint one with normal and abnormal sperm morphology. This course was an excellent source of continuing education for medical technologists and technicians. It was also appropriate for training laboratory personnel, cross training, and clinical laboratory science students.



**Journal Clubs:**

No	Name	Date	Title
1	Dr Faramarz Farrahi	August, 24, 2011	Recurrent implantation failure (Male Aspect)
2	Dr Seyyed Jalil Hosseini	August, 2, 2011	The role of infertility team in providing information for infertile couples atn Royan Institute in comparison with other international fertility centers

**Publication Chart:**



# ANNUAL REPORT

## Embryology Department of RI-RB



ROYAN  
Institute

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### Department Head: Mojtaba Rezazadeh Valojerdi, PhD

■ Anatomy and Embryology (Full Professor)

[m.rezazadeh@royaninstitute.org](mailto:m.rezazadeh@royaninstitute.org)

#### Biography

Educational background: PhD in Anatomy from Glasgow University, Glasgow, England  
Faculty Member in Department of Anatomy, Faculty of Medical Science, Tarbiat Modares University  
Mojtaba Rezazadeh Valojerdi obtained his PhD degree (1990) in Anatomy from the University of Glasgow, UK. At present, he is a full Professor in the Anatomy and Embryology at the University of Tarbiat Modares and the Head of the Department of Embryology at Royan Fertility and Infertility Research Center in Tehran. He is a member of the Research and Ethics Committees at the University of Tarbiat Modarres and has more than 200 publications in national and international journals. He serves as an ad-hoc reviewer of the editorial boards of different national journals concerned with Cell Biology and Human Reproduction. His current research interests include assisted reproduction, embryo and ovarian tissue cryopreservation, and differentiation of stem cells.

#### Department History and Introduction

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

The main focuses of this Department are:

- 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

#### The Groups of Embryology Department

- Clinical Research
- Embryo Biotechnology
- Implantation Biology
- Oocyte Biology
- Ovarian Tissue Banking
- Sperm Biology

#### Goals of the Department

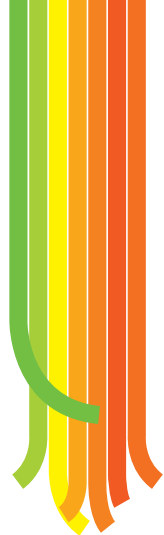
- Increasing the number of high quality human embryos
- Producing transgenic animals with selected genes
- Establishing in vitro human follicle culture following ovarian tissue cryopreservation

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.

#### Main Researches of Embryology Department

- Molecular pathways involved in reproductive system development
- DNA methylation pattern in embryos following vitrification
- Human ovarian and testicular tissue cryopreservation
- In vitro three-dimensional culture of human follicles
- Production of human factor IX in a transgenic goat by nuclear transfer
- Molecular mechanisms involving in follicle in vitro culture, in vitro oocyte maturation, implantation, endometrium receptivity, etc.
- Stem cell differentiation in correlation with reproductive system development



## Clinical Research

### Introduction

Assisted Reproductive Technology (ART) refers to a range of laboratory techniques that combine the sperm and egg for fertilization. Since the birth of the first in vitro fertilization (IVF) or 'test tube' baby in 1978, the field of IVF has been transformed with several technological discoveries that have led to a remarkable expansion of the treatable conditions as well as an outstanding increase in making the dreams of many couples possible. The Embryology Laboratory, where embryos are produced, grown, and nourished during an IVF cycle, is one of the key components of a fertility center. While patients don't necessarily know what happens behind the scenes during an IVF cycle, or how their embryos are produced, having a state-of-the-art Embryology Laboratory is what separates an average fertility center from an excellent one.

The clinical part of the Embryology Department of RI-RB gives our patients access to some of the most accomplished and nationally renowned fertility specialists in this field. A wide range of advanced ART services are also available, and include:

- Intrauterine insemination (IUI)
- In vitro fertilization (IVF)
- Intracytoplasmic sperm injection (ICSI)
- Assisted hatching
- In vitro maturation (IVM)
- Blastocyst culturing
- Embryo cryopreservation
- Preimplantation genetic diagnosis (PGD)
- Donor oocyte (egg) services
- Oocyte cryopreservation (egg freezing) services

After fertilization, embryos are cultured in the Embryology Laboratory under very strict conditions in specialized media in an incubator. Embryos are typically transferred back into the uterus at either the cleavage stage (on day 3 after retrieval) or the blastocyst stage (on day 5 after retrieval).

The clinical part of the Embryology Department of RI-RB offers extensive training in routine and advanced laboratory tests in assisted reproduction techniques (IUI, IVF/ICSI), gamete cryopreservation, and PGD. Through one-on-one training in laboratory procedures, candidates develop technical expertise in all of the essential techniques, including comprehensive semen analysis, sperm preparation procedures, assisted reproduction (IVF/ICSI) techniques, and cryopreservation protocols for semen, testicular, and oocytes/embryos. At the end of the program, candidates receive a Certificate of Training recognizing their achievements.

In addition to patient treatment, we also focus on research about some aspects of the pre-implantation of embryos, such as:

- IVM
- IMSI and the best approaches for sperm selection
- Cryopreservation of gametes and embryos
- Low fertilization
- Effect of oxidative stress on sperm and oocytes

### Laboratory Supervisor:

- **Karimian**, Leila, MSc

### Research Scientists:

- **Rezazadeh Valojerdi**, Mojtaba, PhD
- **Akhondi**, Mohammad Mahdi, PhD
- **Movaghar**, Bahar, PhD



### Group Leader: Poopak Eftekhari-Yazdi, PhD

[eftekhari@royaninstitute.org](mailto:eftekhari@royaninstitute.org)

### Biography

Dr Eftekhari-Yazdi obtained her BSc from the department of biology at Azad University of Mashhad in 1994. She obtained her MSc in the subject of Histology and Embryology in Tarbiat Modares University in 1997. Dr Eftekhari-Yazdi began her PhD in the field of Anatomy at Tarbiat Modares University in 1997 and she joined the Embryology Laboratory at Royan Institute. Her PhD thesis was about human embryo fragmentation and the effect of removal on embryo development. Her supervisor was Prof Valojerdi. She currently works as the Director of the IVF Laboratory at Royan Institute and her major research interests are epigenetics, proteomics, and secretome of embryos as well as the production of cloning and transgenic embryos.

**Research Assistants:**

- **Hasani**, Fatemeh, MSc
- **Behbahanian**, Arash, MSc
- **Nasiri**, Nahid, MSc

**Technician Staffs:**

- **Mohajer-Soltani**, Neda
- **Soleimani**, Mahdi
- **Fouladi**, Hamid Reza
- **Zeinolabedini**, Behnoush
- **Nargesi**, Hamed
- **Badrkhani**, Mojgan
- **Reihani**, Elham

**Publications**

*The factors affecting the outcome of frozen-thawed embryo transfer cycle.* Ashrafi M, Jahangiri N, Hasani F, Akhond M, Madani T. Taivanies J. Obst Gynecol. 2011; 50(2): 159-64.

*Alteration in the mechanical properties of human ovum zona pellucida following fertilization: Experimental and analytical studies.* Khalilian M, Navidbakhsh M, Rezazadeh Valojerdi M, Chizari M, Eftekhari Yazdi P. Experimental Mechanics. 2011; 51: 175–182.

*A case report of bilateral tubal ectopic pregnancy following the five embryo transfer.* Ghafari F, Eftekhari-Yazdi P, Kiani K. Archive of medical science. 2011; 7(6): 1087-1088.





## Embryo Biotechnology

### Introduction

This team is engaged in the development of new embryo-oriented biotechnologies. Their aim is to develop new techniques that will lead to better quality embryo production and more efficiently cloned embryo. The production of a transgenic goat with human coagulation factor IX gene in its milk is one of our priorities in this sub-branch. We are also interested in the production of all types of transgenic animals that contain useful proteins which can later be used in the research laboratory or pharmaceutical industry. Above all, we are researching the role of epigenetics on the growth and development of gametes and embryos. One of the newest issues under research is the study of proteome and secretome in embryos, and the selection of embryos with high quality development based on these two items. This subcategory has had the honor of determining the best way to synchronize necessary cells for nuclear transfer into an enucleated oocyte in order to increase the number of cloned embryos. One of the most significant activities of this sub-branch during the last two years has been the production of two transgenic goats (Shangool and Mangool) with milk that contained human coagulation factor IX. Additionally, another significant activity of this group is the production of cloned mice embryos with the use of an electric Piezo technique.

The approaches are developed in several model species (sheep, goat, and mouse).

Methods used: Micromanipulations of oocytes and embryos, epigenetic characterization of cloned embryos, in vitro maturation, fertilization, and assessment of special protein concentration in embryo secretome.

### Laboratory Head:

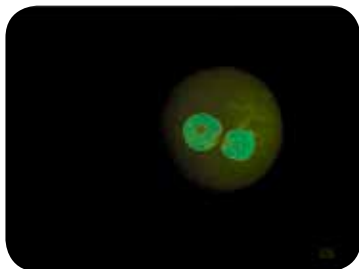
- **Dalman, Azam, MSc**

### Research Assistants:

- **Rajabpour Niknam, Masoumeh, MSc**
- **Vahabi, Zeinab, BSc**
- **Hadi, Mahdi, BSc**

### Student Trainees:

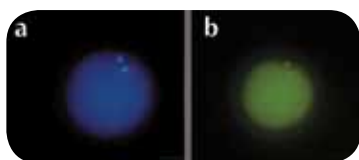
- **Zarei, Maryam**
- **Shamaghdari, Boshra**



It has been shown that aberrant epigenetic regulation can lead to abnormal embryo development. Our aim is to characterise the effect of small molecules (SAHA) on epigenetic remodelling after SCNT and during early embryogenesis. Reprogramming of H4K12 acetylation in cloned embryo, Dalman A, 2012.



The mouse 2-cell reconstructed embryo was cultured in vitro, then morphologically evaluated by nuclear staining with Hoechst 33342 and fluorescence was detected, Dalman A, 2012.



TUNEL Labeling of sheep MII oocytes. (a,b) TUNEL Positive (apoptotic) oocytes, Vahabi Z, 2012.

**Group Leader:**  
**Poopak Eftekhari-Yazdi, PhD**

[eftekhari@royaninstitute.org](mailto:eftekhari@royaninstitute.org)



**Group Leader:**  
**Bahar Movaghar, PhD**

[b.rmovaghar@royaninstitute.org](mailto:b.rmovaghar@royaninstitute.org)

#### Biography

Bahar Movaghar received her BSc from Tehran Medical University in physiotherapy in 1997. She continued her education at Tarbiat Modares University in Tehran and joined Royan Institute for her graduate courses under the supervision of Professor Rezazadeh and graduated in 2001. She began her PhD at Tarbiat Modares University; her thesis was entitled "Regeneration of Transected Rat Sciatic Nerve using in vitro Transdifferentiated BMSCs", under the supervision of Professor Taki Tiraihi, and graduated in 2007. She currently works as an academic staff member in the Embryology Department at Royan Institute. Her major research interests are the molecular mechanisms involved in implantation.

## Implantation Biology

### Introduction

In the Implantation Biology Group we are interested in molecules and pathways that affect implantation. We are also working on endometrium receptivity and its ultrastructural and molecular changes during ovarian stimulation. Some inflammatory and growth factors in blastocysts that are effective in implantation are investigated in our group. We intend to study epigenetical changes in blastocysts obtained from hormone stimulated mice in the near future. We also have performed some research on embryo freezing and the epigenetical effects of vitrification on some genes involved in embryo and placenta growth. We have shown that these genes were downregulated after embryo vitrification and that epigenetic changes played an important role in this process.

### Research Assistants:

- **Khoiastefard, Maryam, MSc**
- **Jahangiri, Maryam, MSc**



## Oocyte Biology

### Introduction

The Oocyte Biology group is interested in ovarian biology and the regulation of mammalian oocyte development, the development of oocyte maturation techniques, and particularly cryopreservation of oocytes and ovarian tissue in experimental models. The research program of this group spans basic discovery research to applied research and clinical trials. A key objective of the discovery research program is to obtain in the ability of having a bank for the cryopreservation of oocyte and ovarian tissue. The group works primarily in animal models but is also actively engaged in pre-clinical trials of research to develop new treatment for female infertility.

### Laboratory Head:

- **Tahaei**, Leila Sadat, MSc

### Research Assistants:

- **Fathi**, Rohollah, PhD student
- **Golkar**, Afsaneh, MSc

### Student Trainees:

- **Mokhber Maleki**, Elham, MSc student
- **Rajabzadeh**, Ali Reza, MSc student
- **Jafarian**, Zahra, MSc student
- **Abedi**, Reyhaneh, MSc student
- **Akhavan Taheri**, Maryam, PhD student

### Graduated Students:

- **Saber**, Maryam, MSc
- **Golkar**, Afsaneh, MSc
- **Tavana**, Somayyeh, MSc
- **Abtahi**, Naeemeh Sadat, MSc
- **Aeinehvand**, Samaneh, MSc
- **Zandevakili**, Maryam, MSc

### Publications

*Development of 4-cell mouse embryos after re-vitrification.* Fathi R, Rezazadeh Valojerdi M, Eftekhari-Yazdi P, Alipour H. CryoLetter. 2012; 64(1): 23-6.

*Heterotopic autotransplantation of vitrified mouse ovary.* Eimani H, Behbahanian A, Zeinali B, Rezazadeh Valojerdi M, Eftekhari P, Shahverdi A, Gourabi H, Golkar-Narenji A. Reproductive Medicine and Biology (RMB). (2011; 10: 267-275.

*Effects of the retinoic acid and granulosa cell co-culture system on the maturation of immature mouse oocytes.* Tahaei L, Eimani H, Eftekhari Yazdi P, Ebrahimi B, Fathi R. Journal assisted reproduction and genetics. 2011; 28: 553-558.

*Effects of saffron (Crocus sativus L.) aqueous extract on in vitro maturation, fertilization and embryo development of mouse oocytes.* Tavana T, Eimani H, Azarnia M, Shahverdi A, Eftekhari-Yazdi P. Cell Journal (Yakhteh). 2012; 13(4): 259-264.

### Journal Clubs:

No	Organizer	Title
1	Leila Sadat Tahaei	The effect of xenotransplantation on vitrified sheep ovarian tissue
2	Samaneh Aeinehvand	The effects of Angiogenesis Factor (VEGF) on the function of autotransplanted vitrified ovaries
3	Ali Reza Rajabzadeh	Study of survival, folliculogenesis, and angiogenesis of isolated pre-antral ovarian follicles from mouse after vitrification and heterotopic transplantation using Fibrin Glue
4	Zahra Jafarian	Effect of papaver rhoeas extract on in vitro maturation and development of immature mouse oocytes treated with chemotherapy drug Doxorubicin
5	Maryam Saber	The effect of Verapamill and Allopurinol on mouse ovarian heterotopic transplantation
6	Leila Sadat Tahaei	G2 phase of cell division



**Group Leader:**  
**Hossein Eimani, PhD**

[h.eimani@royaninstitute.org](mailto:h.eimani@royaninstitute.org)

### Biography

Hussein Eimani received his PhD from Tarbiat Modares University, Tehran, Iran. His research area focused on folliculogenesis and oocyte in vitro maturation and vitrification. Further training and specialization in infertility and assisted reproductive technology was undertaken at Royan Institute, Iran. He is now a full Professor in Embryology. His research focuses on the maturation of immature oocytes and animal cloning, and has led to numerous publications in national and international journals.



**Group Leader:**  
**Bita Ebrahimi, PhD**

b.ebrahimi@royaninstitute.org

**Biography**

Bita Ebrahimi was born in 1975. She received her BSc in physiotherapy from Tehran Medical University in 1997 and continued her MSc and PhD in the field of Anatomical Sciences at Tarbiat Modares University. She graduated in 2010 as the 1<sup>st</sup> rank student. Her PhD thesis entitled "Evaluation of in-vitro maturation and ultrastructure of sheep cumulus-oocyte complexes follow vitrification by conventional, cryotop, and solid surface methods" was under the supervision of Prof Rezazadeh. Her collaboration with Royan Institute started in 2010. She currently works as an academic staff in the Embryology Department of Royan Institute. Her major research subject is molecular mechanism involving in folliculogenesis and ovarian tissue vitrification.

**Ovarian Tissue Banking**

**Introduction**

As a result of developments in current treatment modalities, remarkable improvements have been made in the numbers of survivals from childhood malignancies. Increased awareness of the impact of various cytotoxic treatments on gonadal function has now resulted in a surge in the number of patients seeking help to preserve their fertility. Cryopreservation of embryos is a standard technique for fertility preservation when there is adequate time for ovarian stimulation. If patients have no partner or are unwilling to use donor sperm, oocytes can be frozen instead. The current experience in ovary cryopreservation and transplantation is limited. Nevertheless, at present, it is the only fertility preservation procedure that can be offered to prepubertal girls and can be implemented without any delay in treatment. The main goal of this group is to preserve ovarian tissue by using the best cryopreservation protocol and to establish in vitro cultures of human follicles and investigate the different molecular mechanisms involved in these procedures.

**Laboratory Head:**

- **Abtahi**, Naeimeh Sadat, MSc

**Research Assistants:**

- **Tavana**, Somayeh, PhD Student
- **Farahani Deheshkar**, Nafiseh, MSc
- **Banaei**, Mahdi, BSc

**Student Trainees:**

- **Fatehi**, Roya
- **Sadr**, Zeynab
- **Matini Behzad**, Adele

**Publications:**

*IVM and gene expression of sheep cumulus-oocyte complexes following different methods of vitrification.* Ebrahimi B, Rezazadeh Valojerdi M, Eftekhari-Yazdi P, Baharvand H, Farrokhi A. Reproductive BioMedicine Online 2010; 20: 26–34.

*In vitro maturation, apoptotic gene expression and of numerical chromosomal abnormalities following vitrification of sheep cumulus-oocyte complexes.* Ebrahimi B, Rezazadeh Valojerdi M, Eftekhari-Yazdi P, Baharvand H. J Assist Reprod Genet 2010; 27: 239–246.

*Ultrastructural changes of sheep cumulus-oocyte complexes following different methods of vitrification.* Ebrahimi B, Rezazadeh Valojerdi M, Eftekhari-Yazdi P, Baharvand H. Zygote 2011; 20: 103-115.

*Expression of maturation genes and their receptors during in vitro maturation of sheep COCs in the presence and absence of somatic cells of cumulus origin.* Kyasaria OR, Rezazadeh Valojerdia M, Farrokhi A, Ebrahimi B. Theriogenology. 2012; 77: 12-20.





## Sperm Biology

### Goals of the Group

- Designing new tests for sperm evaluation
- Optimizing cryopreservation of testicular tissue and sperm from humans and animals
- In vitro differentiation of spermatogonial stem cells
- Assessing the effects of environmental factors and nutrition on sperm and relative genetic expression

### Research Scientist:

- **Alizadeh Moghadam Masouleh**, Ali Reza, PhD

### Laboratory Head:

- **Sharbatoghli**, Mina, MSc

### Research Assistants:

- **Esmaeili Borzabadi**, Vahid, MSc
- **Rashki**, Leila, MSc
- **Abbasi Hormozi**, Shima, MSc
- **Sharafi**, Mohsen, PhD

### Student Trainees:

- **Rezaei**, Tohid, DVM
- **Safiri**, Mehran, MSc

### Award

ICAR-2012

Dr Ali Reza Alizadeh has received the "Travel Award for Young Scientists from Developing Countries" presented at the 17<sup>th</sup> International Congress on Animal Reproduction (ICAR). The project entitled 'First Report of Dietary L-carnitine and Fish Oil Effects on Sperm Characteristics in Ram' was founded by a grant from the Royan Institute and the Saveh Branch of Islamic Azad University, which he presented this project in Vancouver, Canada. ([www.icar2012.com](http://www.icar2012.com))

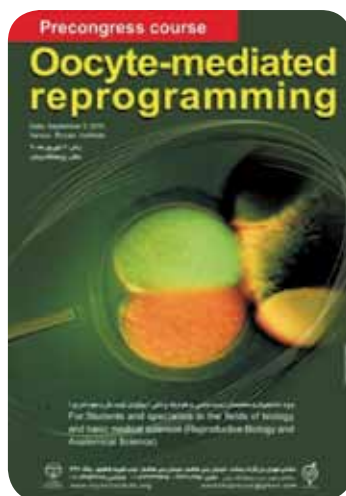
### Publications

*Fatty acid profiles of ram's sperm after removing some fatty acid sources from the diets and persistency of fatty acids in sperm.* Esmaeili V, Shahverdi A, Alizadeh AR, Alipour H, Towhidi A, Zarrabi M. Int J Fertil Steril. 2012; 5(4): 211-216.

## News and Events

### Workshops

- **Sperm Functional Test in the Diagnosis and Treatment of Infertility**
- **Course of Oocyte-mediated reprogramming.** Scientific managers: Dr Michele Boiani and Poopak Eftekhari-Yazdi  
Executive managers: Azam Dalman and Zeinab Vahabi  
September 3, 2011



### Group Leader: **Abdolhossein Shahverdi,** PhD

[shahverdi@royaninstitute.org](mailto:shahverdi@royaninstitute.org)

### Biography

Abdolhossein Shahverdi was born in 1963 in Iran. He received his BSc in Audiology from Iran University in 1986. He studied his MSc and PhD degrees in Anatomical Science at Tarbiat Modares University, and received his PhD degree in 2007. His PhD thesis was entitled "Developmental and Ultrastructural Studies of Zygotes Derived from Reconstructed Oocytes Using Nuclear Transfer and Activated Sperms". Currently, he works as an associate professor and has been an academic member of Royan Institute since 1990. In addition, Dr Shahverdi is a member of the Iranian Society for Anatomy, Iranian Society of Fertility Sterility, Editorial Board of the Iranian Journal of Fertility Sterility, and Executive Board of the Cell Journal (Yakhteh). He published 48 ISI articles and presented 45 abstracts in International & National Congresses. His main research interests are germ cells and sperm biology.



- Workshop of Enucleation and nuclear transfer of mouse oocytes by Piezo.**  
 Scientific managers: Dr. Michele Boiani and Azam Dalman  
 Executive managers: Zeinab Vahabi, Masoumeh Rajabpour Niknam, Mahdi Hadi  
 September 4, 2011
- Workshop of In Vitro Fertilization in mice.**  
 Scientific managers: Azam Dalman  
 Executive managers: Zeinab Vahabi, Mahdi Hadi  
 October 8, 2011



**Journal Clubs:**

No	Organizer	Date	Title
1	Azam Dalman	February 6, 2012	Evaluation of epigenetic marks in human embryos derived from IVF and ICSI
2	Zeinab Vahabi	October 8, 2011	Methods of in vitro maturation of oocytes



# ANNUAL REPORT

## Reproductive Genetics Department of RI-RB

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### Message from the Department Head

There is more and more attention toward genetic sciences, especially among biology and medicine researchers. Genetic background of many diseases with unknown origin is well understood now and many others are in research process. Successful treatment of infertility with assisted reproduction techniques (ART) has many unknown points that discovery of each can help using these treatments more efficiently. Reproductive genetics can help to discover these unclear points and to find new treatments strategies. Last year we organized specialized subgroups to make our future program more convenient. Assigning more specialized staffs and providing suitable infrastructures can make fruitful future. My colleagues have planned to continue their programs for recognizing the genetic factors related to recurrent abortions, fail ART, poor responding to ovarian stimulation medication, epigenetic factors related to infertility and embryo development, genetic manipulation of cells to produce recombinant proteins and transgenic animals.

I would like to express my thanks from my valuable colleagues for their efforts during last year, and extend invitation to all genetic scientists for collaboration in our research program.

### Department History and Introduction

The Genetics Department 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 include 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, and 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 project with the Embryology Group is another main activity of this department.

Activities carried out in collaboration with Royan Institute for Stem Cell Research are karyotyping of stem cell lines following various manipulations, epigenetic and genetic studies of stem cells and iPS cells, in addition to other common research interests.

### Goals of the Department

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

The mission of the Genetics 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 genetics knowledge, which will lead to healthy newborns in a short period of time.



### Department Head: Hamid Gourabi, PhD

■ Medical Physics (Radiobiology)

[gourabi@royaninstitute.org](mailto:gourabi@royaninstitute.org)

### Biography

Dr Hamid Gourabi obtained his PhD degree in 1997 from Tarbiat Modarres University. He was a faculty member of Iran Medical Sciences University until 2001. Dr Gourabi has been a member of Royan Institutes board of directors since its establishment, and he joined as a faculty member in 2003. Since 2004, he has been the Head of the Genetics Department at Royan Institute. His main research interests are reproductive genetics and radiobiology of stem cells. Dr Gourabi has more than 60 published papers, mostly in international scientific journals.

Academic Staff of:

ACECR since 1993

Iran Medical University, 1997-2001

Royan Institute since 2001

Director of PGD Lab since 2002



### The Programs of Reproductive Genetics Department

- Epigenetics
- Genetic Engineering
- Medical Genetics
- PGD
- Pharmacogenetics

### Overview of the Department in 2011

In 2011, 13 research projects were carried out in our departments and 45 projects were undertaken in collaboration with other departments. 23 MSc and 2 PhD theses were ongoing. 7 Masters Students have completed their theses during the past year. Thirteen oral presentations and 26 posters were presented in different national and international congresses. This department published 24 papers that have been listed separately under each program. Additionally, 8 hands-on workshops were held during the past year.

Clinically, more than 2194 genetic consultations, 2795 karyotypes, 865 AZF-microdeletion tests, and 503 PGD tests were performed.

## Epigenetics

### Introduction

Epigenetics refers to DNA and chromatin modifications that persist from one cell division to the next, without any changes in the underlying DNA sequence. Some epigenetic changes show transgenerational inheritance meaning that these changes can be passed from one generation to the next. Epigenetics plays an important role in cellular differentiation, allowing distinct cell types to have specific characteristics despite sharing the same DNA sequence. Some examples of epigenetic processes include imprinting, gene silencing, paramutation, X chromosome inactivation, reprogramming, position effect, maternal effects, heterochromatinization and some carcinogenesis. The mechanisms of epigenetic inheritance systems can be categorized to at least 4 routes by which epigenetic changes persist over time. These routes include DNA methylation, chromatin modifications/variations, non-coding RNAs and ATP-dependent chromatin remodeling.

Because of the critical importance of epigenetics in regulation of development and cellular function/fate, the main interest of this research group is to study the molecular mechanisms of the cellular memory and function, with the special focus on chromatin modifications on the marker genes of different cellular processes. The epigenetics sub-group has held 2 workshops in "Epigenetic Methods" in the past two years, observing different methods of epigenetic analyses at the single gene as well as whole genome levels.

### Research Assistants:

- Favaedi, Raha, MSc
- Azad, Mahnaz, MSc

### Student Trainees:

- Ansari, Hasan
- Ashrafi, Sara
- Fallah Zadeh, Khadijeh
- Moein-Vaziri, Farideh
- Shokraee, Fatemeh
- Mahdian, Soudeh
- Eilami-Nejad, Zahra
- Heydarian, Neda
- Eslami, Hossein

### Publications

Baghban Eslami, M. R., Karimi, N., Shakhoseini, M. *Enhancement of glycosaminoglycan-rich matrix production in human marrow-derived mesenchymal stem cell chondrogenic culture by lithium chloride and SB16763 treatment.* Cell J.2011; 13: 117-126.

Favaedi, R., Shakhoseini, M., Akhoond, M.R. *Comparative epigenetic analysis of Oct4 regulatory region in RA-induced differentiated NT2 cells under adherent and non-adherent culture conditions.* Mol. Cell. Biochem.2012; 363: 129-34.

Jafari S. Hosseini S.M, Forouzanfar P, Hajian M, ... Gourabi H, Shahverdi H, Vosough A, Nasr Esfahani, M.H. *Epigenetic modification does not determine the time of POU5F1 transcription activation in cloned bovine embryos,* J Assist Reprod Genet. 2011 Nov; 28(11):1119-27.

Abdossamadi, S., Rabbani Chadegani, A., Shakhoseini, M. *Identification of low mobility group protein, lmg160, in rat liver chromatin.* FEBS J. 2011; 278- 91.



**Group Leader:**  
**Maryam Shakhoseini, PhD**

[m.shakhoseini@royaninstitute.org](mailto:m.shakhoseini@royaninstitute.org)

### Biography

Maryam Shakhoseini received her BSc degree in Microbiology at 1998 from Department of Biology, University of Tehran. In a straight line, she started her MSc degree in Biochemistry at the Institute of Biochemistry & Biophysics (IBB), University of Tehran, and was graduated at 2001 as the 1<sup>st</sup> rank student. She continued her education at PhD level in Biochemistry at the same department (IBB) and was graduated at 2007 as the 1<sup>st</sup> rank student. Immediately after dissertation, she joined to Stem Cell Dept. in Royan Institute to establish epigenetic techniques to investigate molecular mechanisms of stem cells through differentiation. 2 years later she has moved to Genetic Dept., although she is still in collaboration with the previous department. She has managed several epigenetic and genetic projects in collaboration with Embryology, Gynecology and Andrology Departments in Royan. Since 2007, she has also been the invited academic lecturer of Dept. of Biotechnology, Faculty of Sciences, University of Tehran, teaching Molecular Biology, Molecular Genetics, Molecular Biotechnology, and Gene Expression Regulation courses. Her major research interest is Epigenetic aspects of Development and Reproductive Medicine.

Shahhoseini, M., Saeed, S., Marks, H., Stunnenberg, H.G. *Evidence for a dynamic role of the histone variant H2A.Z in epigenetic regulation of normal/carcinoma switch.* FEBS J. 2011; 278- 8.

Favaedi, R. Shahhoseini, M., Baharvand, H., Akhoond, M.R. *Comparative epigenetic profile of Oct4 regulatory region in embryonal carcinoma cells under retinoic acid induction.* Int. J. Fertil. Stril. 2011; 5- 75.

Azad, M., Sabbaghian, M., Shahhoseini, M. *How a frame shift caused by a single base deletion in SEPT12 gene shed lights as a polymorphism.* Int. J. Fertil. Stril. 2011; 5-74.

Saeidi, S., Shapouri, F., Janan, A., Lakpour, M., Sadighi Gilani, M., Ashrafi, M., Hoseinifar, H., Shahhoseini, M., Sabbaghian, M., Aflatoonian, R. *Expression of intercellular Toll-Like receptors in male genital tract.* Int. J. Fertil. Stril. 2011; 5- 45.

Shapouri, F., Saeidi, S., Janan, A., Lakpour, M., Ashrafi, M., Hoseinifar, H., Shahhoseini, M., Sabbaghian, M., Aflatoonian, R. *Expression of cell surface Toll-Like receptors in the human male reproductive tract.* Int. J. Fertil. Stril. 2011; 5- 46.

Ansari, H., Nemati, Sh., Kiani, S., Baharvand H., Shahhoseini, M. *Expression pattern of REST in hESCs and hiPSCs undergoing neural differentiation,* Cell J. 2011; 13-24.

## Genetic Engineering

### Introduction

Biotechnology is a field of applied biology that involves the use of living organisms and bioprocesses in engineering, technology, medicine and other fields requiring bioproducts. Biotechnology also utilizes these products for manufacturing purposes. Modern use of similar terms includes genetic engineering as well as cell- and tissue culture technologies. The concept encompasses a wide range of procedures (and history) for modifying living organisms according to human purposes-going back to domestication of animals, cultivation of plants and "improvements" to these through breeding programs that employ artificial selection and hybridization. By comparison to biotechnology, bioengineering is generally thought of as a related field with its emphasis more on higher systems approaches (not necessarily directly altering or using biological materials) for interfacing with and utilizing living things.

Biotechnology draws on the pure biological sciences (genetics, microbiology, animal cell culture, molecular biology, biochemistry, embryology, cell biology) and in many instances is also dependent on knowledge and methods from outside the sphere of biology (chemical engineering, bioprocess engineering, information technology, biorobotics). Conversely, modern biological sciences (including concepts such as molecular ecology) are intimately entwined and dependent on the methods developed through biotechnology and what is commonly thought of as the life sciences industry. Modern biotechnology is often associated with the use of genetically altered microorganisms such as *E. coli* or yeast for the production of substances such as synthetic insulin or antibiotics. It can also refer to transgenic animals or transgenic plants, such as Bt corn. Genetically altered mammalian cells, such as Chinese hamster ovary cells (CHO), are also used to manufacture certain pharmaceuticals. Another promising new biotechnology application is the development of plant-made pharmaceuticals.

### Research Assistants:

- **Amiri Yekta**, Amir, MSc
- **Fatemi**, Nayereh Sadat, MSc
- **Bahraminejad**, Elmira, MSc

### Student Trainees:

- **Ahanjan**, Masoumeh, MSc
- **Ebrahimi**, Somayeh, MSc
- **Elyasi Gorji**, Zahra, MSc
- **Ghanbari**, Meysam, MSc
- **Khoshbakht**, Mona, MSc
- **Saeeda**, Somayeh, MSc

### Ongoing Projects:

- Human factor IX production in transgenic goat by nuclear transfer, from 2007
- Production of recombinant human and animal fertility hormones, from 2011
- Production of transgenic chicken with Anti-CD34 Antibody Gene expression in oviduct, from 2011

This sub-group has held annual two workshops on elementary techniques in molecular biology and gene cloning.

### Publications

Amir Amiri Yekta, Azam Dalman, Poopak Eftekhari-Yazdi, Mohammad Hossein Sanati, Hamid Gourabi\*. *Production of transgenic goats, carrying human coagulation factor IX cDNA, by nuclear transfer of transfected fetal fibroblasts*. IEEE:journal 2011; 149-154.

Fazeli AS, Nasrabadi D, Sanati MH, Pouya A, Ibrahim SM, Baharvand H, Salekdeh GH. *Proteome analysis of brain in murine experimental autoimmune encephalomyelitis*. Proteomics 2010 Aug; 10(15): 2822-32.



**Group Leader:**  
**Mohammad H Sanati, PhD**

[mh.sanati@royaninstitute.org](mailto:mh.sanati@royaninstitute.org)

### Biography

Educational Qualifications:1991-1996: PhD (Biotechnology) At Biotechnology Research Group, School Of Biological and Environmental Sciences, Murdoch University, Western Australia 1985-1988: MSc (Biochemistry), Biochemistry Department, School of Medical Sciences, Tarbiat Modarres University, Tehran, Iran 1977-1984: BSc (Chemistry), Chemistry Department, School of Sciences, Ferdowsi University, Mashhad, Iran  
Work Experiences: 2006- Current: Researcher at the Medical Genetic Department, National Institute For Genetic Engineering and Biotechnology, Tehran, Iran. 1997-2005: President of the National Institute for Genetic Engineering and Biotechnology, Tehran, Iran. 1996: Full-time researcher in Murdoch University, production of recombinant monoclonal antibody against the Rizhoctomi Saloon antigens in "Phase Display System".  
1995: Part-time research assistant (work on multiple sclerosis diseases), Murdoch University, Western Australia  
1994: Demonstrator (practical molecular biology for undergraduate students), Murdoch University, Western Australia.



**Group Leader:**  
**Anahita Mohseni Meybodi,**  
**PhD**

[anahitamohseni@royaninstitute.org](mailto:anahitamohseni@royaninstitute.org)

#### Biography

Anahita Mohseni Meybodi was born in 1976. She began working at Royan Institute from 2000 when she started her MSc thesis. She worked on "Human sperm various genetic abnormalities and male infertility" and graduated in 2003 from Islamic Azad university, Science & Research branch. In a straight line, she started her PhD and was graduated in 2008 in the field of Medical Genetics from Tarbiat Modarres University, Tehran, Iran. Her PhD project researched Fanconi anemia patients and the mechanisms of how they repair DNA damages induced by different agents. She currently works as an academic staff and Director of the Medical Genetics Laboratory at Royan institute. She supervises a couple of research projects. Her major research interest has been gene polymorphisms and their role in male and female infertility.

## Medical Genetics

### Introduction

The original goals of medical genetics and reproductive medicine were to maximize fertility, access appropriate genetic testing, and provide prenatal genetic testing and counseling. There are well-described associations between genetic and reproductive abnormalities, for which genetic testing is now being explored.

With recent advances in genetic screening and a better understanding of the genetic background of certain diseases, genetic evaluation is crucial in the work-up of various medical problems, including reproductive failure. Reproductive failure refers to both the inability to conceive (infertility) and the inability to carry a pregnancy successfully to term (spontaneous abortion or recurrent abortion). Embryos that do not carry a full chromosomal component are likely to be lost soon after implantation or do not implant at all. Genetic abnormalities (numerical or structural aberrations) affect on at least 50% of early pregnancy losses. Karyotyping of the parents is now a routine procedure during the work-up of recurrent abortions. Infertility is another form of reproductive failure, and genetic screening plays an increasingly important role in its evaluation. In vitro fertilization (IVF) provides us with a unique situation in which not only the parents but also the embryo can be screened.

Pregnancy rates are between 35% and 50% following IVF treatment among women younger than 40 years. If pregnancy is not achieved during the first 2 or 3 cycles, genetic testing, when available, should be offered to the couples. This could be useful in those selected cases in which preimplantation genetic diagnosis could identify healthy embryos, possibly improving outcome. In other cases, early genetic testing of couples could identify those for whom the use of donor gametes would be indicated. Now through the assistance of reproductive and genetic medicine, medical miracles allow the detection of genetic disorders through prenatal diagnosis and the ability of infertile individuals to become genetic parents. Referred to as the new parenthood, these technologies allow for the conception of genetically exceptional babies by eliminating genetic defects and enhancing desirable qualities as well as the ability of individuals with a genetic disorder to reproduce without transmitting a given disorder. Such technological advances have influenced consumer (and often caregiver) expectations of reproductive medicine and medical genetics that result in unrealistic or misguided anticipations of feasibility, success and applicability of these medical interventions. Furthermore, the ability of reproductive medicine and medical genetics to facilitate the conception of a healthy infant has become fraught with moral dilemmas and technological complications.

### Research Assistants:

- **Almadani**, Seyyed Navid, MD
- **Bazrgar**, Masoud, PhD student
- **Anissi Hemaseh**, Khadijeh, MSc
- **Asadpour**, Ummolbanin, MSc
- **Habibi**, Roghayeh, MSc
- **Kalantari**, Hamid, MSc
- **Mansouri**, Zahra, MSc
- **Masoodi**, Najmeh Sadat, MSc student
- **Zar'i Moradi**, Shabnam, MSc
- **Borjian**, Parnaz, MSc Student
- **Mokhtari**, Pegah, BSc
- **Fakhri**, Mostafa, Msc
- **Hosseinifar**, Hani, Msc
- **Vaziri**, Hamed, Msc

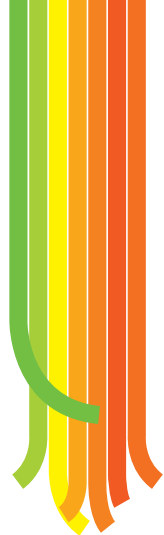
### Student Trainees:

- **Moazenchi**, Maedeh
- **Ghezelayagh**, Zeinab
- **Eslami**, Ali

Hajian M, Hosseini S.M, Forouzanfar P, Abedi P,....., Moulavi F, Gourabi H, Shahverdi H, Vosough A, Amiri-Yekta A, Nasr Esfahani M.H-*Conservation cloning of vulnerable Esfahan mouflon (Ovis orientalis isphahanica ):in vitro and in vivo studies*. European Journal of Wildlife Research. 2011 Jan.

Nasr Esfahani ,M.H, Hosseini S.M, Hajian M, Gourabi H, Shahverdi H, Vosough A, Vojgani M- *Development of anoptimi- zed zona-free method of somatic cell nuclear transfer in the goat*, Cell Reprogram. 2011 Apr; 13(2):157-70

Jafarpour F, Hajian M,...., Ghaedi K, Gourabi H, Shahverdi H, Vosough A, Nasr-Esfahani M.H -*Somatic Cell-Induced Hyperacetylation, But Not Hypomethylation Positively and Reversibly Affects the Efficiency of In Vitro Cloned Blastocyst Production in Cattle*, Cell Reprogram. 2011 Dec; 13(6):483-93.

**Award**

Anahita Mohseni Meybodi, Award winner of Best Poster Presentation in the 23<sup>th</sup> international symposium of Fanconi anemia, 2011, Barcelona, Spain

**Core Facility:****DNA Bank**

DNA bank is a repository of DNA, usually used for research. Royan DNA Bank, for example, collects the DNA of male and female from infertile patients and couples with repeated miscarriages, for scientific research. Most DNA provided by DNA banks is used for studies that attempt to determine the reason behind idiopathic infertility and abortion, as well as to investigate genetic diseases related to infertility and abortion.

Couples: 583 (ART Fail:153, Abortion: 370, Fertile control: 60)

Male: 1665 Female: 354

Total: 3185

**Projects of Medical Genetics**

- Investigation for an association of Haplotypes and gene Mutations of USP26 (Ubiquitin Specific Protease 26) with Azoospermia and Oligospermia in Royan Institute patients.
- Investigation for an association of CGG triples repeat alleles of Fragile X gene (FMR1) with ovarian stimulation rates and premature ovarian failure.
- Association of MICA gene polymorphism with Chlamydia Trachomatis infection in male infertility in Royan Institute patients.
- Investigation of FMR1 gene expression rate in blood and ovary granulosa cells in patients with to premature ovarian failure.
- Investigation for an association between CAG and GGN triple repeat alleles of the Androgen Receptor gene with different situations of infertility in men.
- Epigenetic patterns and gene expression of FMR1 gene in blood and granulosa cells in women with premature ovarian failure.
- Investigation of genetic variation and gene expression of the FSH receptor gene in blood and granulosa cells of patients with Premature Ovarian Failure, referred to Royan Institute.

**Publications**

Sabbaghian M, Mohseni Meybodi A, Rahimian M, Sadighi Gilani MA. *Occurrence of 47,X,i(X)(q10),Y Klinefelter variant with hypogonadotropic hypogonadism: A case report, Fertility and Sterility.* 2011; Aug; 96(2): 115-117.

Bazrgar M, Peiravian F, Abedpour F, Karimi M. *Causes for hospitalization and death in Iranian patients with Beta Thalassemia Major.* Ped Hematol Oncol. 2011; 28(2):134-139.

H Mozdarani, K Abed Ashtiani, A Mohseni-Meybodi. *Evaluation of concentration and storage effects of mitomycin C in the diagnosis of Fanconi anemia among idiopathic aplastic anemioa patients.* Indian J Hum Genet.2011; 17(3): 145-151.

Mohseni Meybodi A, Mozdarani H, Zari Moradi Sh, Akhoond MR, *Importance of sperm glutathione treatment in ART.* J Assist Reprod Genet. 2012.

Totonchi M, Mohseni Meybodi A, Borjian Boroujeni P, Almadani N, Sedighi Gilan MA, Gourabi H, *Clinical data for 185 infertile Iranian menwith Y-chromosome microdeletion.* J Assist Reprod Genet. 2012.

Shahbazi E, Kiani S, Gourabi H, Baharvand H, *Electrospun Nanofibrillar Surfaces Promote Neuronal Differentiation and Function from Human Embryonic Stem Cells,*Tissue Eng Part A,2011 Dec;17(23-24):3021-31.

Barekati Z, Golkar-Narenji A, Totonchi M, Radpour R, Gourabi H, *Effects of Amifostine in Combination With Cyclophosphamide on Female Reproductive System.* Reprod Sci. 2012 May; 19(5):539-46. Epub 2012 Jan 19.

Amps K,Andrews PW, Anyfantis G,··· Armstrong L, Salekdeh GH, Gourabi H, Baharvand H, Zhou Q, *Screening ethnically diverse human embryonic stem cells identifies a chromosome 20 minimal amplicon conferring growth advantage,* Nat Biotechnol. 2011 Nov 27; 29(12):1132-44. doi: 10.1038/nbt.2051.

Eimani H, Behbahanian A, Zeinali B, Rezazade M, Eftekhari P, Shahverdi A, Gourabi H, Golkar A. *Heterotopic autotransplantation of vitrified mouse ovary,* Reproductive Medicine and Biology,2011 –number (4)267-275.

Afsaneh Golkar-Narenji, Hamid Gourabi, Hussein Eimani, Zeinab Barekati and Aliasghar Akhlaghi, *Superovulation, in vitro fertilization(IVF)and in vitro development (IVD) protocols for inbred BALB/cJ mice in comparison with outbred NMRI mice,* Reproductive Medicine and Biology ,2012, DOI: 10.1007/s12522-012-0127.

**Journal Clubs**

No	Organizer	Date	Title
1	Anahita Mohseni Meybodi	July 07, 2011	USP genes and their effects in male infertility
2	Hamid Kalantari	June 08, 2011	Prenatal Diagnosis: progress through plasma nucleic acid
3	Shabnam Zari Moradi and Roghayeh Habibi	October 10, 2011	MLPA introduction and application



**Group Leader:**  
**Parvaneh Afsharian, PhD**

pafshar@royaninstitute.org

**Biography**

Parvaneh Afsharian received her first BSc in Chemistry. One year later, she was graduated in Biology (in BSc level) from Biology department at the Ferdowsi University of Mashhad. Her MSc subject was Genetics in Azad University, Tehran. Her project (Chromosomal abnormalities in patients with the pubertal and reproductive failures) was done in Clinical Genetics Department, Iranian Blood Transfusion Organisation in collaboration with Royan Inst. The next year in 2000, she has started her research in Genetics Dept. in Royan Inst. as an academic staff of ACECR and 3 years later she moved to Department of Medicine in Karolinska Institute (KI), Stockholm, Sweden to start her PhD research in Pharmacogenetics of Bone Marrow Transplantation Chemotherapy. Immediately after PhD program in 2007, she started her first postdoc in Experimental Cancer Medicine group under supervision of Professor M. Hassan in Lab Medicine Dept., KI and in 2008 she joined the professor Inge Olsson group in Lund University to investigate "The Localization of Target Therapy in Hematopoietic Stem Cells". Since 2011, she works as an academic member and director of Pharmacogenetics group in Royan institute. Her major research interest has been Pharmacogenetics aspects of Reproductive Medicine and infertility.

## Pharmacogenetics

### Introduction

Each individual can respond to the same doses of a drug in a different way, regarding to their own genetic variation patterns. Pharmacogenetics (PG) is considered as the study or clinical testing of these genetic variations that gives rise to differing response to drugs. PG also refers to genetic differences in metabolic pathways which can affect individual responses to drugs, both in terms of therapeutic effect as well as adverse effects. Thus PG studies are committed to select the best therapy for every patient with a minimum risk of complications. Furthermore, these studies allow the development of clinical tests based on the presence of profiles of biomolecules and other biological markers useful for routine diagnosis.

Since genetic variations play an important role in reproductive medicine, pharmacogenetics studies open a new field to modify and develop the treatments of infertile couples. For instance, the application of PG to assisted reproductive techniques (ART) will help clinicians to improve the efficacy of hormone treatments that are being routinely applied during ART protocols. As an example, FSH- and estrogen-receptors are genetic markers involving controlled ovarian hyperstimulation as clinical studies have demonstrated that the p.N680S polymorphism of the FSH-receptor gene determines the less ovarian response to FSH stimulation in patients undergoing IVF. In women with homozygous Ser/Ser in their FSH-receptor, the FSH receptor appears to be more resistant to treatment. Therefore, genotyping of patients scheduled for ovarian stimulation could be an attractive tool to individualize FSH dosing according to genetic differences in ovarian sensitivity. Consequently, pharmacogenetics can assist physicians with prescribing medicine to achieve the controlled ovarian stimulation.

Our research outlines focus on genes that are involved in male/female infertility, particularly in ART-protocols response.

### Research Assistants:

- **Zari Moradi**, Shabnam, MSc
- **Khosravi Far**, Mona, MSc
- **Mohseni Meybodi**, Anahita, PhD
- **Mansouri**, Zahra, MSc

### Student Trainees:

- **Ghezelayagh**, Zahra
- **Nazouri**, Azadeh
- **Modaresi**, Monir
- **Tarahomi**, Nafiseh
- **Keshmiripour**, Shirin
- **Chekini**, Zahra

### Projects

- Genetic and Pharmacogenetic aspects of ovulation induction in anovulatory women
- The study of genetic variants and expression of the follicular stimulating hormone receptor (FSHR) gene in patients with Polycystic Ovary Syndrome (PCOS)
- Gene expression and gene polymorphism study of the Estrogen receptor (ER) and Aromatase (CYP19) in infertile men referred to Royan Institute
- Genetic variation analysis of MIF in endometriosis patients referred to Royan Institute

### Journal Clubs:

No	Organizer	Date	Title
1	Parvaneh Afsharian	January 3, 2012	Pharmacogenetics aspects of PCOS





## News and Events

### Workshops

- **Workshop: Genetic Engineering & Molecular Cloning.**  
Theory & Practical: 1. Genetic engineering, 2. Cloning of PCR product into T/A vector, 3. Transformation of recombinant vector into bacterial host, 4. Colony pick up & Colony PCR, 5. Plasmid extraction, 6. Digestion, 7. Gel electrophoresis & analysis.  
Scientific Manager: Amir Amiri Yekta; Executive Manager: Totonchi M. June 7-8, 2011
- **Primary Methods in Molecular Biology**  
Theory & Practical: 1. GLP, 2. Gene expression biology, 3. Primer design, 4. DNA extraction, 5. RNA extraction, 6. DNase treatment, 7. RT-PCR, 8. Gel electrophoresis & Data analysis.  
Scientific Manager: Totonchi M; Executive Manager: Amir Amiri Yekta. May 3-4, 2011
- **Culture, Harvest and Banding of Human Lymphocyte Chromosomes**  
Theory & Practical: 1. Culture of lymphocytes, 2. Harvesting of lymphocytes, 3. Smear preparation and G banding of chromosomes, 4. An introduction on karyotyping.  
Scientific Manager: Anahita Mohseni Meybodi; Executive Manager: Shabnam Zari Moradi. June 23, 2011
- **Genetic Counselling in Infertility.**  
Theory & Practical:
  - Principles & Indications of Clinical Genetic Counseling
  - Pedigree Drawing Milestones (theoretical & practical)
  - Genetic Inheritance Patterns
  - Chromosomal Abnormalities
  - Genetic Aspects of Recurrent Miscarriage
  - Genetic Screening in Obstetric Clinic
  - Prenatal & Neonatal Screening
  - Principles & Indications of PGD & PGS
  - Genetic Approach in Infertility CenterScientific Manager: Navid Almadani; Executive Manager: Shabnam Zari Moradi, November 22-23 2011
- **FISH (Hands-on workshop on Fluorescent In Situ Hybridization)**  
Subjects: 1. Interphase lymphocyte slide preparation by direct harvest, 2. Interphase FISH, 3. Metaphase FISH, 4. Whole Chromosome Paints. Application: 1. Genetic Research, 2. Medical Genetics. Scientific Manager: Hamed Vaziri; Executive Manager: Hamed Vaziri. December 6-7 2011
- **Sperm Functional Tests in the Diagnosis and Treatment of Infertility.** Executive Manager: Hani Hosseinifar
- **Semen Analysis.** Executive Manager: Hani Hosseinifar
- **RNAi Technics,** Executive Manager: M Totonchi



# ANNUAL REPORT

## Epidemiology and Reproductive Health Department of RI-RB



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Annual Report



### Department Head: Reza Omani Samani, MD

■ Medical Doctor, Bioethics, Faculty of Medicine, Iran University of Medical Science, Tehran, Iran

[samani@royaninstitute.org](mailto:samani@royaninstitute.org)

#### Biography

Dr Samani achieved his MD from University of Iran Medical Science in 1996. He has been working in this department since 2001. He has been involved mostly in ethical issues of infertility. By this background he applied for PhD of Bioethics in Tehran University of Medical Science and he was accepted there in early 2011. He currently works as Head of the department of Epidemiology and Reproductive Health in Royan Institute.

#### Message from the Department Head

This department was established in 1999 in Royan Institute. The aim of this department was to do extensive researches on epidemiological aspects of infertility and reproduction and also on reproductive and sexual health. In 2000 after establishment of Ethical committee in the Institute, the ethics was added to the duties of this department. In 2003 it was divided to three subgroups: Biostatistics, Epidemiology and Bioethics. Then in 2008 Bioethics subgroup was changed to "Bioethics and law" because of so many legal issues in infertility treatment and reproduction and large number of researches undergoing in this field. Finally in 2010, three subgroups names changed to: Biostatistics and methodological subgroup, Reproductive health, Epidemiological and social subgroup, Bioethical, legal and Ethics, and psychological subgroup.

#### Department History and Introduction

The Epidemiology and Reproductive Health Department was established in 2000 with the aim of promoting reproductive health by epidemiological research in the field of reproduction. This department is responsible for checking all research proposals in three faculties 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 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.

#### The Department Focuses on:

- Social and occupational factors influencing reproduction and fertility
- Attitudes, knowledge and practice of the society regarding reproductive issues
- Quality of life, marital and sexual satisfaction and influential factors among infertile couples
- Psychological issues of infertility and interventions to improve them
- Statistical methods with intention to increase the accuracy of statistical analysis
- Ethical, legal and religious aspects of reproduction
- Designing Clinical trials
- Sexual health education
- Interpretation of statistical results in medical research
- Evaluation of diagnostic test accuracy

#### The Department's Main Activities and Researches:

- Giving information to the Surrogate child: (What and When)
- Ethical challenges of cell therapy and possible solutions
- The role of stem cells in the burn
- Patient Bill of Rights
- Views in favor of commercialization Surrogacy



- Mutual obligations of the contract in Surrogacy
- Relationship between Surrogacy and Adoption
- Review the draft bill for adding some points to the Act of Embryo Donation
- Psychological and cultural problems of Surrogacy
- Medical hegemony in the definition of ethics body in Iran
- Nature of the relationship between physician and patient from Imamieh point of view
- Doctor and patient relationship
- Applying artificial neural network to predicting the outcome of ART cycles in the patients who refer to Royan institute
- Attitude towards the child and the parent specially in HIV positives
- Survey of sexual function in infertile women
- Development and standardization of data collection tools to study knowledge and attitude towards Methods of gamete donation
- Experience of infertility among embryo recipients
- Using ART for addicted couples from legal and moral point of view
- Review the necessity of obtaining permission of spouse for using the medical treatment for wife
- Review of reproductive rights in local and international legal system
- The relationship between chemical pregnancy, risk factors, clinical and cellular factors in infertile people using structural equation model
- Using methods of correction of sensitivity and specificity of diagnostic tests to estimate the accuracy of transvaginal ultrasonography in diagnostic endometrial polyps when verification bias is present
- Ethical challenges of human transplantation using transgenic animals organ
- The results of infertility treatment in older women
- Vaginismus treatment after 20 years: Case report
- Writing a book about assisted reproductive treatments History in Iran
- Collecting ART patient records
- Design of forecast models using decision trees to identify infertile women with endometriosis
- Review of assisted reproductive therapy in postmenopausal women with advanced age from medical and ethical perspective
- Professionals' attitudes towards the welfare of children born after assisted reproductive techniques

#### Programs and Directors

1. Developmental Outcomes of IVF Children, Reza Omani Samani, MD
2. ART History in Iran, Narges Bagheri Lankarani, PhD
3. Epidemiologic aspect of infertility, Gholamreza Khalili, MD
4. Predicting ART success rate, Mohammad Reza Akhoond, PhD
5. Ethics and legal aspects of ART, Mohamad Reza Rezaniya Moalem, PhD
6. Clinical trials in cell therapy: Design and statistical method, Ali Akhlaghi, MSc
7. Bio statistics and Methodology in Cellular and Molecular Researches, Mohammad Chehrizi, MSc
8. ART surveillance, Azadeh Ghaheri, MSc
9. Ethical aspects of care and use of lab animals, Shima Behnammanesh, MA
10. Ethical aspects of ART and new biologic methods, Leila Alizadeh, BSc
11. Psychological aspect of Assisted Reproductive Technology, Shokoufeh Sabeti, MD

#### Overview of the Department in 2011

- Numerous researches were initiated in 2011 in addition to the continuation of previously started projects
- Congress was carried out under the name of the first annual congress of ethics and reproductive rights
- The 6<sup>th</sup> symposium of nursing role in infertility



**Group Leader:**  
**Mohammad Reza Rezaniya Moalem, MA**

rezaniyamoalem@royaninstitute.org

#### Biography

He achieved his BA in law from university of Tehran in 1996. He continued his education in University of Qom and graduated with MA of Private law in 1999. He has been working in this department since 2005. He has been involved mostly in ethical and jurisprudential issues of infertility. By this background he applied for PhD and he graduated from University of Shahid Motahari in 2009.

## Ethics and Legal Aspect of ART

### Introduction

Assisted reproductive technologies are widely practised around the world for the treatment of all forms of infertility. Currently, the application of this technology is common in the Islamic world. This group discusses derivation of Islamic rulings and its impact on the ethics of contemporary issues, including family formation and assisted reproduction. It is important for the Muslims from all around the world to know the current situation of Islamic decrees about assisted reproduction, especially Shī'ah Muslims, because in Shī'ah Islam, third party assisted reproduction is accepted. As the law in Iran and many other Islamic countries are based on Islam, legal researches and pursuing guidelines and legislations is another aim of this group.

### Research assistants:

- **Behnammanesh**, Shima, MA
- **Azin**, Mohammad, MA
- **Shariati-Nasab**, Sadegh, MA
- **Merghati**, Taha, PhD
- **Omani Samani**, Reza, MD

### Publications

*Ethical challenges regarding Xenotransplantation of transgenic animals to human beings*  
Behnam Manesh Sh. Hakim Research Journal 2012; 15(1): 13- 21.

*Ethical issues in stem cell research and cell therapy.* Omani Samani R. Archives of Iranian Medicine. May 2011; 14(3): 227-229.



## Epidemiology and Biostatistics in ART

### Introduction

Infertility is a major public health problem worldwide that has been encountered more during recent years. Clinically a couple is considered to be infertile after at least one year without contraception and without pregnancy (Weinberg and Wilcox 1998; Savitz et al. 2002). Factors affecting fertility can be varied in different parts of the world. The epidemiological knowledge about infertility in Iran is sparse; as regards fertility treatment had developed substantially during the 1980's, and Royan institute is one of largest center in our country that many infertile men and women with different geographical areas and different ethnic groups refer to this center around the country. It is tried to study the important variables such as psychosocial, demographic, social, geographical, and etc which effect on fertility. Also, the associations between those variables among women and men in ART through epidemiological methodology such as case-control, retrospective cohort or interventional study are included. Hope that the activities of this group can be effective in providing some important data about the epidemiologic and etiologic factors of infertility in this part of the world and can show the priority of future plan for complementary assessment and preventive programs in general population.

### Research Assistants:

- **Akhoond**, Mohammad Reza, PhD
- **Akhlaghi**, Ali Asghar, MSc
- **Chehrazi**, Mohammad, MSc
- **Shamsipour**, Mansour, MSc
- **Mounesan**, Leila, MSc
- **Shabani**, Fatemeh, BSc
- **Sazvar**, Saeedeh, BSc
- **Ghaheeri**, Azadeh, MSc
- **Cheraghi**, Rezvan, MSc
- **Hesam**, Saeed, MSc

### Publications

*Comparison of Cabergoline and Intravenous Albumin in The Prevention of Ovarian Hyperstimulation Syndrome: A Randomized Clinical Trial*, Tehraninejad ES, Hafezi M, Arabipoor A, Azimineko E, Chehrazi M, Bahmanabadi A. J Assist Reprod Genet. 2012 Mar; 29(3):259-64.

*Comparative Epigenetic Analysis of Oct4 Regulatory Region in RA-Induced Differentiated NT2 Cells under Adherent and Non-Adherent Culture Conditions*, Favaedi R, Shahhoseini M, Akhoond MR. Mol Cell Biochem. 2012 Apr; 363(1-2):129-34.

*Improvement in Pregnancy Rate by Removal of Cervical Discharge Prior to Embryo Transfer in ICSI Cycles: A Randomized Clinical Trial*, A Moini, K Kiani, A Bahmanabadi, MR Akhoond, A Akhlaghi. The Australian and New Zealand Journal of Obstetrics and Gynecology 9 Jun 2011

*Evaluation of Sperm Preparation Methods and Their Correlation with Conventional Semen Parameters, Intracellular ROS, DFI, MMP and Apoptosis in Normospermic Semen Samples* L Rashki Ghaleno, M Rezazadeh Valojerdi, E Jaan Zamin, M Chehrazi, M Sharbatoghli, R Salman Yazdi, International Journal of Andrology. 2011.

*Improvement in Pregnancy Rate by Removal of Cervical Discharge Prior to Embryo Transfer in ICSI Cycles: A Randomized Clinical Trial*. A Moini, K Kiani, A Bahmanabadi, M Akhoond, A Akhlaghi. The Australian and New Zealand Journal of Obstetrics and Gynecology, 2011.

*Quantum Dot Labeling Using Positive Charged Peptides in Human Hematopoietic and Mesenchymal Stem Cell*. S Ranjbarvaziri, S Kiani, A Akhlaghi, A Vosough, H Baharvand, N Aghdami, Biomaterials, 2011

Dibaj Sh, Omani Samani R. *Letter to Editor*. J Reprod Infertil. 2011; 12(2):165-165.



### Group Leader: Gholamreza Khalili, MD

[rkhaliie@royaninstitute.org](mailto:rkhaliie@royaninstitute.org)

### Biography

Dr Khalili has been involved with Epidemiology and Reproductive health for past two years as a research fellow. He achieved his MD from university of Tehran in 1999. He continued his education in University of Tehran and currently he is a PhD student in Epidemiology field since 2001.

*Superovulation, in vitro fertilization (IVF) and in vitro development (IVD) protocols for inbred BALB/cJ mice in comparison with outbred NMRI mice.* A Golkar-Narenji, HGourabi, H Eimani, Z Barekati, A Akhlaghi. *Reproductive Medicine and Biology.* 2012: 1-8.

*The effect of adding oral oestradiol to progesterone as luteal phase support in ART cycles –a randomized controlled study.* A Moini, Sh Zadeh Modarress, EAmirchaghmaghi, N Mirghavam, SKhafri, MR Akhoond, R Salman Yazdi. *Arch Med Sci.* 2011; 7, 1: 112-116

*The Factors Affecting the Outcome Of Frozen-Thawed Embryo Transfer Cycle,* Ashrafi M, Jahangiri N, Hassani F, Akhoond MR, Madani T. *Taiwan J Obstet Gynecol.* 2011 Jun; 50(2): 159-64.



**Group Leader:**  
**Narges Bagheri**  
**Lanakarani, PhD**

[nargesbagheri@royaninstitute.org](mailto:nargesbagheri@royaninstitute.org)

#### Biography

Dr Lanakarani has been involved with Epidemiology and Reproductive health for the past two years as a research fellow. She received her PhD from the University of Wollongong in Australia in 2008.

## Reproductive Health

### Introduction

One side of every innovation in the field of medicine and high-technology which has something to do with medicine is human being. Moreover it cannot be found any kind of people living out of societies throughout the history, which means human are social and cultural animals. This kind of creation, similar to others, has necessary and basic needs for survival. So, the main difference between human and other kind of animals is having culture and an economical system in order to live with each other and improve the qualities of life.

ART is a sort of innovations coming from this system in order to help to maintain and improve it. Therefore, not only it is supposed to be studied the process of constructing ART, but also it intended to do research on how it works, who local socio-economic system accept, change and internalize that, and what intended or unintended consequences are.

### Research Assistants:

- **Karimi**, Morteza, MSc
- **Sabeti**, Shokoufeh, MD
- **Izadyar**, Nasrin, MSc
- **Ahmadi**, Zahra, BSc
- **Ezabadi**, Zahra, MSc
- **Irani**, Shohreh, PhD
- **Kashfi**, Fahimeh, MSc
- **Malekzadeh**, Farideh, MSc

### Publications

*Anti-Coagulation During Pregnancy in Women with Mechanical Heart Valves: A Prospective Study.* AJ Khamoushi, F Kashfi, S Hosseini, A R Alizadeh Ghavidel, N Samiei, M Haddadzadeh. *I J F S.* Apr-Jun 2011. 5: 1: 47-51

*The Relationship between Occupation and Semen Quality,* Vaziri MH, Sadighi Gilani MA, Kavousi A, Firoozeh M, Khani Jazani R, Vosough Taqi Dizaj A, Mohseni H, Bagheri Lanakarani N, Azizi M, Salman Yazdi R. *International Journal of Fertility And Sterility,* september 2011; 5(2): 66-71.

## News and Events

### Workshops

- **Introduction to ENDNOTE:** Held on June 14, 2011 from early morning to 4:00 PM at the Royan Institute in Tehran, Iran. This workshop runs at least once a year to help researchers write their articles.
- **Designing a Clinical trial:** Held from July 13-14, 2011 to help researchers have a better understanding of interventional studies in which the research subjects are assigned by the investigator to a treatment or other intervention and their outcomes are measured.







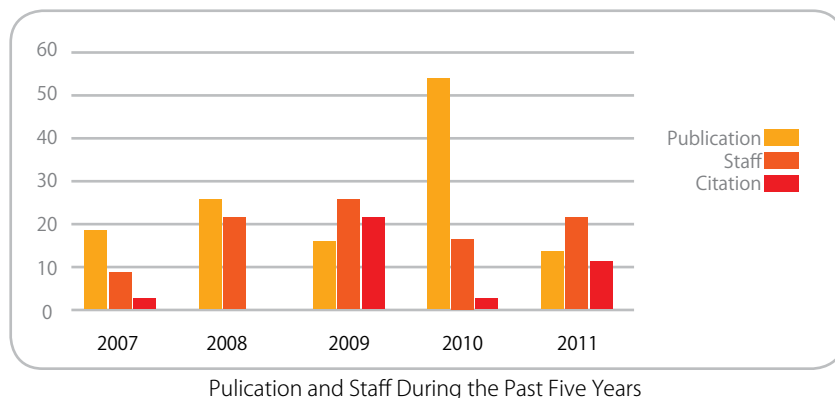
- **Sexual Health:** Held on November 9-11, 2011. Provided detailed instructions on issues relating to human sexuality, including: human sexual anatomy, sexual reproduction, sexual intercourse, reproductive health, emotional relations, reproductive rights and responsibilities, abstinence, birth control, and other aspects of human sexual behavior. Common avenues for sex education are caregivers and public health campaigns that could help young couples.
- **Interpretation of Statistical Results in Medical Research:** It was held on December 14, 2011. The aim of this workshop was to introduce how to interpret scientific articles to fellow researchers.
- **The First Annual Congress of Reproductive Ethics and Law:** This was a 3-day congress held on January 4-6, 2012. It was a multidisciplinary congress that had been held as a symposium and seminar in the past. Because assisted reproductive techniques are closely related to religious beliefs, this congress tried to gather the religious controversies about these procedures, especially surrogacy, in one place. Then, by considering the legal and ethical aspects, tried to clear some of legal obstacles in order to pave the way for future laws.



**Journal Clubs:**

No	Organizer	Date	Title
1	Shiva Dibaj	05/07/2011	Bias in clinical trial
2	Leila Alizadeh	27/09/2011	Post-humus

**Staff, Publication, Budget, and Citation Charts:**



**Other Activities:**

Own projects	19
Joint projects	70
Supervision of graduated students	5
Consultant for Research Methodology	140
Statistical analysis	73
Article review	88





# ANNUAL REPORT

## Reproductive Imaging Department of RI-RB



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### Department Head: Firoozeh Ahmadi, MD

■ Radiologist

[f\\_ahmadi@royaninstitute.org](mailto:f_ahmadi@royaninstitute.org)

#### Biography

Educational background: Radiology, Iran University of Medical Science, Tehran, Iran (1994-1997)  
General Physician, Iran University of Medical Science, Tehran, Iran (1986-1993)  
Associate Professor, Reproductive Medicine Research Center, Royan Institute, ACECR (2008- Present)  
Head of Reproductive Imaging Department, Royan Institute (2008-present)

#### Message from the Department Head

Infertility is a widespread, growing problem. The physical and psychological impact of infertility can be crushing to the infertile persons and to their family. Ultrasound plays a great role in the assessment and management of infertility. It is also an important tool by which it is possible to monitor the growth of the fetus development during the pregnancy, and screen for fetal anomalies.

The mission of our department is to provide comprehensive infertility evaluations using the latest knowledge and innovative research to provide the highest quality of infertility management.

The goals of the department are to conduct research in the field of male and female infertility in order to provide modern, high quality services for infertile couples.

The department's vision is to perform national and international multicenter research with the collaboration of universities and other infertility centers to provide educational courses in diagnostic ultrasound, including transvaginal, color Doppler, power Doppler, 3D/4D imaging and radiology for radiologists, gynecologists and fellowships.

#### Department History and Introduction

The Reproductive Imaging Department was established in 2008. Our department performs female and male infertility assessment and pregnancy monitoring using 2D, 3D, color Doppler, ultrasound, hysterosalpingography, 3D hysterosonography, vasography, and transrectal ultrasonography techniques.

The department also offers a fellowship in reproductive imaging for radiologists in order to establish a high standard of education and training in the field of reproductive imaging.

#### Research Scientists:

- **Ahmadi**, Firoozeh, MD (Radiologist)
- **Hodshenas**, Safa, MD (Radiologist)
- **Niknejadi**, Maryam, MD (Radiologist)
- **Salamati**, Masoumeh, MD (Radiologist)
- **Vosoug**, Ahmad, MD (Radiologist)
- **Zafarani**, Fatemeh, MSc

#### Research Assistants:

- **Akhbari**, Farnaz, BSc
- **Eslami**, Bita, MSc
- **Haghighi**, Hadieh, BSc
- **Irani**, Shohreh, PhD
- **Javam**, Maryam, BSc
- **Moinian**, Dina, MSc
- **Niknejad**, Fatemeh, BSc
- **Rashidi**, Zohreh, BSc
- **Tehrani**, Fattaneh, BSc
- **Poyan**, Akram, BSc
- **Ghaderi**, Farahnaz, BSc

#### Other Members:

- **Abolhasani**, Jamileh
- **Rozbehani**, Masoumeh
- **Tamhidi**, Nadia

**Students Trainees:**

- **Rohaninejad**, Somayeh, MSc
- **Abtahi**, Naemeh Sadat, MSc
- **Safavi**, Fatemeh, MSc

**Overview of the Group in 2012****Projects:**

Continuing projects in the assessment of female and male infertility, and fetal screening anomalies with more focus on:

- Ultrasonographic chart standardization for Iranian fetuses in order to study early prenatal abnormalities
- Comparative studies of different imaging modalities for assessment of female/male infertility and fetal screening to determine diagnostic accuracy with regards to the golden standard.
- Hysterosalpingography for endometrial investigation and tubal evaluation
- 3D hysterosonography for detection of uterine anomalies
- Diagnostic and interventional imaging in male infertility

**Education:**

providing leadership and knowledge in the field of reproductive medicine by short conducting the following:

- Short reproductive imaging course (2-4 weeks)
- Long reproductive imaging course (2-6 months)

**Special Clinical Services:**

- Hysterosalpingography
- 3D Sonohysterography
- 2D/3D /color Doppler, ultrasound in obstetrics and gynecology
- Diagnostic and interventional imaging in male infertility 2D/3D/color Doppler/trans rectal sonography

### Group Leader: Firoozeh Ahmadi, MD

f\_ahmadi@royaninstitute.org

## Ultrasonography and Sonohysteroscopy

### Publications

*Application of 3D Ultrasonography in Detection of Uterine Abnormalities: Pictorial Review.* F Ahmadi, F Zafarani, H Haghighi, M Niknejadi, A Vosough Taqi Dizaj. Int J Fertil Steril. 2011; 4(4):144-147.

*Conservation Cloning of Vulnerable Esfahan Mouflon(Ovis Orientalis Isphahanica): in Vitro and in Vivo Studies.* Hajian M, Hosseini SM, Forouzanfar M, Abedi P, Ostadhosseini S, Hosseini L, Moulavi F, Gourabi H, Shahverdi AH, Vosough Taghi Dizaj A, Kalantari SA, Fotouhi Z, Iranpour Z, Mahyar H, Amiri-Yekta A, Nasr-Esfahani MH. EJWR-D, 57(4)2011; 959-969.

*Effect of Ovarian Cyclic Status on In Vitro Embryo Production in Cattle.* A Pirestani, SM Hosseini, M Hajian, M Frouzanfar, F Moulavi, P Abedi, H Gourabi, A Shahverdi, A Vosough Taqi Dizaj, MH Nasr Esfahani. Int J Fertil Steril. 2011; 4(4): 172-5.

*Quantum dot labelling using positive charged peptides in human hematopoietic and mesenchymal stem cells.* S Ranjbarvaziri, S Kiani, A Akhlaghi, A Vosough, H Baharvand, N Aghdami. Biomaterials. 2011; 32: 5195-5205.

*Autologous Transplantation of Bone Marrow –derived Mononuclear and CD133+cells in Patients with Decompensated Cirrhosis.* Nikeghbalian S, Pournasr B, Aghdami N, Rasekhi A, Geramizadeh B, Hosseini Asl SM, Ramzi M, Kakaei F, Namiri M, Malekzadeh R, Vosough Dizaj A, Malek-Hosseini SA, Baharvand H. Archives of Iranian Medicine.

*Dizygotic twin pregnancy with a complete hydatidiform mole and a coexistent viable fetus,* Moini A, Ahmadi F, Eslami B, Zafarani F. Iran J Radiol. 2011; 8(4): 249-252.

*Detection of Congenital Mullerian Anomalies Using Real-time 3D,* Ahmadi F, Haghighi H. journal of reproduction & infertility. January/March. 2012; 13(1): 65-66.

*Improved in vitro development of cloned bovine embryos using Sadenosylhomocysteine, a non-toxic epigenetic modifying reagent.* Jafari, Hosseini, Hajian, Forouzanfar, Jafar pour, Abedi, Ostad Hosseini, Abbasi, Gorabi, Shahverdi, Vosough, Anjomshoaa, Haron, Noorshariza, Yakub, NasrEsfahani. Mol Reprod Dev Aug. 2011; 78(8): 576-584.

*Comparing intramuscular progesterone, vaginal progesterone and 17 $\alpha$ -hydroxyprogesterone caproate in IVF and ICSI cycle.* Moini A, Zafarani F, Eslami B, Sadeghi M, Kamyabi Z, Jahangiri N. IJRM. 2011.

*Detection of Congenital Mullerian Anomalies by Real-time 3D.* Ahmadi F, Haghighi H. Reproduction & Infertility. 2012; 13(1): 65-66.

### News and Events

#### Workshops:

- **Hysterosalpingography**  
This pre-congress was held on September 6<sup>th</sup> 2011. The chairman of this pre-congress was Dr Ahmadi.
- **Application of Color Doppler Sonography in Fetal Assessment**  
This pre-congress has been organized by the Department of Reproductive Imaging to provide an overview of the role of Doppler ultrasound in prenatal fetal assessment. The selective use of fetal Doppler leads to significant reduction in prenatal mortality and morbidity. This pre-congress was held on September 6<sup>th</sup> 2011. The chairman of this pre-congress was Dr Sanei. It was a great success, with around 20 radiologists who attended.





- Imaging in Infertility**  
 Imaging in Infertility Symposium was held on September 6<sup>th</sup> 2011 to provide an overview of the key role of modern imaging technologies in the diagnosis and treatment of infertility. It was organized by the Department of Reproductive Imaging at Royan Institute and the chairman was Ms Zafarani. A total of 204 midwives participated in this symposium.

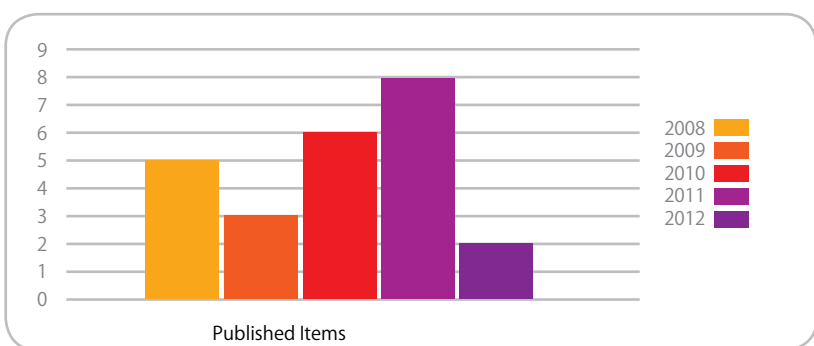
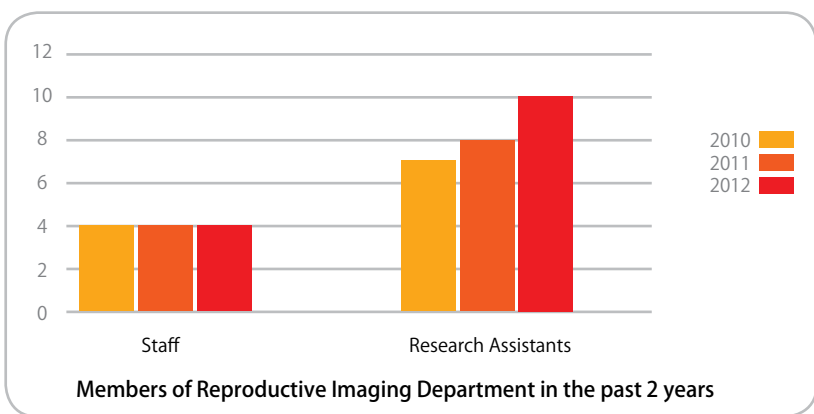


- Bone Cytometry**  
 A one day event focusing on Bone cytometry was held on June 10<sup>th</sup> 2011. The presenter was Dr Fatehi. It was a great success with more than 30 participants.
- Fetal Non-stress Test (NST)**  
 One day event focusing on NST was held on October 28<sup>th</sup> 2011. The presenter was Dr Kalantari, and it was a great success with more than 30 radiologists who attended.
- Ultrasound Evaluation of Regional Lymph Nodes in Breast Cancer and Hysterosalpingography**  
 Ultrasound Evaluation of Regional Lymph Nodes in Breast Cancer and Hysterosalpingography were two workshops held at the 4<sup>th</sup> annual Congress of Women Imaging on February 19<sup>th</sup>- 21<sup>st</sup> 2012. They were organized by Gondishapor University in Ahvaz and the speakers were Dr Ahmadi and Dr Salamaty from the Department of Reproductive Imaging.
- Comparative Study of Imaging Findings in Patient with Genital Tract Endometriosis**  
 This workshop was held on 3<sup>rd</sup> of Feb, 2012 The chairman of this workshop was Dr Niknejadi and it was a great success with about 30 radiologists.

**Journal Clubs:**

No	Organizer	Date	Title
1	Dr Maryam Niknejadi	November, 1 <sup>st</sup> 2011	The application of three-dimensional ultrasound in detection of uterine abnormalities

**Staff Publication Charts**



# ANNUAL REPORT

## Royan Infertility Clinic of RI-RB



**Clinic Head:**  
**Tahereh Ma'dani, MD**

[tmadani@royaninstitute.org](mailto:tmadani@royaninstitute.org)

### Biography

Dr Tahereh Ma'dani obtained her medical degree in 1984 from Shiraz University of Medical Sciences, Iran, and completed her obstetrics and gynecology specialty in 1989 at Iran University of Medical Sciences. She then became an Associate Professor at Iran University of Medical Sciences. Currently she is the Head of Royan Infertility Clinic. She is especially interested in assisted reproductive technology (OHSS, IVM) and reproductive immunology. She has managed several research projects and has a range of national and international publications and presentations.

### Introduction

Royan Infertility Clinic is the second clinic for treatment of infertility in Iran and the first one in Tehran. Although there are more than 50 infertility clinics throughout Iran, after 21 years of experience in this field and due to the high rate of success, many patients prefer to have their treatments in this clinic. Each year we have numerous foreign patients who come to Iran for infertility treatment. Different services including diagnostic and operative laparoscopy, IUI, ovulation induction, IVF, ICSI, ZIFT, IVM, PGD, PESA/TESE, microscopic TESA, vasovasostomy, vasoepididymostomy, TURD, gamete and embryo cryopreservation, assisted hatching, karyotyping, molecular genetic tests such as Factor V Leiden, Factor II and MTHFR gene, as well as others routinely offered to patients.

Royan Infertility Clinic includes different sections for the assessment of different aspects of infertility and developing the best treatment methods:

- Endocrinology and Metabolism Clinic
- Nutrition Clinic
- Endoscopy Clinic
- Endometriosis Clinic
- Recurrent Abortion Clinic
- Prenatology Clinic
- IVF Failure Clinic
- Male Infertility Clinic
- Psycho- Social Support and Counseling Clinic
- Genetic Counseling Clinic
- Imaging modalities such as rectal and vaginal ultrasonography

### Statistics of Royan Infertility Clinic Activities and Treatment Cycles in 2011-2012:

Total number of Visited Patients + Specialized Counseling	64973
Genetic Counseling	2128
Psychological Counseling	989
Diagnostic Laparoscopy	57
Diagnostic Hysteroscopy + Office Hysteroscopy	1053
Laparohysteroscopy	189
Hysterosonography	728
Varicocelectomy	202
PESA/TESE, TESE Microscopy	1748
PGD	432
Embryo Transfer & Freezing	1619
IUI	2683
ZIFT	25
ICSI/IVF cycle	4900
Specialized Sonography + Radiology	19975
Operative Hysteroscopy	583
Monitoring Sonography	42499
Operative Laparoscopy	123

# ANNUAL REPORT

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

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Annual Report

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



**Department Head:**  
**Hossein Baharvand, PhD**

[baharvand@royaninstitute.org](mailto:baharvand@royaninstitute.org)

#### Biography

Born in 1972, Hossein Baharvand received his PhD degree from University for Teacher Training (TARBIAT MOALEM), Tehran in 2004 in the field of Developmental Biology. He joined Royan institute when he was MSc student in 1995. He is currently professor and director of Royan Institute for Stem Cell Biology and Technology (2002-now) and head of Department of Developmental Biology at University of Science and Culture (2006-now). He established the first mouse and human embryonic stem cells in Iran (2003). Later his team has generated several mouse and human embryonic and induced pluripotent stem cells (2008). This has enabled them to pursue many avenues of research into translational research and regenerative medicine. He has published 130 international and 98 national peer-reviewed papers, as well as five chapters in international books, six books in Persian, and translated six English text books into Persian. He was editor of three international books (2009, 2012, Humana press, Springer, USA). He is editorial board member of eight international journals and was as invited speaker in several meetings. He has received 18 international and national prizes including 10<sup>th</sup> (2004), 12<sup>th</sup> (2006), and 17<sup>th</sup> (2012) annual Razi research festival on medical sciences, 27<sup>th</sup> annual book of the year of the Islamic republic of Iran (2010), Academy of Medical Sciences of Iran (Dr Hadavi's Award, 2010), Science and Technology Prize of the Islamic Educational, Scientific, and Cultural Organization (ISESCO) in the field of Biology (2010).

#### 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, the Department of Stem Cells expanded to twelve main research groups that conduct studies on stem cells and developmental biology, molecular systems' biology, and regenerative medicine.

Throughout, our vision 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.

#### Research Programs and Directors:

- Biology of Pluripotent Stem Cells
  - Epigenetic Reprogramming
  - Hepatocytes
  - Pancreatic Beta Cells
  - Germ Cells
  - Neural Cells- Developmental Biology
- Dr Baharvand
- Neural Cells-Traumatic Nerve Injury
- Dr Kiani
- Neural Cells-Neurodegenerative diseases
- Dr Javan
- Bone and Cartilage/Mesenchymal Stem Cells
- Dr Baghaban Eslaminejad
- Cardiomyocytes and Endothelial Cells
  - Skin Cells
  - Regenerative Medicine
- Dr Aghdami
- Molecular Systems Biology
- Dr Hosseini Salekdeh
- Cancer and Hematopoietic Stem Cells
  - Public Cord Blood Bank
- Dr Ebrahimi

#### Core Facilities:

- Royan Stem Cell Bank (RSCB)
- Molecular Biology Lab
- Electrophysiology Lab
- Cytometry and Imaging Lab
- History Lab
- Gene Targeting Lab
- Viral Transduction Lab
- Nano/Tissue Engineering Lab
- "Stem Cell for All" Lab

# ANNUAL REPORT

## Research Programs of RI-SCBT



**Chief Researcher:**  
**Seyedeh Nafiseh Hassani**

**Group Leader:**  
**Hossein Baharvand, PhD**

[snafisehassani@royaninstitute.org](mailto:snafisehassani@royaninstitute.org)

### Biography

Seyedeh Nafiseh Hassani received her BSc in Cell and Molecular Biology from Tehran University in 2002. She continued her education in same field at Khatam University in Tehran. She passed her thesis by Dr Rafati at Pasteur Institute and graduated with MSc in 2005. In 2008, she began a PhD degree in Developmental Biology in a joint program between Royan Institute and the University of Science and Culture. Currently, she is working on her PhD thesis under the supervision of Dr Baharvand. Her major research interest is pluripotent signaling pathways in stem cells.

## Biology of Pluripotent Stem Cells

### Introduction

Our first priority was the derivation and maintenance of embryonic and pluripotent stem cells from mice and human. Accordingly, we could derive 20 lines of human embryonic stem cells and more than 170 lines of mouse embryonic stem cells from 2002 until now. In recent years, we have focused on the generation of new embryonic stem cell lines for achievement of these goals:

1. Identification of signaling pathways in pluripotent stem cells
2. Improvement of culture medium and extracellular matrix for pluripotent stem cells
3. Scale-up culture of human pluripotent stem cells (hESCs and HiPSCs) in bioreactors

### Research Assistant:

- **Abasalizadeh, Saeed, MSc**

### Technical Staffs:

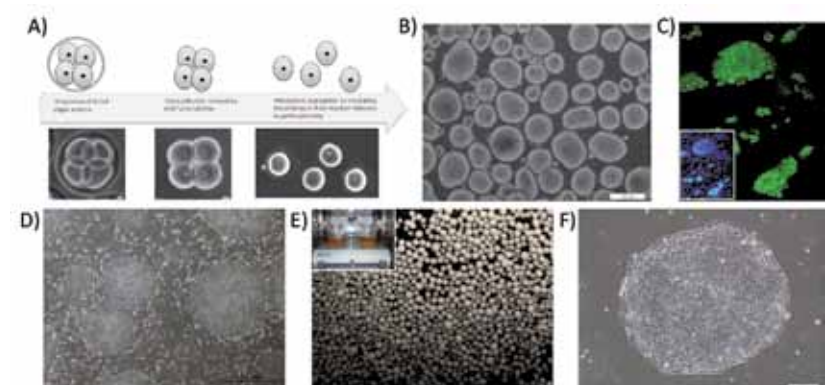
- **Pakzad, Mohammad, MSc**
- **Rezaei, Mehran, BSc**
- **Taee, Adeleh, BSc**
- **Mollamohamadi, Sepideh, BSc**

### Students:

- **Farzaneh, Maryam, MSc**
- **Milani, Arezoo, MSc**

### Postdoc:

- **Gharaati, Mohammad Reza, PhD**



A) Derivation of mouse embryonic stem (ES) cells from single blastomeres. B) Suspension culture of mouse ES cells. C) Immuno staining for pluripotency marker gene, Oct4 (green). Staining of nucleus are shown by DAPI (blue). D) Suspension culture of human pluripotent stem cells in bioreactor. E) Human ES cells in defined culture condition



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- Faradonbeh MZ, Gharechahi J, Mollamohammadi S, Pakzad M, Taei A, Rassouli H, Baharvand H, Salekdeh GH. *An orthogonal comparison of the proteome of human embryonic stem cells with that of human induced pluripotent stem cells of different genetic background.* Mol Biosyst. 2012 Jun; 8(6): 1833-40.
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- Gheisari Y, Baharvand H, Nayernia K, Vasei M. *Stem Cell and tissue engineering research in the Islamic Republic of Iran.* Stem Cell Rev. 2012. [Epub ahead of print]
- Abbasalizadeh S, RezaeiLarijani M, Samadian A, Baharvand H. *Bioprocess Development for Mass Production of Size-controlled Human Pluripotent Stem Cell Aggregates in Stirred Suspension Bioreactor.* Tissue Eng Part C Methods. 2012.



**Chief Researcher:**  
**Mehdi Totonchi**

**Group Leader:**  
**Hossein Baharvand, PhD**

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#### Biography

Mehdi Totonchi was born in 1979 and received his BSc in Biology at the University of Bu-Ali Sina in Hamedan from 1997-2002. In 2005, he got his MSc in the field of Molecular Genetics at Azad University of Research Sciences. For the next three years, he was research assistant in the Department of Genetics and Stem Cells at Royan Institute. There, he was involved in the generation of the first induced pluripotent stem cell (iPSC) in Iran. In 2008, he began his PhD at a joint program between University of Science and Culture and Royan Institute in the field of Developmental Biology.

## Epigenetic Reprogramming

### Introduction

Epigenetic reprogramming, which considered the biological breakthrough of the decade, can be categorized into in vitro and in vivo trials. In recent years, there has been an increased interest in the study of induced pluripotent stem cells (iPSC) biology and cell fate conversion because of the potential of iPSC in regenerative medicine, disease modeling, drug discovery and in vitro analysis of development, which have led scientists to enthusiastically embrace this field.

Our group performs its assignments both as a viral transduction core facility and in independent research projects. Since the establishment of first iPSC lines, our group decided to narrow its activities to some major fields, including:

- Establishment of patient specific iPSCs, genetic correction and functional analysis of these cells in order to study the disease mechanisms, development and disease modeling for drug discovery trials. iPSC technology has provided scientists with patient-derived pluripotent stem cells that can be differentiated towards interesting cells affected by certain diseases. To reach this goal, we have established iPSC lines from some diseases.
- Movement towards production of iPSCs. Regarding this, we have launched some projects to generate safer iPSCs using small molecules, recombinant proteins and synthetic mRNAs.
- Direct transdifferentiation of terminally differentiated cells and studying cell fate conversion. Due to the importance of this issue in regenerative medicine, our group has set this goal as one of its highest priorities and enthusiastically follows this plan.
- Computational modeling of genetic/epigenetic mutual interaction within pluripotent and differentiated cells. The Waddington landscape approach to this problem has recently provided insights into several key issues of differentiation. Our aim is to develop a computational platform for quantitative analysis and prediction of events during pluripotency and differentiation.

### Research Assistant:

- Taghizadeh, Zeinab, MSc

### Technical Staffs:

- Hajikaram, Maryam, MSc
- Hesaraki, Mehdi, MSc

### Students:

- Moradi, Sharif, PhD student (Developmental Biology)
- Sharifi Zarchi, Ali, PhD student (Bioinformatics)

A diagram to show the definition of transdifferentiation, which is the direct conversion from one mature somatic cell type into another functional mature or progenitor cell type in the same or another lineage of the embryonic germ layers. (B. Pournasr et al, Concise Review: Alchemy of Biology: Generating Desired Cell Types from Abundant and Accessible Cells, 2011, Stem Cells, 29:1933–1941)



### Publications

Pournasr B, Khaloughi K, Salekdeh GH, Totonchi M, Shahbazi E, Baharvand H. *Concise review: alchemy of biology: generating desired cell types from abundant and accessible cells*. Stem Cells. 2011; 29(12):1933–41.

Zahabi A, Shahbazi E, Ahmadideh H, Hasani N, Totonchi M, Taei A, Masoudi N, Ebrahimi M, Aghdami N, Seifinejad A, Mehrnejad F, Daftarian N, Salekdeh GH, Baharvand, H. *A new efficient protocol for directed differentiation of retinal pigmented epithelial cells from normal and retinal disease induced pluripotent stem cells*. Stem Cells Dev. 2011 Dec 6. Epub ahead of print.

Hosseini SM, Hajian M, Forouzanfar M, Moulavi F, Abedi P, Asgari V, Tanhaei S, Abbasi H, Jafarpour F, Ostadosseini S, Karamali F, Karbaliiae K, Baharvand H, Nasr-Esfahani M. *H. Enucleated ovine oocyte supports human somatic cells reprogramming back to the embryonic stage*. Cell Reprogram. 2012, 14(2):155–63



## Hepatocytes

### Introduction

Cell-based therapy with the hope of replacement of new hepatocytes in the injured organ motivates scientists to produce large amounts of the cells ex-vivo. Having functional hepatocyte in the lab, one needs to have extensive knowledge regarding real, functional hepatocytes that can be obtained in a primary culture from the liver. It is also necessary to have the basic knowledge of mechanisms involving liver formation during embryogenesis, which can be simulated in the lab by using human pluripotent stem cells in addition to using a rodent model.

Therefore, our group has focused on hepatocyte differentiation of pluripotent stem cells as well as direct conversion of accessible cells such as fibroblasts to hepatocytes; a new era called transdifferentiation. The main goal of our group is improving the situation of patients suffering liver disease in addition to finding unknown basic phenomena during human hepatogenesis using pluripotent stem cells as a model.

### Research Scientists:

- **Pyriaee, Abbas**, PhD
- **Moslem, Mohsen**, PhD

### Research Assistant:

- **Farzaneh, Zahra**, MSc

### Students:

- **Vosough, Masoud**, PhD
- **Yahoo, Neda**, PhD
- **Lotfinia, Madjid**, PhD
- **Heidarian, Zeinab**, PhD
- **Ghanian, Hossein**, MSc



**Chief Researcher:**  
**Behshad Pournasr**

**Group Leader:**  
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### Biography

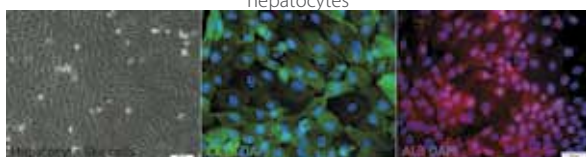
Behshad Pournasr received his BSc in Cell and Molecular Biology from the Faculty of Science, Tehran University in 2000. He continued his education at Isfahan University of Medical Sciences. He joined the Department of Immunology and worked under the supervision of Dr Pourazar, completing his study in 2003. He began working at Royan Institute from 2006 as a research assistant. In 2009, he began a PhD position in Developmental Biology in a joint program between Royan Institute and the University of Science and Culture. His major research interest is the biology of hepatocytes and hepatogenesis.



Mass Differentiation of Human Pluripotent Stem Cells in Suspension Culture



Mass Differentiation of Human Pluripotent Stem Cells to the definitive endoderm and then to hepatocytes



Acquiring Functional Hepatocyte-derived Pluripotent Stem Cells on a homemade Matrix



Direct Conversion of Mouse Fibroblast to Hepatocyte-Like Cells

## Publications

- Moslem M, Valojerdi M, Pournasr B, Mohammadnejad A, Baharvand H. *Therapeutic Potential of Human-induced Pluripotent Stem Cell-derived Mesenchymal Stem Cells in Mice with Lethal Fulminant Hepatic Failure*. Cell Transplantation. 2012
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## Pancreatic Beta Cells

### Introduction

Type 1 diabetes mellitus (T1DM) is one of the most common metabolic disorders and characterized by the autoimmune destruction of the insulin producing pancreatic  $\beta$ -cells. There is a great hope to use renewable sources of cells that could replace pancreatic  $\beta$ -cells.

There are several approaches being considered for the generation of  $\beta$ -cells:

- Differentiation of embryonic stem cells, induced pluripotent stem (iPS) cells, adult pancreatic cells and adult stem cells to the  $\beta$ -cell lineage
- Conversion of other terminally differentiated cells to  $\beta$ -cells in a process called "Transdifferentiation".
- Promote the replication of existing  $\beta$ -cells either in vivo or in vitro.

There are several reports of differentiation of cell populations into  $\beta$ -cells, definitive endoderm, and pancreatic progenitors, using growth factors and small molecules. However, success in final step of directed differentiation to generate functional mature  $\beta$ -cells in sufficient quantities has yet to be achieved in vitro.

Our group's areas of focus include:

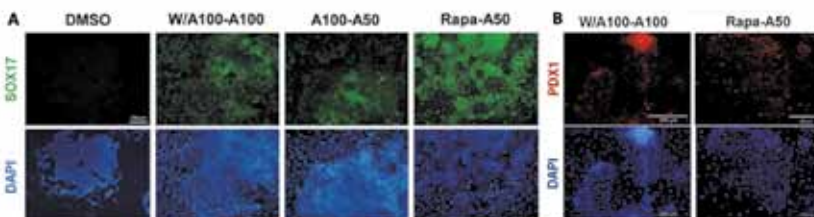
- manipulating signaling pathways to enhance differentiation of human pluripotent stem cells to insulin producing cells by growth factors and small molecules;
- Transdifferentiation of terminally differentiated cells such as fibroblast to  $\beta$ -cells.
- Gene manipulation of regulatory networks in pancreas development to enhance the differentiation of mouse embryonic stem cells to  $\beta$ -cells.
- Islet transplantation in T1DM mice model and investigating the effect of immune modulators and angiogenic factors on islets survival and functions after transplantation

### Research Assistants:

- **Moradmand**, Azadeh, BSc
- **Khalooghi**, Keynoosh, MSc
- **Nezari**, Hossein, MSc
- **Khosravi**, Mohsen, MD

### Students:

- **Moradmand**, Azadeh, MSc
- **Kazemi**, Mohamad, MSc
- **Tahamtani**, Yaser, PhD
- **Hajizadeh**, Ensieh, PhD
- **Soltanian**, Anahita, PhD



(A) Immunofluorescent staining of human embryonic stem cells (hESCs) treated with three endodermal differentiation protocols. Treating hESCs with small molecule Rapamycin and 50 ng/ml activin A (Rapa-A50) can efficiently produce SOX17 (definitive endoderm marker) positive populations. Two other groups (W/A100-A100 & A100-A100) consist of usual growth factor methods for endodermal differentiation of hESCs.

(B) Further differentiation of the produced definitive endoderm cells (A) into pancreatic progenitor cells (PDX1 is the main marker expressed in pancreatic progenitor cells).

### Publication

Pournasr B, Khalooghi K, Salekdeh GH, Totonchi M, Shahbazi E, Baharvand H. *Concise review: alchemy of biology: generating desired cell types from abundant and accessible cells*. Stem Cells. 2011; 29(12):1933-41.



**Chief Researcher:**  
**Ali Farrokhi**

**Group Leader:**  
**Hossein Baharvand, PhD**

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### Biography

Ali Farrokhi completed his BSc degree in Genetics from Shahid Chamran University of Ahvaz in 2003. In 2004, he became a research assistant at Royan Institute. He received his MSc in Cell and Molecular Biology from Tehran University in 2007. From 2007 until now, he has been the chief researcher of pancreatic  $\beta$ -cell program at Royan Institute.

**Group Leader:**  
**Hossein Baharvand, PhD**

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## Germ Cells

### Introduction

Spermatogonial stem cells (SSCs) are unipotent precursor cells for sperm generation in the testis. SSCs represent an extremely low proportion of the cells of the testis, but they can be isolated and propagated in vitro. More recently, it was found that these cells can be reprogrammed spontaneously to multipotent cells in vitro, named gPSC, that have the capability to differentiate into various differentiated cell lineages. In fact, these multipotent cells can act like embryonic stem (ES) cells in their differentiation properties and growth characteristics of the colonies they form in culture. Thus, they are also named ES-like cells. Less ethical concerns that derivation of these cells face with, in addition to lack of immunogenicity associated with ESCs, and production of them without the need for viral genes which currently used in iPSCs generation, had made gPSCs a novel opportunities in regenerative medicine. Given how low efficient and lengthy the process of gPSCs production can be, we reasoned that the usage of small molecules as a tool for manipulating signaling pathways provide the ability to generate gPSCs in a more efficient and faster manner. Our group has succeeded in developing a robust and reproducible protocol for obtaining gPSCs from testicular cells through manipulating signaling pathways by small molecules. Moreover we are attempting to find an efficient way for differentiating SSCs to sperm and mass production of ovarian stem cell in vitro.

### Research Scientist:

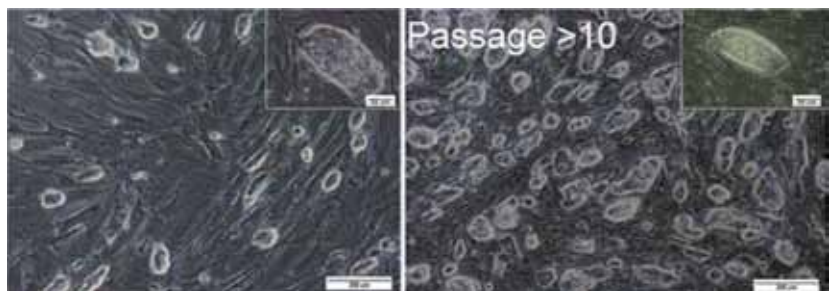
- **Shahverdi**, Abdolhossein, PhD

### Research Assistant:

- **Moraveji**, Faezeh, MSc

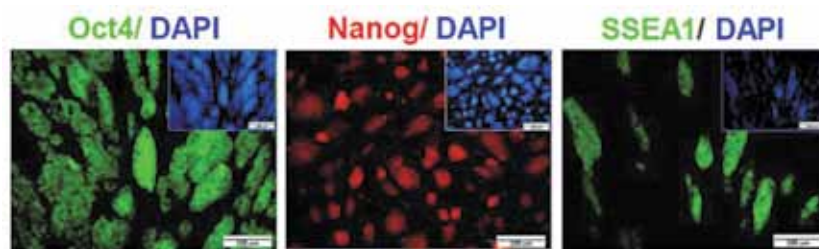
### Students:

- **Attari**, Farnoosh, PhD
- **Esfandiari**, Fereshteh, PhD
- **Mohamadi**, Alireza, PhD
- **Abolfathi**, Mohsen, MSc



Picture 1: After passaging, typical mESC-like colonies were observed at Day 14. These colonies could be passaged every 2–3 Days (passage 12)





Picture 2: The expression of mESC-specific markers and immunofluorescence staining for Oct4, Nanog and SSEA1 in the gPSC lines established by small molecule after at least 20 passages

#### Publications

Moraveji S F, Attari F, Shahverdi A, Sepehri H, Farrokhi A, Hassani S N, Fonoudi H, Aghdami N, Baharvand H. *Inhibition of Glycogen Synthase Kinase-3 Promotes Efficient Derivation of Pluripotent Stem Cells from Neonatal Mouse Testis*. Human Reproduction, 2012. [Epub ahead of print]

Bahadorani M, Hosseini SM, Abedi P, Hajian M, Hosseini SE, Vahdati A, Baharvand H, Nasr-Esfahani MH. *Short-term in-vitro culture of goat enriched spermatogonial stem cells using different serum concentrations*. J Assist Reprod Genet. 2012; 29(1): 39-46.

Tavakolifar F, Shahverdi A, Pirouz M, Shakeri M, Koruji M, Baharvand H. *Comparison of Neonatal- and Adult-derived Sertoli Cells in Support of Expansion of Mouse Spermatogonial Stem Cells in vitro*. International Journal of Fertility and Sterility. 2012, 5(4): 217-224

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**Chief Researcher:**  
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**Group Leader:**  
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**Biography**

Ebrahim Shahbazi obtained his BSc degree from the department of biology at Mohaghegh Ardebili university of Ardebil in 2004. He received his MSc in Developmental biology in 2008 joint program between Royan Institute and Science & Culture University. He began working at Royan institute from 2008 as a research assistant. His major research interest is biology of neural cells and neurogenesis.

**Neural Cells- Developmental Biology**

**Introduction**

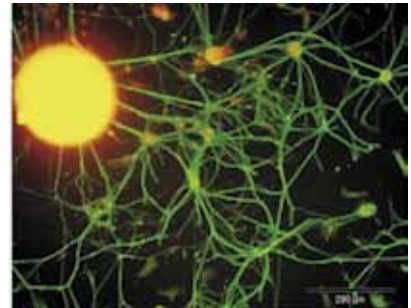
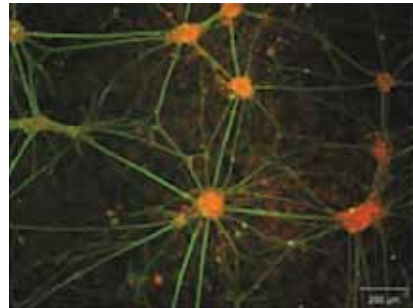
Neural development comprises the processes that generate, shape and reshape the nervous system, from the earliest stages of embryogenesis to the final years of life. This field of study draws on both neuroscience and developmental biology to provide insight into the cellular and molecular mechanisms by which complex nervous system has been developed. Defects in neural development can lead to cognitive, motor and intellectual disability, as well as neurological disorders. The major focus of our group is to develop new efficient protocols generating neural cell types from either Pluripotent or somatic cells (i.e. mouse/human fibroblasts). These approaches are based on programming, reprogramming and direct transdifferentiation. The availability of new functional self-renewing stem cells with more specific characteristics has provided new perspectives for the development of neuroregenerative therapies.

**Research Assistants:**

- **Nemati, Shiva, MSc**
- **Pouya, Alireza, MSc**
- **Khayatan, Fahimeh, MSc**
- **Ansari, Hassan, MSc**

**Students:**

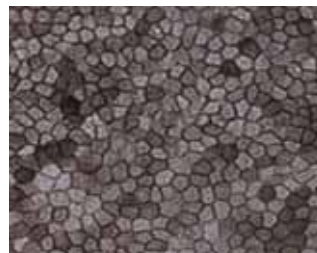
- **Fathi, Ali, PhD**
- **Jalili, Sasan, MSc**
- **Parvini, Maryam, PhD**
- **Safarpour, Atefeh, PhD**
- **Karamali, Fereshteh, PhD**
- **Mirakhori, Fahimeh, PhD**



Neural cells derived from human pluripotent stem cells



Neural progenitor cells in the present of small molecule CHIR



Retinal pigmented epithelial cells derived from human pluripotent stem cells

## Neural Cells-Traumatic Nerve Injury

### Introduction

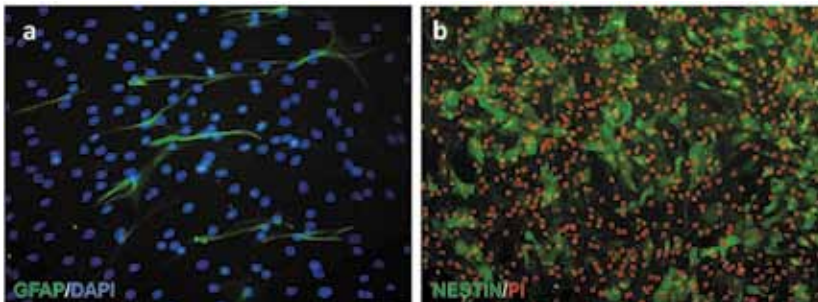
The possibility of isolation and culturing endogenous neural stem cells and producing neural progenitors from pluripotent stem cells promise new advantages in repairing neural injuries. The main goal of this program is to isolate endogenous neural stem cells and produce defined neural progenitors from embryonic and induced-pluripotent stem cells as well as their transplantation to animal models (rats and primates) of spinal cord injuries.

### Research Assistants:

- **Ghandipour**, Mahdiyeh, MSc
- **Arab**, Leila, MD

### Students:

- **Rostami**, Ali Akbar, MSc
- **Zafarani**, Fatemeh, PhD
- **Valizadeh**, Zahra, MSc
- **Alemzadeh**, Seyed Amirpoua, MD



Isolated neural stem cells from sub-ventricular zone (a) monkey, (b) rat.



### Group Leader: Sahar Kiani, PhD

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### Biography

Sahar Kiani received her BSc from the Department of Biology at Azad University in 2001. She continued her education in the Medical University of Mashhad. She joined the laboratory of Professor Boskabady at the Medical University of Mashhad and graduated with an MSc in Physiology in 2003. Then, she began her PhD at Tarbiat Modares University and Royan Institute, emphasizing the electrophysiology of human embryonic stem cells during neural differentiation, in the laboratory of Professor Baharvand at Royan Institute in 2006 and graduated in 2010. She currently works as a member of the academic staff at Royan Institute. Her major research interest has been motor neurons, particularly spinal cord injuries.



**Group Leader:**  
**Mohammad Javan, PhD**

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**Biography**

Mohammad Javan received his BSc from department of Biology, Mashhad University in 1994. He continued his studies in Shahid Beheshti University in Tehran and graduated with an MSc in Physiology in 1977. Then, he began his PhD at Shahid Beheshti University of Medical Science and graduated in 2003. He passed his post-doctoral studies in Kyorin University Medical School, Tokyo in molecular pharmacology. From 2005, he joined the department of Physiology in Tarbiat Modares University, Tehran. Currently, he is an associate professor in physiology department and holds a part time PI position in Royan Institute. His major research interest has been repair in neurodegenerative diseases, particularly multiple sclerosis, neural stem cells and oligodendrocyte precursors.

**Neural Cells-Neurodegenerative diseases**

**Introduction**

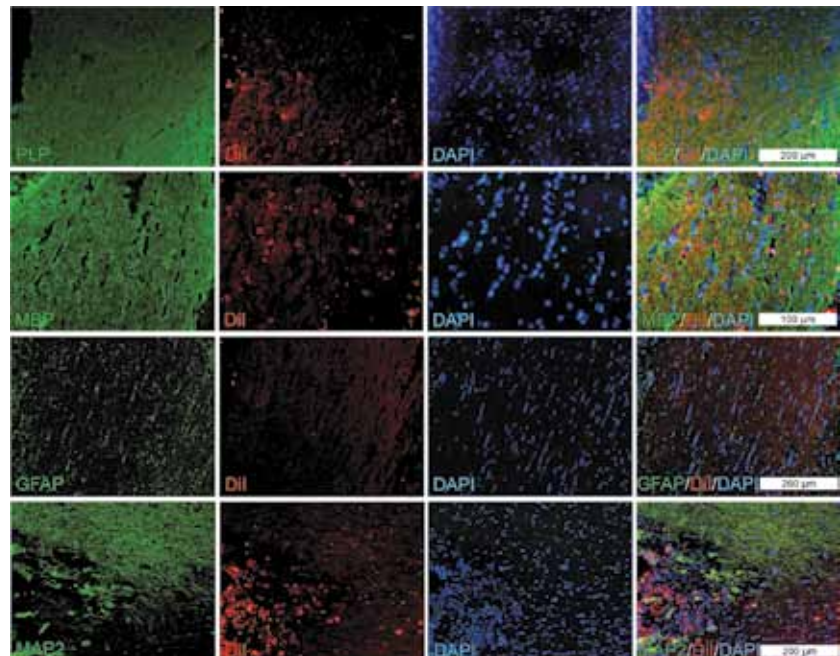
The major research interest of this program is to understand the cellular and molecular mechanisms underlying neurodegenerative diseases. We are interested in brain repair following neurodegenerative diseases, especially multiple sclerosis. In collaboration with Tarbiat Modares University Department of Physiology this program tries to enhance endogenous stem/progenitor cells mediated myelin repair using experimental model of multiple sclerosis and also optic nerve injury. We try to increase the repair by increasing endogenous stem cells migration using knocking down of some myelin inhibitory protein, growth factors and also magnetic fields. Since the limited number of endogenous stem cells is suggested as the main cause of myelin repair failure in the context of demyelinating diseases, in the recent years we have tried to use somatic cell-reprogramming strategies for partial reprogramming of neural stem/progenitor cells to increase the repair capacity within the brain. These attempts include application of reprogramming factors, miRNAs and epigenetic modifiers. Furthermore, we try to differentiate OPCs from different source of human stem cells, optimize the differentiation protocols and also assessing their remyelinating efficacy in different animal models.

**Research Assistant:**

- **Malvandi, Amir Mohammad, MSc**

**Students:**

- **Malakoutikhah, Mahboubeh, MSc**
- **Pachenari, Narges, MSc**
- **Bayat, Mahnaz, PhD**
- **Satarian, Leila, PhD**
- **Ghasemi, Maryam, PhD**
- **Hemati, Nima, MD**
- **Hashemi, Shokouh-Sadat, MD**



Immunofluorescence staining of transplanted cells. The hiPSC1-derived OPs were labeled with DiI before transplantation into chiasm and immunostained with antibodies against PLP, MBP, GFAP, or MAP2 eight weeks after transplantation. The majority of DiI-labeled cells showed PLP and/or MBP reactivity, and a few of them were GFAP+ and/or MAP2+. Pouya et al., 2011, PLOS One

**Publications (of all 3 neural cells research programs)**

Ghoochani A, Shabani K, Peymani M, Ghaedi K, Karamali F, Karbalaie K, Tanhaie S, Salamian A, Esmaeili A, Valian-Borujeni S, Hashemi M, Nasr-Esfahani MH, Baharvand H. *The influence of peroxisome proliferator-activated receptor  $\gamma$  (1) during differentiation of mouse embryonic stem cells to neural cells.* Differentiation. 2012;83(1):60-7

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**Group Leader:**  
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**Biography**

Mohamadreza Baghaban Eslaminejad has obtained PhD degree in anatomical sciences from Tarbiyat Modarress University in 2004. Since then he has worked in Royan Institute as an academic staff. At beginning he established a lab for adult stem cells at Royan Institute in order to start the investigation regarding mesenchymal stem cells (MSCs). The objective of the lab was to make MSCs applicable at human orthopedic diseases in particular as those related to bone and cartilage large lesions. To achieve these goals he had conducted multiple basic animal studies using mice, rabbit and even dog models. The results of such studies have been published in the form of approximately 150 full paper and abstracts in international and national journals as well as conferences. At present his researches achieve to clinical trial. In this context several clinical trials have been finished and many are ongoing. During the years of investigations, Dr Eslaminejad has been honored by several awards: 1- Winner of the 7th Royan International Research award on reproductive biomedicine and stem cells, 2006; 2- Distinguished investigator of Tehran province in year 2007; 3- Selected researcher in 14th Razi Research Festival on Medical Sciences Award, 2008; 4- Iranian Excellent Researcher in 10th Festival of Appreciation of Selective Researchers and Technologists, 1388, Tehran; 5- The editorial board member of two international journals.

## Bone and Cartilage/Mesenchymal Stem Cells

### Introduction

The lab for MSCs/ bone and cartilage is active on the following topics:

- Basic biology of MSCs
- Extraction of MSCs from multiple tissue sources including adipose tissue, dental sources, blood and etc and comparing them with the aim of achieving to a reliable source for MSCs
- Bone and cartilage engineering using MSCs
- Experimental studies regarding bone and cartilage regeneration using animal models
- Clinical trials regarding the application of MSC in cell-based treatment of bone and cartilage hard-to-cure lesions.

### Research Assistants:

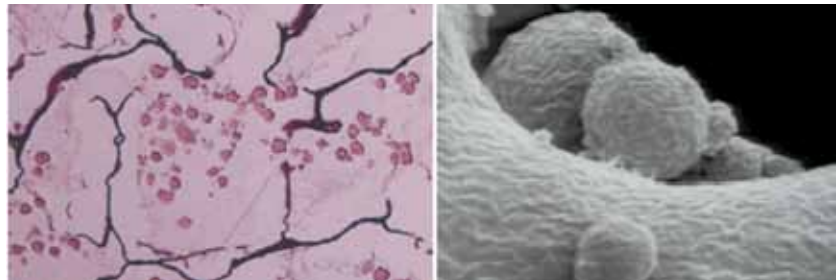
- **Bagheri**, Fatemeh, MSc
- **Bordbar**, Sima, MSc
- **Taghiar**, Lila, MSc
- **Jahangir**, Shahrbanoo, MSc
- **Fani**, Nesa, MSc
- **Zomorrodian**, Elham, MSc

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- **Safari**, Fatemeh, MSc
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- **Zaare**, Mohammad Ali, PhD
- **Faghihi**, Faaeze, PhD
- **Ghasemzade**, Mohammad, PhD
- **Karimi**, Tahereh, PhD



MSCs loaded onto porous scaffold

### Publications

Farrokhi A, Eslaminejad MB, Nazarian H, Moradmam A, Samadian A, Akhlaghi A. *Appropriate Reference Gene Selection for Real-time PCR Data Normalization during Rat Mesenchymal Stem Cell Differentiation*. Cell. Mol. Biol. 2012; 58(Supp): 1660-1670.

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Khojasteh A, BaghabanEslaminejad M, Nazarian H, Morad G, Dashti SG, Behnia H, Stevens M. *Vertical bone augmentation with simultaneous implant placement using particulate mineralized bone and mesenchymal stem cells: a preliminary study in rabbit*. J Oral Implantol. 2011.



## Cardiomyocytes and Endothelial Cells

### Introduction

In cardiovascular group our main goal is investigating mechanisms which lead to efficient production of cardiovascular cells from different sources such as embryonic and adult stem cells. Enhancing current protocols or finding new methods for differentiation toward cardiovascular cells with modern technologies like small molecules, protein transduction, gene delivery and nano-technology are among the activities that are ongoing in this group. For example, protein transduction of ISL1, GATA4 and NKX2.5 is used to improve the efficiency of cardiac differentiation from embryonic stem cells. The application of desired proteins instead of their genes increases the safety of these methods and paves the way for further application of them.

The other activities of this group are differentiation of cardiac stem cells derived from adult hearts by growth factors and tissue engineering of this organ. In one of our ongoing projects, a pericardium-scaffold is used to enhance the cardiomyocytes differentiation efficiency of cardiac stem cells derived from patients with defects in heart valves.

In recent years, studies with the aim of reprogramming and trans-differentiation of dermal and heart fibroblasts into cardiac cells have been considered in our group. In these studies we have tried to produce safe cells in addition to increasing the efficiency. So, small molecules and protein transduction is used in this methods as an alternative of gene delivery in trans-differentiation of fibroblasts into cardiomyocytes. The consequences of these studies are to understand the mechanisms of heart regeneration and testing these mechanisms on animal models to enhance the regeneration after heart diseases such as infarction.

There are similar plans for differentiation to smooth muscle cells and endothelial cells. The aim of the projects of this part are increasing the differentiation efficiency of embryonic stem cells into smooth muscle cells and testing endothelial cells derived from induced pluripotent stem cells on animal model of Scleroderma. Now, with the availability of methods for differentiation of vascular cells from induced pluripotent stem cells we are trying to produce and analyze these cells from patients with Scleroderma.

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- **Rajabi**, Sareh, PhD

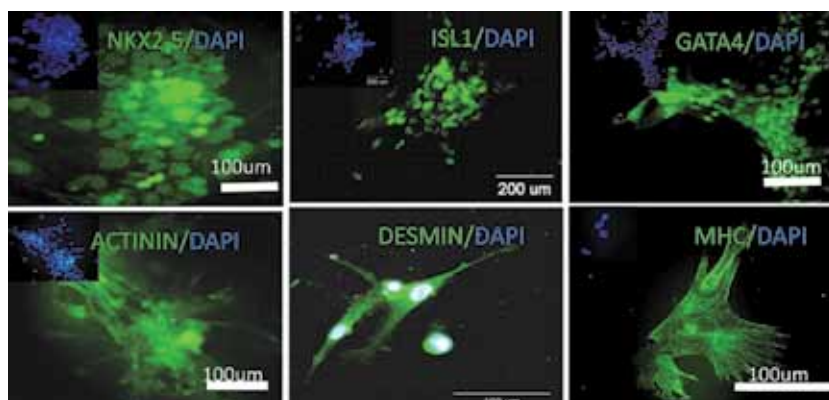


### Group Leader: Nasser Aghdami, MD, PhD

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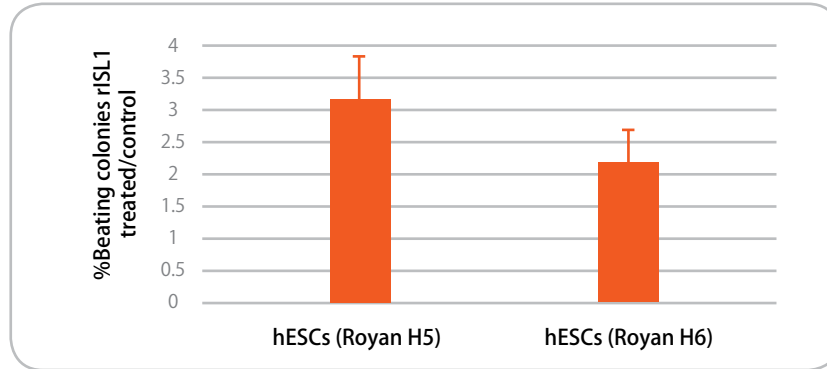
### Biography

Nasser Aghdami received his MD from Urmia University of Medical Sciences in 1998 and his PhD in Immunology from Tarbiat Modarres University in 2007. From 2006-2008 he was the Head of the Transplantation Laboratory at Royan institute. Since 2008 he is the Head of the Department of Regenerative Medicine and also Royan Cell Therapy Center.



Immunofluorescence staining of cardiomyocytes differentiated cells from human embryonic stem cells showed the expressions of NKX2.5, GATA4, ISL1, ACTININ, DESMIN, and MHC which are the markers of cardiac cells.





ISL1 protein transduction resulted in a  $3.2 \pm 0.5$  fold increase in the number of beating colonies. ISL1 also caused a  $2.2 \pm 0.4$  fold increase in the other hESC line (Royan H6;  $P < 0.05$ ).

#### Publications

Ahmadian Kia N, Bahrami AR, Ebrahimi M, Matin MM, Neshati Z, Almohaddesin MR, Aghdami N, Bidkhorri HR. *Comparative analysis of chemokine receptor's expression in mesenchymal stem cells derived from human bone marrow and adipose tissue*. J Mol Neurosci. 2011; 44(3): 178-85.

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## Skin Cells

### Introduction

Ability of skin cells in healing skin diseases and their use in beauty category has led skin cells group to try to develop suitable methods on proliferation and different cell types culture in skin tissue such as fibroblast, keratinocyte, melanocyte and hair stem cells.

Our aim is to apply these cells in vitiligo, burn, wrinkle, acne scar, epidermolysis bullosa and alopecia patients' treatment.

At this stage we purify and characterize these cells. Followed by above mentioned activities, related patients are being cured. Nowadays we are using epidermal and fibroblast cells for vitiligo and wrinkle in therapeutic phase. So in future we can treat numerous patients when we finish these projects:

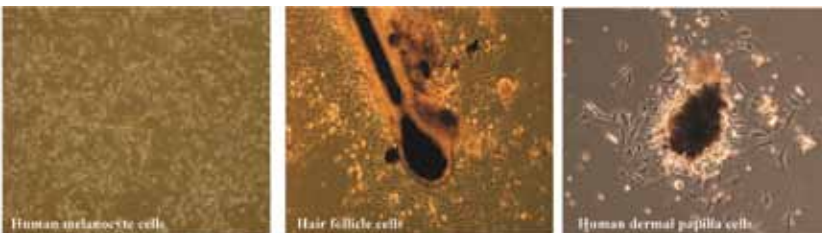
- Hair induction by transplantation of human follicular stem cells, dermal papilla cells or their combination with or without laser pretreatment in Nude Balb/c mice
- Evaluation of the attachment and proliferation of fibroblasts and keratinocytes on fibrin based scaffolds for skin tissue engineering
- Comparison between effects of fat injection and adipose derived stem cells in deep burn wound healing on mice
- Effect of fibroblast cultured in fibrin glue on bone devoid of periosteum as a supporting tissue on survival of skin graft in rabbit
- Investigate the effect of mesenchymal stem cells derived from adipose tissue (ADSC-CM) on synthesis and degradation of hyaluronic acid in human dermal fibroblast

### Research Assistant:

- **Sajadian, Sahar**, MSc

### Students:

- **Taghiabadi, Ehsan**, MSc
- **Jalili, Sasan**, MSc
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Human melanocyte, hair and dermal papilla explants were expanded. Hair follicle explants give rise to epithelial outgrowths. The dermal papilla cells grew out like a sun flower.



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### Biography

Parvaneh Mohammadi studied for a BSc in animal biology at Shahid Chamran University, Ahwaz, Iran from 2002 to 2006. She received her MSc in developmental biology at the joint program between Royan institute and the University of Science and Culture in 2009. She began working at Royan institute as a research assistant. In 2010 she began a PhD position in developmental biology in a joint program between Royan institute and the University of Science and Culture. Her major research interest is the biology of epithelial stem cells.

### Group Leader: Nasser Aghdami, MD, PhD

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## Regenerative Medicine

### Introduction

Although recent advances in medical sciences have made patients' survival increase in some cases, but still there are diseases which remained uncured. Progressive tissue diseases such as heart diseases, neurological diseases and bone and cartilage disorders are some examples of uncured diseases. In this type of disorders, an organ loses some parts of its performance because of various causes. Unfortunately, despite considerable researches on these diseases, there is not yet suitable treatment. Currently patient with such diseases have limited options for treating, and regenerative medicine is one of the best choices. Regenerative medicine is replacing lost tissue with new functional tissue. In this method, medical doctors use drugs to stimulate the body's repair mechanisms, cells especially stem cells to compensate for lost tissue and tissue engineering for producing tissue in the laboratory and transplantation into the damaged tissue. In regenerative medicine group, the main goal is clinical studies in various stages of the following diseases:

- Dermal diseases
- Cardiovascular diseases
- Orthopedic diseases
- Neurological diseases
- Ophthalmic diseases
- Gastrointestinal diseases
- Purogenital diseases

The other goal of this group is establishing cell banks for storing cells required for clinical applications in future. These banks include:

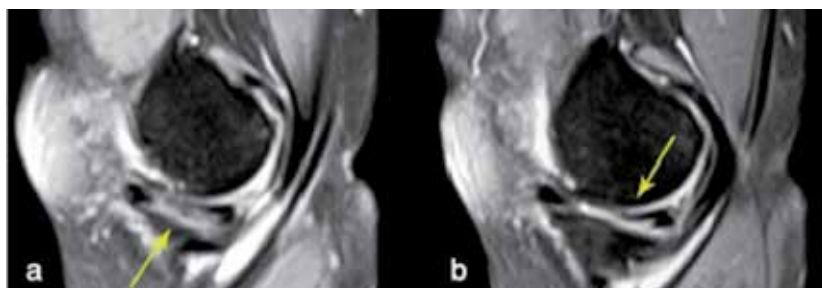
- Public cord blood bank
- Peripheral blood cells bank
- Fibroblast cells bank
- Mesenchymal cell bank

### Research Assistant

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- **Naffisi**, Shahriar, MD
- **Orouji**, Zahra, MD
- **Rafiee**, Baradaran, MD (Ophthalmologist)
- **Rezvani**, Mohammad, MD (Dermatologist)
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- **Vosough**, Ahmad, MD (Radiologist)
- **Zaali**, Alireza, MD
- **Zafarghandi**, Mohammad, MD (Vascular Surgery)



Establishing national standards, providing quality control procedures for manufacturing products in single units or in use and improving laboratory services according to general manufacturing practice (GMP), general clinical practice (GCP) and general laboratory practice (GLP) rules are the other activities of this group.



MR image at sagittal plane of the same patient depicted in b. shows increased signal intensity due to subchondral edema before stem cell injection. B. 6 months after stem cell injection demonstrating disappearance of signal changes. Arrows head shows a slight increase in cartilage thickness.

#### Publications

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**Group Leader:**  
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**PhD**

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**Biography**

Dr Salekdeh's research work focuses on proteome and molecular systems biology. He is a council member of the Asia Oceania Human Proteome Organization (AOHUPO) and member of HUPO educational committee. He is the Director of the Human Y Chromosome Proteome Project (an official project of HUPO) and Chair of AOHUPO Embryonic Stem Cell (ESC) Membrane Proteome Initiative (AOHUPO ESC-MPI). On a national level, Dr Salekdeh is a co-founder of the Iranian Proteomics Society and President of this society since 2004. He is also the Head of the Molecular Systems Biology Department at Royan Institute. He is on a number of editorial boards, including the Proteomics Journal. He has received several awards and honors including, the National Biotechnology Award (2007), National Razi Medical Science Award for Advanced Technologies (2009), the Khwarizmi International Award for Fundamental Research (2010) and Hadavi award from the Iranian Academy of Medical Sciences (2010). He has published more than 60 papers in international journals including Nature Biotechnology, Nature Protocols, Trends in Plant Science, Journal of Hepatology, Molecular Cellular Proteomics, Stem Cells, and Journal of Proteome Research.

## Molecular Systems Biology

### Introduction

Cellular functions are controlled by different complex and inter-related mechanisms. Characterization of these mechanisms can lead to a better understanding of the cellular regulatory processes. "Molecular systems biology" program is integrating high-throughput "-omics" technologies such as genomics, epigenomics, transcriptomics and proteomics as well as bioinformatics in an interactive and collaborative environment to use the acquired knowledge in order to understand and control cellular behavior.

The main project includes the following items:

- To discover the mechanisms which regulate the differentiation of human embryonic stem cells (hESCs) by employing transcriptomics, epigenomics and proteomics approaches.
- Exploiting recombinant protein technology to increase the efficiency of human embryonic stem cell differentiation.
- Asia Oceania Human Proteome Organization (AOHUPO) project entitled AOHUPO human Embryonic Stem Cells Membrane Proteome Initiative (AOHUPO hESC-MPI) chaired by Royan Institute. This project aims to analyze hESC membrane proteome in several laboratories across Asia Oceania to identify novel plasma membrane proteins in hESC and its differentiated cells. This is a multi-laboratories project involving laboratories in Australia, China, Singapore, Taiwan, South Korea, Japan, and Iran (Royan Institute). Each lab employs its best technology for analyzing hESC-MPI samples to provide a more inclusive and comprehensive portrait of hESC proteome particularly membrane proteome.
- Human Y chromosome proteome project. This ongoing project seeks to identify the function of all proteins encoded by chromosome Y and any potential connection with various disorders like infertility. This project is under Human Proteome Project (HPP) leading by Human Proteome Organization (HUPO). Currently, more than 20 countries are exploring 19 human chromosomes throughout human proteome projects (HPP).

### Research Assistants:

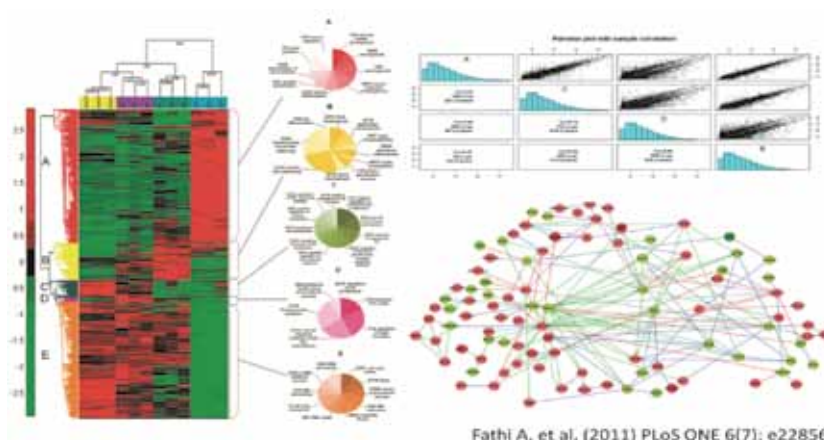
- **Alikahni**, Mehdi, MSc
- **Mousavi**, Seyyed Ahmad, BSc
- **Rasouli**, Hasan, MSc
- **Sharifi**, Mehdi, MSc
- **Tale Ahmad**, Sarah, MSc
- **Vakilian**, Haghighat, MSc
- **Shekari**, Faeze, MSc
- **Fathi**, Ali, MSc

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- **Habibi Rezaii**, Lida, MSc

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- **Fathi**, Ali, PhD
- **Jangravi**, Zohreh, PhD
- **Nasrabadi**, Davood, PhD
- **Arefnejad**, Babak, PhD
- **Rastgar**, Diba, MSc



Hierarchical and functional clustering as well as and regulatory networks of differentially expressed genes in neural differentiation of human embryonic stem cells

### Publications

Legrain P, Aebersold R, Archakov A, Bairoch A, Bala K, Beretta L, Bergeron J, Borchers CH, Corthals GL, Costello CE, Deutsch EW, Domon B, Hancock W, He F, Hochstrasser D, Marko-Varga G, Salekdeh GH, Sechi S, Snyder M, Srivastava S, Uhlén M, Wu CH, Yamamoto T, Paik YK, Omenn GS. *The human proteome project: current state and future direction*. Mol Cell Proteomics. 2011; 10(7): M111.

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ZamaniFaradonbeh M, Gharechahi J, Mollamohammadi S, Pakzad M, Taei A, Rassouli H, Baharvand H, Hosseini Salekdeh G. *An orthogonal comparison of the proteome of human embryonic stem cells with human induced pluripotent stem cells of different genetic background*. Mol. Biosyst. 2012, 8: 1833-1840.

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Paik YK, Omenn GS, Uhlén M, Hanash S, Marko-Varga G, Aebersold R, Bairoch A, Yamamoto T, Legrain P, Lee HJ, Na K, Jeong SK, He F, Binz PA, Nishimura T, Keown P, Baker MS, Yoo JS, Garin J, Archakov A, Bergeron J, Salekdeh GH, Hancock WS. *Standard guidelines for the chromosome-centric human proteome project*. J Proteome Res. 2012 Apr 6; 11(4): 2005-13.



**Group Leader:**  
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**Biography**

Marzieh Ebrahimi received her BSc in Cell and Molecular Biology from the Department of Biology at Tehran University in 1996. To pursue the underlying sciences in more depth, she obtained a Master degree and PhD in Immunology from the Medical Faculty at Tarbiat Modarres University in 2000 and 2007, with a focus on tumor therapy by proteins derived from garlic and activation of DCs derived from cord blood stem cells using tumor lysate. Since July 2009- July 2010, she worked in the Oncology Surgery, ZLF, Unihospitale of Basel, Switzerland as a guest researcher. In Jun 2009, she received an award from the Iranian Presidential Office, Center for Women and Family Affairs as a Woman Elite.

Dr Ebrahimi began research in field of stem cells in the Department of Stem Cells at Royan Institute in 2003 as a researcher and in 2007, she got an assistant professor. Currently, she is the leader of the Hematopoietic and Cancer Stem Cells Group, the Royan Public Cord Blood Bank programs, and Head of the Cytometry Laboratory.

**Cancer and Hematopoietic Stem Cells**

**Introduction**

Hematopoietic stem cells (HSCs) are responsible for the constant renewal of blood and immune cells. Since more than 50 years ago, these cells have been developed to treat many diseases. Research in this area is an integrated research discipline that seeks to understand how different cells emerge from a stem cell source, which developmental pathway promotes HSCs differentiation, how the micro environment affects efficiency of cell function and other questions in the field of basic research. Also, many questions must be addressed in patients who receive HSCs for treatment in different disease areas. With this intent, the Hematopoietic Stem Cells Group began its activity in 2005. The main goal in this group is the high throughput expansion of HSCs using bioreactors, evaluation of cord blood mesenchymal cells (UC-M.SCs) effects on HSCs expansion efficacy, differentiation of HSCs into insulin secreting cells and the production of functional blood cells from different sources of stem cells, such as embryonic stem cells.

In 2009, research on cancer stem cells was added to the previous activities of our group, therefore our group name changed to the Hematopoietic and Cancer Stem Cells Group. The main focus of cancer stem cell research is on isolation and characterization of cancer stem cells from different types of solid cancers including, prostate, gastric, breast and melanoma cancers from patient tissue or cell lines. In addition, we are attempting to find and target the pathways activated in metastatic cells by using micro-RNAs and regulation of methylation or acetylation of epithelial mesenchymal transition (EMT) regulators.

**Research Scientist:**

- **Abroun, Saeed, PhD**

**Research Assistants:**

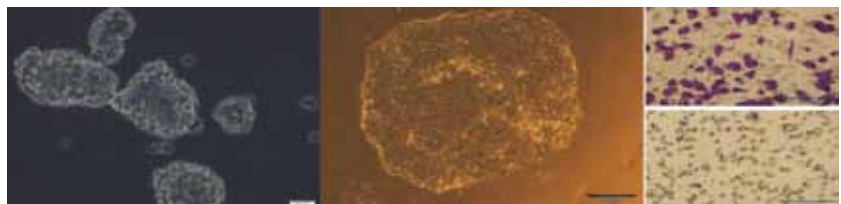
- **Baghsheikhi, Amir Hossein, BSc**
- **Khoshchereh, Reyhaneh, MSc**
- **Ganji, Fatemeh, MSc**

**Technical Staff:**

- **Firouzi, Javad, BSc**

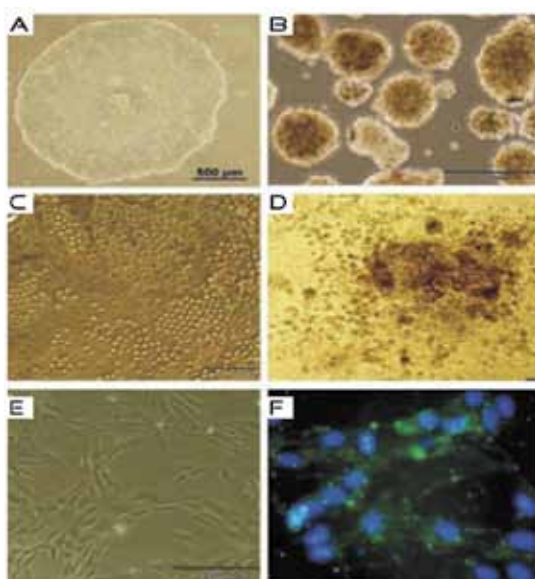
**Students:**

- **Rajabi, Motahareh, MSc**
- **Shokraee, Fatameh, MSc**
- **Mohammadi, Maryam, MSc**
- **Mehdipour, Maryam, MSc**
- **Abdollahi, Pegah, MSc**
- **Haji Moradi, Bitra, PhD**
- **Roudi, Raheleh, PhD**
- **Sabet, Nasrollah, PhD**
- **Nouri, Masoumeh, PhD**



1. Prostosphere formation in prostate cancer stem cells 2.Colonies formed by prostate cancer stem cells 3.Invaded (Up) and no Invaded (Down) cells of prostate cancer cells





A) Embryonic stem cell culture on Matrigel B) Suspension culture of Embryonic stem cell C) Differentiation of blast colonies on thin layer of Matrigel D) Blast colonies-derived CFU-Mixed in methylcellulose base media E) Blast colonies-derived endothelial cells F) Immuno-micrograph illustrating expression of CD31 markers on endothelial cells. Nuclei stained with DAPI.

### Publications

N. Shayan, M.Ebrahimi, B.Beiki, E. Janzamin, *Use of Non-rotational Computer Controlled Suspension Bioreactor for Expansion of Non-purified Cord Blood Mononuclear Cells (CB-MNC)*, *Biotechnology letter*, 2012,

Azarpira N., Amini M., Kojuori J., Ebrahimi M., Karimian Z., Saadat I, Bagheri lankarani J, *Assesment of scientific thinking in basic science in the Iranian second national Olympiad*, *BMC* 2012 5:61

Ahmadian Kia N, Bahrami AR, Ebrahimi M, Matin MM, Neshati Z, Almohaddesin MR, Aghdami N, Bidkhori HR. *Comparative analysis of chemokine receptor's expression in mesenchymal stem cells derived from human bone marrow and adipose tissue*. *J Mol Neurosci*. 201; 44(3): 178-85.

Zahabi A, Shahbazi E, Ahmadideh H, Hasani N, Totonchi M, Taei A, Masoudi N, Ebrahimi M, Aghdami N, Seifinejad A, Mehrnejad F, Daftarian N, Salekdeh GH, Baharvand H. *A new efficient protocol for directed differentiation of retinal pigmented epithelial cells from normal and retinal disease induced pluripotent stem cells*. *Stem Cells Dev*. 2011 Dec 6. Epub ahead of print.

Khoshchehreh R, Ebrahimi M, Baghban EslamiNejad M, Aghdami N, Baharvand H, *In-vitro Potential of Human Bone Marrow and Umbilical Cord Vein Mesenchymal Stem Cells to Differentiate into Insulin Producing Cells*, *Iranian Journal of Endocrinology and Metabolism*. 2011; 13: 384-397





## Public Cord Blood Bank

### Introduction

Cord blood hematopoietic stem cells (HSCs) as well as bone marrow stem cells are responsible for the constant renewal of blood and immune cells. Since the first cord blood transplant performed in 1988 by Elian Gluckman, cord blood transplantation has been increasingly used as a new source of HSC, and many countries established cord blood banks. At that time, most attempts focused on differentiation of HSCs into other cells to develop new therapy in diseases that need stem cells. However, since 1988, cord blood stem cells are well known, but many questions remain to be addressed such as which kind of stem cells in cord blood or bone marrow help to reconstruct immunity and blood cells, which developmental pathway promotes HSCs expansion and differentiation, and numerous other questions. Royan Public Cord Blood Bank was established in 2007. The main goal of this bank is the storage of high quality cord blood units, development of new methods for cryopreservation and thawing cells, improving quality control experiments to select the best units for transplantation and the development of new criteria for donors.

Selecting healthy donors, shipping cord blood units, processing the units using red blood cell depletion and decreasing volume and cryopreservation of cord blood samples are performed in the Public Cord Blood Bank. We have cryopreserved about 4350 units that include  $>8 \times 10^8$  cells which have successfully passed microbial testing, viral testing and the numbers of CD34+ cells as well as their colony forming potential before long term storage.

Royan Public Cord Blood Bank technicians are experts in freezing all types of stem samples such as bone marrow, peripheral blood, mesenchymal cells from different sources as well as fibroblasts and keratinocytes which come to our lab.

HLA typing of units gives us valuable genetic information about our Iranian nation.

Recently, our Research and Development Group began work on developing our techniques, standardizing our methods and producing products from cord blood serum. We are happy that we can assist other researchers who work in the field of cord blood stem cells by providing cells for them.

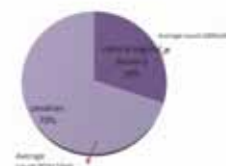
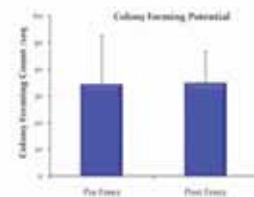
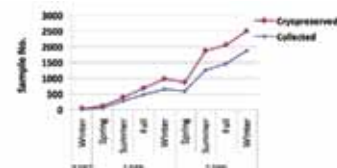
**In the beginning of 2012, we were registered as BMDW (Bone Marrow Donors Worldwide) to share all HLA data to patients and specialist.**

### Technical Staffs:

- **Hosseini**, Seyyed Mahdi, BSc
- **Mir Morsali**, Lida, BSc
- **Mohammad**, Monireh, BSc
- **Momeni**, Maryam, MSc
- **Shayan**, Niloufar, MSc
- **Shirzad**, Negin, MSc
- **Karimi**, Negar, MSc
- **Soltan Alizadeh**, Fatemeh, BSc
- **Molaie**, Maryam, BSc
- **Hassani**, Elham, BSc

### Group Leader: Marzieh Ebrahimi, PhD

mebrahimi@royaninstitute.org



# ANNUAL REPORT

## Core facilities of RI-SCBT

### Royan Stem Cell Bank (RSCB)

#### Introduction

Today, the Biology of Stem Cells as a growing scientific field, has afforded the possibility for scientists to work and research extensively in fields such as Developmental Biology, Drug industry, Toxicology, Disease Modeling and Cell Therapy. According to the growing demands of scientific research for stem cell lines including embryonic Stem Cells, Adult Stem Cells, Induced Pluripotent Stem Cells and Embryonic Carcinoma Cells, Royan Institute decided to invest on and establish a Human and other Mammalian Stem Cell Bank. Because of being well-founded of required equipment and having enough experience, Royan Institute, in parallel with other qualified research centers of the world, is proud to offer the results of one decade research in the form of production and maintenance of more than 300 stem cell lines with different origins listed below:

- Adult Human Stem Cells
- Human Embryonic Stem Cells (hESCs)
- Mouse Embryonic Stem Cells (mESCs) including different strains like C57BL/6, BALB/c, NMRI, NIH/Swiss, FVB/N, DBA/2, and SW.
- Human Induced Pluripotent Stem Cells with normal karyotypes and different disease phenotypes including Bombay Blood Group, Familial Hypercholesterolemia, Glycogen Storage, Type I Tyrosinemia, Hereditary Cholestasis, Retinitis Pigmentosa, Leber's Congenital Amaurosis, Usher Syndrome, Age Related Macular Degeneration, Leber's Hereditary Optic Neuropathy, Cligler Najjar Syndrome.
- Mouse Induced Pluripotent Stem Cells (NMRI Strain)
- Human Carcinoma Stem Cells

RSCB Data base software contains accurate information about its cell lines like type of the cell, its origin, its passage number, number of cryopreserved vials of a specific cell line, the exact place of the vial in the liquid and vapor-phase nitrogen storage tanks and its freeze and thaw dates.

Stem Cell lines available in RSCB are checked regularly for stem cell characteristics and lack of bacterial, fungal and Mycoplasma contamination with accurate techniques.

For cell line authentication and identification, STR (Short Tandem Repeat) Profiling will be done in the near future for discrimination of different cell lines.

For simulation of the current operating procedures in the Bank in order to prevent the unwanted changes done by different persons, SOP (Standard Operating Procedures) have been codified which explain accurately current methods for maintenance and deposition of the cells. These SOPs are available in Royan Stem Cell Bank web site.

According to these data, RSCB is ready to provide written contract in order to collaborate closely with research and therapeutic societies for providing high quality and authenticated stem cell lines with respect to financial and moral rights.

#### Technical Staffs:

- **Pakzad**, Mohammad, MSc
- **Haghparast**, Newsha, MSc



#### Laboratory Head: Hossein Baharvand, PhD

baharvand@royaninstitute.org



**Laboratory Head:**  
**Ali Fathi**

a.fathi@royaninstitute.org

## Molecular Biology Lab

### Introduction

The pivotal differences among different cell types, such as neurons, hepatocytes, osteocytes and blood cells are not due to the differences in DNA sequence of the genome but are linked to the differential expression of tissue-specific genes during development. The Molecular Biology Core facility was established to help the researchers of RI-SCBT obtain molecular data (DNA and RNA level) for their cellular experiments. In our molecular biology laboratory PCR and quantitative real-time PCR routinely applied in stem cell research. This technique enables investigators to evaluate low-abundance mRNAs, often obtained from their scarce cell cultures and tissue samples.

### Activities and Services:

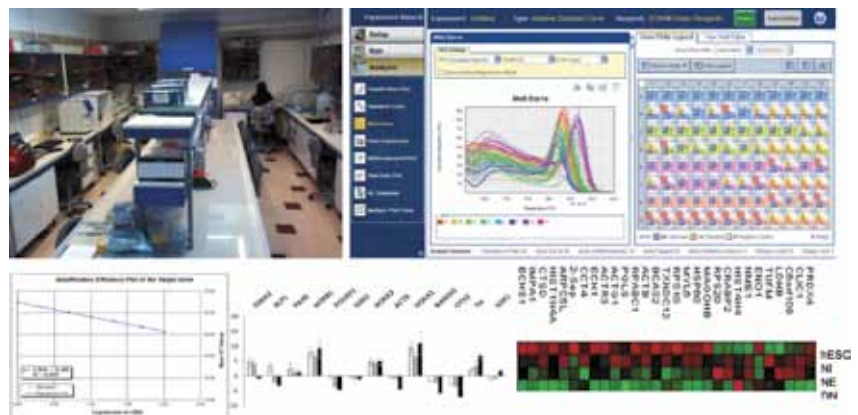
- Primer designing and banking
- RNA extraction from cultured cells or tissues samples
- Checking RNA purity and quantity
- cDNA synthesis (reverse transcription)
- PCR (polymerase chain reaction)
- Gel electrophoresis
- RT-PCR analysis
- Real-time PCR (ABI 7500 Applied Biosystem and Rotor Gene 6000 Corbett systems are available)
- Real-time PCR data analysis
- Gene isolation and cloning

We are collaborating in more than 40 research projects and our aim is providing high quality data for research and practice.

Working in the MB lab needs permission from principal investigators in the RI-SCBT and researchers or students should pass the qualities of working with molecular samples according our guidelines in addition of GLP.

### Technical Staffs:

- **Samadian**, Azam, BSc
- **Sayyhpour**, Forough Azam, BSc





## Electrophysiology Lab

### Introduction

The Electrophysiology Laboratory performs experiments pertaining to the functional analyses of differentiated cells. In this lab we can record inward ionic currents and action potentials of these cells with patch clamp recording. Additionally, we perform extracellular recording from the brain and spinal cord. Microelectrode array is a new setup in our lab that enables us to record extracellular events in cultured cells.

### Technical Staff:

- Hashemizadeh, Shiva, MSc



### Laboratory Head: Sahar Kiani, PhD

sahar\_kiani@royaninstitute.org



**Laboratory Head:  
Marzieh Ebrahimi, PhD**

mebrahimi@royaninstitute.org

## Cytometry and Imaging Lab

### Introduction

This lab, established in 2007, is equipped with a FACSCalibur. Flow cytometry, typically using fluorescent probes which bind to specific cell-associated molecules, allows for measurements of various phenotypic, biochemical and molecular characteristics of individual cells (or particles) suspended in a fluid stream. Since the latter part of 2010, we began to sort different types of stem cells using BD FACS Aria II.

The key aims of our facility are analyzing, sorting and imaging of numerous samples and cells needed by researchers. Moreover, we hold flowcytometry workshop yearly to train users for obtaining the best possible flowcytometry data for their experiments. Our cytometry facility is available for use by outside groups on a special basis.

### Technical Staffs:

- **Janzamin, Ehsan, BSc**
- **Khosravani, Pardis, MSc**
- **Sahraneshin Samani, Fazel, MSc**

### Flowcytometry

Our mission is to provide state of the art multicolor flow cytometry services to the research staff at RI-SCBT. Our educational program provides didactic lectures and hands-on experience with isolation, preparation and staining of all types of human and animal cells, instrument setup and acquisition, and data analysis.



A Becton-Dickinson FACSCalibur is available to provide analytic capability. The FACSCalibur has a five parameter analysis capability – forward and side scatter and three colors of fluorescence using 488 excitations. The instrument currently uses a MAC G5 computer for instrument control and data acquisition. The software running the FACSCalibur is Cell Quest.

BD FACS Aria Cell Sorter I improvements in fluidics and optics have allowed for higher speed sorting (25,000 events/sec at 70psi using a 70um nozzle) with enhanced overall sensitivity

### Imaging



IX71 inverted microscope      BX51 microscope

Immuno stained cells or tissues can be observed as well as precise, high quality photographs taken by the BX51 and IX71 microscopes located in the imaging room.





## Histology Lab

### Introduction

This lab was established to provide histology services and support investigators associated with RI-SCBT. The mission of the Histology Core is to provide the necessary training and/or services that will enable investigators to study their research samples.

The Histology Core provides full service histology, training and equipment use for frozen tissues and tissues embedded in paraffin or resin and a variety of counterstaining procedures. Cell and tissue processing for transmission and scanning electron microscopy and ultra-thin sectioning for transmission electron microscopy are also available. Specialized histological procedures are available as well for unique samples such as in vitro cultured cells, tissues, embryos and engineered tissues.

The Core is managed and operated by a full-time histotechnologist with more than five years of experience in this field. The Core Director oversees all operations and assists in the interpretation and evaluation of histological specimens.

### Services Available:

- Setting up and optimizing of histological approaches for scientific project
- Training on any aspect of histology
- Tissue processing for LM, IHC, IF, SEM and TEM
- Decalcification of bone and teeth specimens
- Sectioning for LM, IHC,IF, and TEM
- Routine and special staining for LM and TEM

Users of the Histology Core can choose to submit full service jobs and allow Core personnel to proceed the samples, or they can sign up to use the equipments themselves. Training on any aspect of the histological process is available on request. After training, users have free access to the equipments in the Core facility. It also assists in the setting up and optimizing of histological approaches specific for each scientific project, delivering protocols that can be tested either by the researchers themselves, the laboratory technicians or both.

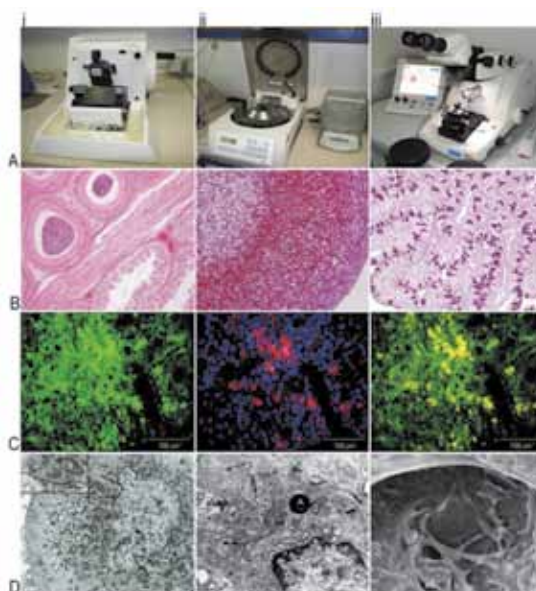
### Technical Staffs:

- **Ajdari, Zahra**, BSc
- **Najar-Asl, Mostafa**, BSc



**Laboratory Head:**  
**Abbas Piryaee, PhD**

[piryae\\_a@royaninstitute.org](mailto:piryae_a@royaninstitute.org)



A, Several lab equipments: (i) microtome, (ii) TEM sample preparation equipment, (iii) ultra-microtome. B, photomicrograph of sections of (i) mouse testis and epididymis (H&E staining), (ii) cartilage cells differentiated from mesenchymal stem cells using micromass culture method (Safranin-O staining), (iii) mouse intestinal villi (PAS staining). C, immunofluorescent staining of the liver frozen sections, (i) Albumin expression (green), (ii) nucleuses (blue) and transplanted cells (red), (iii) merge of the ii and iii which the Albumin secreting transplanted cells are shown with yellow. D, transmission electron micrographs of (i) mesenchymal stem cells of bone marrow, (ii) cardiomyocytes derived from human embryonic stem cells, (iii) scanning electron micrograph of the fibroblast cells cultured on 3-D scaffold.



**Laboratory Head:  
Ali Farrokhi**

alifarrokhi@royaninstitute.org

**Gene Targeting Lab**

**Introduction**

Royan Transgenic Core Facility provides all appropriate procedures and technology for production of transgenic, knockout and knock-in mice. This Core offers the following services to Royan Institute as well as researchers from external institutions:

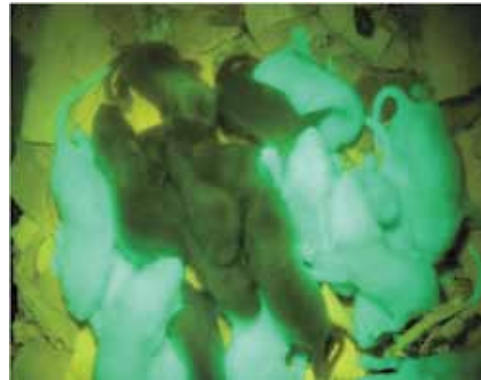
- Pronuclear microinjection for production of standard transgenic mice
- ES blastocyst injection which involves injections of gene targeted mouse embryonic stem cells into blastocysts for the production of knockout and knock-in mice
- Preparation of pre-implantation mouse embryos
- Aggregation Chimeras: Combining ES Cells, Diploid, and Tetraploid Embryos
- Embryo cryopreservation
- Consultation services for the design of transgenes, animal husbandry and genotypic analysis of transgenic animals.

**Technical Staffs:**

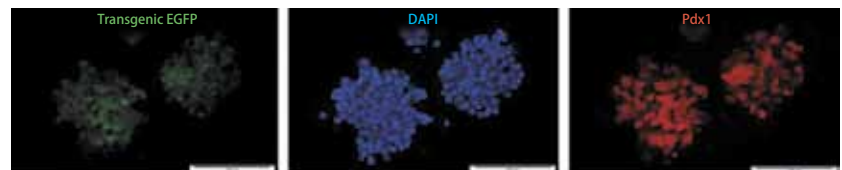
- **Asgari**, Behrouz, BSc
- **Sahraie**, Saiedeh, MSc
- **Tavakolrad**, Poya, BSc



Injection of ESCs into blastocyst and production of chimera followed by germ line transmission to next generation



pCAG-EGFP IRES PuroR transgenic mice



Islets of Langerhans isolated from "Pdx1-EGFP" transgenic mice



## Viral Transduction Lab

### Introduction

RNA viruses, one of the diverse groups of virus, can infect a broad spectrum of cells from prokaryotic to eukaryotic. Among them, the Retroviridae family is more applicable in molecular biology studies. Retroviruses that replicate in the host cell by the reverse transcriptase enzyme are one of the interesting viruses used in molecular biology. These viruses can incorporate into the host genome after the production of DNA from its RNA genome, by an integrase enzyme. The retroviral genome consists of 3 ORFs, including gag, pol and env genes. The core and structural proteins of the virus are encoded by the gag sequence; the enzymes required for its life cycle including RT, protease and integrase are encoded by the pol sequence; and coat proteins are encoded by the env gene. Regulatory sequences of the retrovirus genome consist of two long terminal repeats (LTRs) on both sides of the coding sequence. 5'LTR, which acts as a promoter and transcription start site and 3'LTR which is involved in posttranscriptional processing (i.e., polyadenylation). The packaging signal placed just after the 5'LTR is responsible for packaging all sequences as a retrovirus genome. Lentiviruses are other members of the Retroviridae family with complex a genome that could infect both dividing and non-dividing cells. By replacing viral genes with our gene of interest and placing a transgene juxtaposed to the packaging signal on one vector, and engineering viral coding genes on the other vectors, it is possible to produce recombinant viruses carrying the gene of interest that capable of transduction into any target cell.

We began our work by first establishing human iPS cells in 2008. Currently, we have the capability to produce iPS cells from any cell type.

Other works currently ongoing in the Viral Transduction lab include:

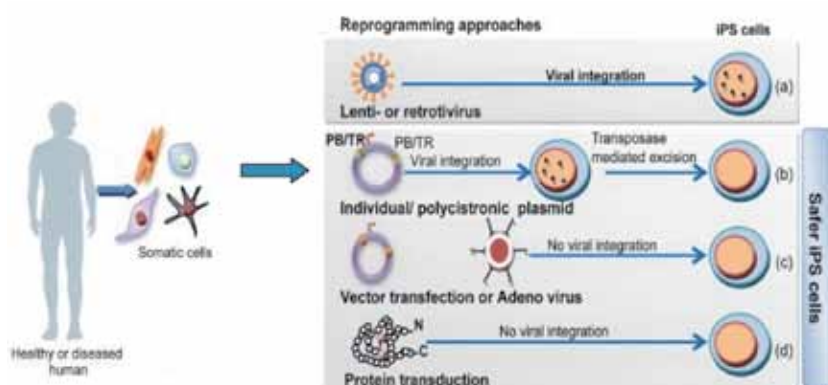
- RNAi trials for gene silencing and functional analysis studies,
- Over-expression and ectopic expression of genes for functional analysis
- PPI studies
- Establishment of Vector Bank
- Generation of Safe iPS cells using miRNAs and minicircles
- Viral transduction training

### Technical Staffs:

- **Hajikaram**, Maryam, MSc
- **Hesaraki**, Mahdi, MSc

### Laboratory Head: Mehdi Totonchi

[m.totonchi@royaninstitute.org](mailto:m.totonchi@royaninstitute.org)



Generation of human induced pluripotent stem cells  
(Asgari Set.al, Induced pluripotent stem cells: a new era for hepatology, 2010, J Hepatol, Oct;53(4):738-51)

**Laboratory Head:**  
**Hossein Baharvand, PhD**

baharvand@royaninstitute.org

**Nano/Tissue Engineering Lab**

**Introduction**

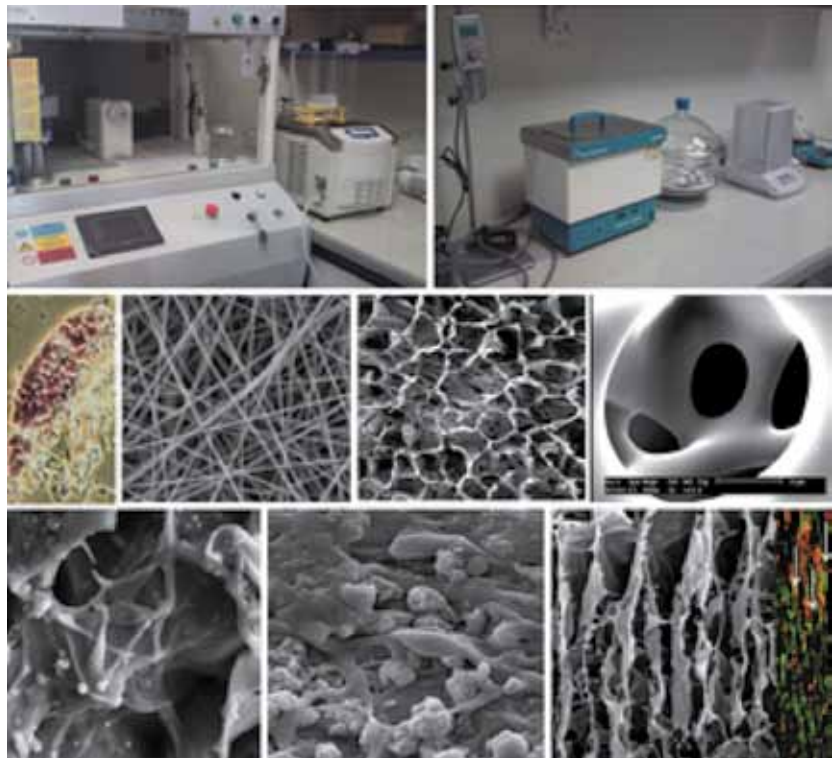
Stem cells are the most promising cell sources for therapeutic purposes. Clinical and pharmaceutical application of stem cells highly requires achieving a predictable and reproducible behavior of these cells in vitro and in vivo. For this aim, a well-defined and fully characterized microenvironment that mimics stem cells niche is inevitable. Biomaterial technology when combined with emerging stem cell technology provides a promising strategy for tissue engineering. New technologies, such as nanotechnology and also new fabrication techniques help biomaterial and biomedical scientists in designing new scaffolds to direct stem cells fate. For this approach, collaborative efforts between cell biologists and tissue engineers are essential.

The core consists of bioengineers and biologists with tight collaboration in following programs:

- Designing and bioactive modification of nanostructures
- Fabrication of electrical conductive substrates for neural and cardiac tissue engineering
- Growth factor delivery from hydro gels for promoting angiogenesis
- Hybrid scaffolds for skin tissue engineering.

**Technical Staffs:**

- **Khayyatan**, Fahimeh, MSc
- **Kazemi Ashtiani**, Mohammad, BSc
- **Jalili**, Sasan, BSc





### “Stem Cells for All” Lab

#### Introduction

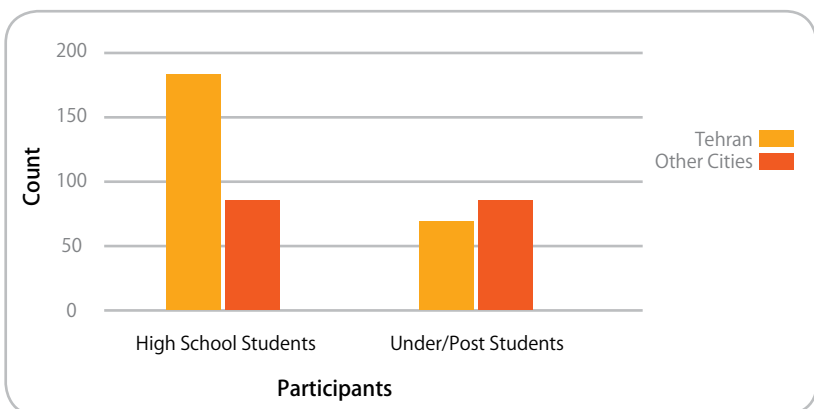
In order to expand knowledge of stem cells and creating the appropriate infra structure for the future, Royan Institute has established and equipped an educational lab for high school students, teachers and under/ post graduate students. Our prospective has been familiarizing of Biology teachers and elite students with basic knowledge and practical aspects of stem cell science and technology which leads to quality promotion of education, increasing students' trends to continue their academic training in this fields and develop targeted students and researchers for future. Since establishment (January 2012) till now, as it has been shown below, approximately 300 high school students and 150 under/post graduate students have been trained in this laboratory.

#### Lecturers:

- **Tavakolifar**, Faranak, MSc
- **Khaki Najafabadi**, Irandokt, MSc

**Laboratory Head:**  
**Hossein Baharvand, PhD**

[baharvand@royaninstitute.org](mailto:baharvand@royaninstitute.org)



Graph of Participant's number, which shows that 186 high school students from Tehran, 90 high school students from other cities of Iran (Esfahan, Fars, Alborz, Varamin ), 68 under/post graduate students from Tehran, and 84 under/post graduate students other cities of Iran (like Gilan, Azarbaiejan, Esfahan, Alborz) have been trained in this laboratory.



# ANNUAL REPORT

Royan Institute for Animal Biotechnology (RI-AB)



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**Department Head:**  
**Mohammad Hossein Nasr-Esfahani, PhD**

■ Embryologist

[mh.nasr-esfahani@royaninstitute.org](mailto:mh.nasr-esfahani@royaninstitute.org)

**Biography**

Dr Nasr-Esfahani graduated in the field of Embryology from the University of Cambridge, UK in 1991. He started his career as a clinical embryologist at Born Hall Assisted Reproductive Center in Cambridge, where the first in vitro fertilization (IVF) child was born, and has been active since then as a clinical embryologist. In 1992 he began his academic career in Iran and became actively involved in Royan Institute research projects. He established the Royan Institute for Biotechnology in 2004 in Isfahan. Since then this group has achieved outstanding results under his supervision. Dr Nasr-Esfahani has supervised over 167 projects and has 130 national and 88 international publications. He is also the author of three books, several chapter books, the editors of IJFS, and a member of several editorial boards for different journals.

**Message from the Department Director**

Recent advances in the past decade have shortened the gap between basic science and its applications. This phenomenon is at its utmost in the field of biotechnology. In Royan Institute for Animal Biotechnology, we hope to participate in this endeavor, and through this improve the standards of life for the mankind and help those in needs. Therefore, we believe this vision can only come true through interactive scientific communication between experienced researcher and the young researcher. Therefore, we hope by encouraged interactivity and opportunity for scientific discussion between student and the scientist, in addition to expanding our research facilities, to broaden our boundaries of science and make science applicable for those in need.

**Department History and Introduction**

In 1983, Dr Kazemi Ashtiani, the founder of the Royan Institute, established Royan institute of Animal Biotechnology, as the third branch of Royan Research Institute. At present, this branch has 100 research faculties and students working in 5 departments to expand the knowledge of science in their areas. The intensive seminar schedule in each department has encouraged interactivity and opportunity for scientific discussion between students and scientists, with the intent to facilitate the progress of science in their fields. In 2010, through this interactive and integrative science, we have achieved a number of important goals: the establishment of zona-free somatic cell nuclear transfer (SCNT) in goats, the effect of epigenetic modifier on the outcome of SCNT and vitrified embryos, the introducing of a novel approach for the selection of intact sperm for ICSI based on sperm functional characteristics, developed an understanding of the role of embryonic structure in neurogenesis based, assessed the role of PEP, (peroxisomal protein) and PPAR  $\gamma$  in neurogenesis for the first time, and finally understanding the role of biotechnology in the production of biological products.

**The Projects of Animal Biotechnology:**

- Embryology
- Andrology
- Stem Cells
- Genetic
- Recombinant Protein

**Office Staffs:**

- **Khodaei**, Seyyed Hamed, MSc
- **Mansouri**, Samaneh, MSc
- **Fouladgar**, Maryam, BSc
- **Motiei**, Mehmoosh, BSc
- **Shokouhi**, Mostafa, BSc
- **Jafari**, Ahmad
- **Heydari**, Homayoun
- **Khajeh**, Ali Asghar
- **Dadgostar**, Ahmad Reza
- **Shakeri**, Maryam
- **Shokouhi**, Farshad
- **Salehi**, Hamid
- **Nikbakht**, Javad
- **Yazdekhesti**, Hamid

# ANNUAL REPORT

## Projects of RI-AB

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Annual Report

ROYAN Institute for Projects of RI-AB

## Embryology

### Introduction

The mechanisms of in vivo and in vitro embryo development are of paramount importance in the field of assisted reproductive technology, dairy farming, and biopharming. Although much effort has been put into the establishment of sequential media, further advances are required in order to overcome in vitro stress for embryo development. Thus a major goal of this group is the optimization of culture media. In the field of somatic cell nuclear transfer, despite great advances achieved in recent years, there is also a need to set-up species-specific protocols to achieve higher efficiency. This implies the need for focus on both the cellular and molecular bases of cellular reprogramming. The search for alternative method for the production of transgenic animals may provide a useful platform for further studies. Cryopreservation of reproductive elements (sperm, oocyte, and embryo) is one of the other programs scheduled in this department. Finally, there is a critical need to reconsider the efficiency of the current in vitro oocyte maturation protocols to access maximum oocyte capability.

### Main Goals Within This Research Area

- Establishment of different methods for somatic cell nuclear transfer or cloning
- Production of transgenic animals via cloning, sperm and germ cells
- Production of novel culture media for in vitro embryo development
- Cryopreservation of gametes, embryos, and reproductive tissues
- Increasing cloning efficiency by epigenetic modification
- The mission of this department is to achieve world-class applicative approaches in transgenesis in the hope of producing recombinant proteins

### Focused Areas of Department

- Somatic cell nuclear transfer
- Transgenesis
- Cryobiology
- Epigenetic reprogramming

### Research Assistants:

- **Ostad Hosseini**, Somayeh, DVM
- **Jafarpoor**, Farnoush, PhD
- **Hajian**, Mahdi, MSc
- **Sadeghi**, Nima, DVM
- **Asgari**, Vajihe, MSc
- **Forouzanfar**, Mohsen, PhD
- **Nasiri**, Zahra, MSc

### Lab Technicians:

- **Tanhaeivash**, Nima, BSc

### Student Trainees:

- **Fekri**, Saman, MSc
- **Abbasi**, Hasan, PhD
- **Sekhavati**, Mohammad Hadi, PhD
- **Jafari**, Shahram, PhD
- **Esmailzadeh**, Forouzan, PhD
- **Kiani**, Maryam, MSc
- **Bakhtari**, Azizollah, PhD
- **Bonakdar**, Elham, PhD
- **Gharibi**, Shahin, MSc
- **Hodaei**, Mehrdad, MSc
- **Rohollahi**, Shiva, MSc
- **Hosseinnia**, Pourya, PhD



**Chief Researcher:**  
**Sayed Mortaza Hosseini,**  
**DVM**

[smhosseini@royaninstitute.org](mailto:smhosseini@royaninstitute.org)

### Biography

Morteza S. Hosseini has been working on different aspects of in vitro embryo production since 2003. His doctorate investigated the effect of cumulus cells on developmental competence of in vitro matured sheep oocytes, focusing on cumulus cell-oocyte interactions. The team he is involved in is now a registered animal biotechnology research group known worldwide for their achievements in cloning domestic achievement and wild animal species, and the establishment of a herd of transgenic goats that produce human-tissue-plasminogen activator in their milk.



#### Previous Student Trainees:

- **Kargar**, Safieh, MSc
- **Bahadorani**, Mehrnoush, PhD
- **Gharibzadeh**, Zahra, MSc

#### Dairy Assist Center (DAC):

The Dairy Assist Center (DAC) is a newly designed center within the department of Reproduction and Development that provides R&D support for expanding the dairy industry throughout the country. Over the years with excellent experience in the field of mammalian in vitro embryo development, embryo transfer, and genetics, DAC has gained prominence as a front-ranking research center whose purpose is to create the first joint effort to offer a continuum of academic, technical and applied collaboration with local and national industrial dairy complexes.

#### Main Missions of DRC

- **Sperm Technologies:**  
Although expensive, many farmers are concerned or even dissatisfied with the results of some semen batches used for artificial insemination. They can now accurately be informed of the quality of purchased semen with the use of a dozen semen tests such as: morphology, motility, and integrity (DNA/plasmalemma/cytoplasm), etc. The semen's fertilization potential can also be checked by IVF experiments.
- **Ovary and Oocyte Technology:**  
Champion dairy cattle are frequently lost due to sudden death, critical fractures, or acute diseases. In these situations, there are only two biotechnological approaches to sustain the reproductive performances of these champions: a) obtaining immature oocytes to be used for either IVF or freezing and b) cryopreservation of ovarian tissue for future use.
- **Embryo Technologies:**  
In order to assist those dairy owners who desire to increase the numbers of their champion cattle, several technologies have been established to distribute superior genetic constitutes throughout the country. Some of these technologies include: multiple ovulation, artificial insemination, embryo flushing, embryo transfer, in vitro fertilization with sexed semen, sperm sexing, intracytoplasmic sperm injection, in vitro embryo culture, embryo sexing, embryo splitting, assisted zona drilling, embryo freezing and embryo banking.

#### Publications

*Application of in vitro production-embryo transfer in the protection and development of lactational potential of superior cows.* Pirestani A, Nasr Esfahani M.H, Hosseini S.M, Moulavi F, Hajian M, Forouzanfar M, Abedi P, Ostad-Hosseini S, Hosseini L. African Journal of Biotechnology. 2012; 11(5): 1287-92.

*Effects of different feeder layers on short-term culture of prepubertal bovine testicular germ cells in-vitro.* Nasiri Z, Hosseini SM, Hajian M, Abedi P, Bahadorani M, Baharvand H, Nasr-Esfahani MH. Theriogenology. 2012. (77):1519–28.

*Development of an optimized zona-free method of Somatic Cell Nuclear Transfer in the goat.* Nasr-Esfahani MH, Hosseini SM, Hajian M, Forouzanfar M, Ostad- Hosseini S, Abedi P, Khazaie Y, Dormiani K, Ghaedi K, Forouzanfar M, Gourabi H., Shahverdi AH, Vosough AD, Vojgani H. Cellular Reprogramming 2011; 13(00).

*Potential applications of sheep oocytes as affected by vitrification and in vitro aging.* Hosseini S.M, Asgari V, Ostad-Hosseini S, Hajian M, Piryaei A, Najarasl M, Nasr-Esfahani MH. Theriogenology. 2011; (in press).

*Comparative immunohistochemical analysis of VASA, PLZF and THY1 in goats and sheep suggests that these markers are also conserved in these species.* Bahadorani M, Hosseini SM, Abedi P, Hajian M, Afrough M, Azhdari- Tafti Z, Azizi H, Hosseini SE, Vahdati A, Baharvand H, Nasr-Esfahani MH. Cytology & Histology. 2011. 2. (6).

*Developmental Competence and Pluripotency Gene Expression of Cattle Cloned Embryos Derived from Donor Cells Treated with 5-aza-2'-deoxycytidine.* Jafarpour F, Hosseini SM, Hajian M, Forouzanfar M, Abedi P, Hosseini L, Ostadhosseini S, Gholami S, Nasr Esfahani MH, International Journal of Fertility and Sterility 2011; 4(4):148-155.

*Time dependent effect of post warming interval on microtubule organization, meiotic status, and parthenogenetic activation of vitrified in vitro matured sheep oocytes.* Asgari V, Hosseini S.M, Ostadhosseini S, Hajian M, Nasr-Esfahani M.H Theriogenology (75) 904–910.2011

*Effect of Ovarian Cyclic Status on In Vitro Embryo Production in Cattle.* Pirestani A, Hosseini S.M, Hajian M, Forouzanfar M, Moulavi F, Abedi P, Gourabi H, Shahverdi A, VosoughTaqiDizaj A, Esfahani M.H. International Journal of Fertility and Sterility. 2011 4(4): 172-175.

*Effect of culture condition and cell-permeable superoxide dismutase on levels of reactive oxygen species (ROS) production in "in vitro" produced sheep embryos.* Ostad-Hosseini S, Aghaee F, Hosseini S. M, Hajian M, Forouzanfar M, Noorbakhshnia M, Gourabi H, Shahverdi AH, Vosough-Taghidizaj A. Nasr-Esfahani M.H. Small Ruminant Research 2011



*Short-term in-vitro culture of goat enriched spermatogonial stem cells using different serum concentrations.* Bahadorani M, Hosseini S.M, Abedi P, Hajian M, Hosseini S.E, Vahdati A, Baharvand H, Nasr-Esfahani M.H. J Assist Reprod Genet 2011; (in press).

*Epigenetic modification does not determine the time of POU5F1 transcription activation in cloned bovine embryos.* Jafari S, Hosseini S. M, Hajian M, Forouzanfar M, Jafarpour F, Abedi P, Ostad- Hosseini S, Abbasi H, Gourabi H, Shahverdi A.H, Dizaj-Vosough A, Anjomshoaa M, Haron A,W, Nordin N, Yaakub H, Nasr-Esfahani M.H. J Assist Reprod Genet 2011. DOI 10.1007/s10815-011-9638-1.

*Somatic Cell Induced Hyperacetylation, but not Hypomethylation, Positively and Reversibly Affect the Efficiency of In Vitro Cloned Blastocyst Production in Cattle.* Jafarpour F, Hosseini S.M, Hajian M, Forouzanfar M, Ostadhosseini S, Abedi P, Ghaedi K, Gholami S, Gourabi H, Shahverdi A. H, Vosough Taghi Dizaj A, Nasr-Esfahani M.H. Cellular Reprogramming. 1-35. 2011

*Improved in vitro development of cloned bovine embryos using S- denosylhomocysteine, a non-toxic epigenetic modifying reagent.* Jafari SH, Hosseini SM, Hajian M, Fourouzanfar M, Jafarpour F, Abedi P, Ostadhosseini S, Abbasi H, Gourabi H, SHahverdi A. H, Vosough A, Anjomshoaa M, Haron W, Noorshariza N, Yakub H, Nasr-Esfahani MH. Molecular Reproduction & Development 2011.

*Effect of culture system on developmental competence, cryosurvival and DNA-fragmentation of in vitro bovine blastocysts.* Hajian M, Hosseini S.M, Asgari V, Ostad-Hosseini S, Forouzanfar M, Nasr-Esfahani M.H. International Journal of Fertility and Sterility 2011. 5 (1): 21-6.

*Effect of ovarian cyclic status on in vitro embryo production in cattle.* Pirestani A, Hosseini S. M, Hajian M, Forouzanfar M, Moulavi F, Abedi P, Gourabi H, Shahverdi A, Vosough Taqidizaj A, Nasr- Esfahani M. H. International Journal of Fertility and Sterility 2011, 4 (4): 172-5.





**Chief Researcher:  
Marziyeh Tavalaei**

tavalaei.m@royaninstitute.org

**Biography**

Marziyeh Tavalaei received her MSc degree in Physiological Science at Azad University, Damghan, Iran, in 2005 and has been an academic member of Royan Institute in Tehran, Iran (Isfahan Campus). Her research interest is male infertility, focusing particularly on sperm functional tests, novel and routine sperm selection procedures and the etiology of varicocele. She has been involved in numerous projects and has published 27 international papers, 15 national papers, and two books (1-Sperm: Identification and Selection of Sperm from the Molecular and Clinical Aspect in ICSI Candidates: 2-WHO Laboratory Manual for the examination and Processing of Human Semen).

## Andrology

### Introduction

This department focuses on male infertility; its main research interest is to improve the outcomes of male infertility treatment. This group has pioneered the establishment of novel sperm selection procedures for the treatment of ICSI, the results of which have been published in international journals. The main goal of this department is to optimize sperm selection for ICSI and to improve the healthy baby take-home rate of ICSI through understanding sperm functional characteristics and sperm biology.

Main goals within this research area:

- Establishment of a screening test for the assessment of sperm integrity
- Establishment of novel sperm selection procedures for ART

### Focused Areas of Department:

- Novel sperm selection procedure
- Sperm functional tests
- Sperm biology
- Etiology of varicocele
- Artificial oocyte activation
- Freezing human sperm
- Animal models for infertility

### Research Assistant:

- **Deemeh**, Mohammad Reza, MSc

### Lab Technicians:

- **Arbabian**, Maryam, BSc
- **Aazadi**, Leila, MSc

### Student Trainees:

- **Charehjooy**, Nasim, MSc
- **Javadian**, Soudabeh, MSc
- **Bateni**, Zahra, MSc
- **Zahedi**, Alieh, MSc
- **Atrian**, Afsoun, MSc
- **Bahreini**, Mahsa, MSc
- **Barekat**, Forough Sadat, MSc

### Previous Student Trainees:

- **Motiei**, Marjan, MSc
- **Basiri**, Farzaneh, MSc
- **Bahrani**, Soulmaz, MSc
- **Skandari**, Marzieh, MSc
- **Aghajani**, Samaneh, MSc
- **Shaygannia**, Erfaneh, MSc

### Publications

*There an association between HOST grades and sperm quality?* Bassiri F, Tavalaei M, Shiravi A.H, Mansouri S, Nasr-Esfahani M.H. Human Reproduction. 2012.

*Evaluation of HSPA2 in fertile and infertile individuals.* Motiei M, Tavalaei M, Rabiei F, Hajhosseini R, Nasr-Esfahani M.H. Andrologia 2012.

*A Proper Ubiquitination Effect on the Fertilization Outcome Post-ICSI.* Eskandari-Shahraki M, Tavalaei M, Deemeh MR, JelodarGh, Nasr-Esfahani M.H. Andrologia 2011 (in press).



*Origin and Role of DNA Damage in Varicocele.*Tavalaee M, Abasi H, Nasr-Esfahani M.H. International Journal of Fertility and Sterility. 2012.

*The role and effect of HSPA2 in male infertility.*Motiei M, Tavalaee M, Nasr-Esfahani M.H. Journal of Iranian Anatomical Sciences, Vol 9, No 37, Winter 2012 (Review)

*High total acrosin activity in varicocele individuals.*Navaeian-KalatE, DeemehM.R, TavalaeeM, AbasiH, ModaresiM&Nasr-Esfahani MH. Andrologia. 2012(in press)

*DHR123: an alternative probe for assessment of ROS in human Spermatozoa.*Kiani-Esfahani A, Tavalaee M, Deemeh M.R, Hamiditabar M andNasr-Esfahani M.H. Systems Biology in Reproductive Medicine. 2012(in press)

*Density gradient centrifugation before or after magnetic-activated cell sorting:which technique is more useful for clinical sperm selection?.*Tavalaee M,DeemehM.R,Arbajian M,Nasr-Esfahani MH. J Assist ReprodGenet.29(1):31-8. 2012

*Evaluation of ubiquitin and annexin V in sperm population selected based on density gradient centrifugation and zeta potential (DGC-Zeta).*Zarei M,ShayganniaE,TavalaeeM,DeemehM.R,ArabiM,Forouzanfar M,JavadiGh.R,Nasr-Esfahani MH. J Assist Reprod Genet.29:365–371. 2012

*Quantitative Expression of Phospholipase C Zeta, as an Index to Assess Fertilization Potential of a Semen Sample.* Aghajanpour S, Ghaedi K, Salamian A, Deemeh MR, Tavalaee M, Moshtaghian J, Parrington J, Nasr-Esfahani MH. Human Reproduction 2011. In press

*Decisive factors in medical tourism destination choice: A case study of Isfahan, Iran and fertility treatments.* Moghimehfar F, Nasr-EsfahaniMH.Tourism Management 2011

*Flow Cytometry: A Novel Approach for Indirect Assessment of Protamine Deficiency by CMA3 Staining, Taking into Account the Presence of M540 or Apoptotic Bodies.* Fathi Z, Tavalaee M, Kiani A, Deemeh MR, Modaresi M, Nasr Esfahani MH. International Journal of Fertility and Sterility 2011. In press

*Effects of human placental serum on proliferation and morphology of human adipose tissue-derived stem cells.* Shafaei H, Esmaeili A, Mardani M, Razavi S, Hashemibeni B, Nasr-Esfahani MH, Shiran MB, Esfandiari E. Bone Marrow Transplant.46(11):1464-71. 2011

*New era in sperm selection for ICSI.*Nasr-Esfahani M.H, Deemeh M.R, and TavalaeeM. International Journal of Andrology. 1–10. 2011

#### Book Publications

*Sperm: Identification and selection of sperm from Sperm the biological and clinical aspect in ICSI patients (2010)*, is written by Dr MH.Nasr-Esfahani and MarziyehTavalaee. ISBN: 978-964-8115-83-3.

*WHO laboratory manual for the Examination and processing of human semen*, Translated by Dr MH.Nasr-Esfahani and MarziyehTavalaee (ISBN: 978-600-6040-00-4).

An english book chapter (Collaborated) *“Mechanism of human oocyte activation during ICSI and methodology of overcoming low or failed fertilization”*

An english book chapter *“Sperm Selection for ICSI Using the Hyaluronic Acid Binding Assay”*



**Chief Researcher:  
Khadijeh Karbalaie**

karbalaie@royaninstitute.org

**Biography**

After graduation with a BSc in Zoology, she became interested in Cellular and Molecular Biology and obtained her MSc on this topic. She joined Royan Institute as Research Assistant in the Stem Cell Department and was actively involved in different projects. Presently she is a PhD student in Molecular Genetics (2010) in the Department of Biology at the Faculty of Science at Isfahan University.

## Stem Cell

### Introduction

The Stem Cell Department was established in 2005 to advance the research on stem cell biology. This group works on different types of stem cells including human and mouse embryonic stem cells, adult stem cells such as bone marrow mesenchymal stem cells and dental pulp mesenchymal stem cells, which was first established by this group in Iran. This group has an interest in differentiating these cells into neurons for possible future clinical application in neurodegenerative disorders such as Parkinson and Alzheimer's disease. In addition, this group has focused on tissue engineering using nanofiber technology for three-dimensional cell culture and cell transplantation as well as drug screening and toxicity assays using stem cells. The research in this department is mainly carried out under the supervision of Dr H. Baharvand.

### Research Assistant:

- **Karamali**, Fereshteh, MSc

### Lab Technicians:

- **Shoarayenejati**, Ali Reza, BSc
- **Nematollahi**, Marzieh, BSc
- **Ejeian**, Fatemeh, MSc

### Student Trainees:

- **Masaeli**, Elaheh, PhD
- **Rasekhian**, Parsa, PhD
- **Mirhosseini**, Seyyed Mohammad Mahdi, MD
- **Piri**, Mohammad Reza, MD
- **Pourveiseh**, Azadeh, MSc
- **Beigi**, Mohammad Hossein, MSc
- **Jahanmard**, Fatemeh, MSc
- **Dormiani**, Kianoush, PhD
- **Kashfi**, Shirin, PhD

### Previous Student Trainees:

- **Salehi**, Hossein, PhD
- **Niapour**, Ali, PhD
- **Taghipour**, Zahra, PhD

### Publications

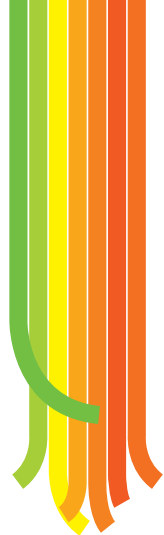
*Differentiation of human embryonic stem cell-derived retinal progenitors into retinal cells by Sonic hedgehog and/or retinal pigmented epithelium and transplantation into the subretinal space of sodium iodate-injected rabbits.* Amirpour N, Karamali F, Rabiee F, Rezaei L, Esfandiari E, Razavi S, Dehghani A, Razmjou H, Nasr-Esfahani MH, Baharvand H. Stem Cells Developments.21(1):42-53. 2012

*Differentiation of human ES cell-derived neural progenitors to neuronal cells with regional specific identity by co-culturing of notochord and somite.* Salehi H, KarbalaieKh, Salamian A, Kiani A, RazaviSh, Nasr-Esfahani M.H, Baharvand H. Stem Cell Research (8), 120–133. 2012

*Application of conductive polymers, scaffolds and electrical stimulation for nerve tissue engineering.* Ghasemi-Mobarakeh.L, Molamma P Prabhakaran, Morshed M, Nasr-Esfahani M.H, Baharvand M, Kiani S, Al-DeyabS. Journal Of Tissue Engineering and Regenerative Medicine 2011.

*Transplantation of Undifferentiated and Induced Human Exfoliated Deciduous Teeth-derived Stem Cells Promote Functional Recovery of Rat Spinal Cord Contusion Injury Model.* Taghipour Z, KarbalaieKh, KianiA, Niapour A, Bahramian H, Nasr-Esfahani M.H, BaharvandH. Stem Cells Development. 2011 (in press)

*Neuronal induction and regional identity by co-culture of adherent human embryonic stem cells with chicken notochords and somites.* Salehi H, Karbalaie KH, Razavi SH, Tanhaee S, Nematollahi M, Sagha M, Nasr-Esfahani MH and Baharvand H. The International Journal of Developmental Biology, 321-326. 2011



*Induced in vitro differentiation of neural-like cells from human exfoliated deciduous teeth-derived stem cells.* Nourbakhsh N, Soleimani M, Taghipour Z, Karbalaie KH, Mmousavi S, Talebi A, Nadalfi F, Tanhaei S, Kiyani GH-A, Nematollahi M, Rabeif, Mardani M, Bahramiyan H, TorabianejadM, Nasr-Esfahani MH and Baharvand H. The International Journal of Developmental Biology, 189-195. 2011

*Treatment of full thickness cartilage defects in human knees with Autologous Chondrocyte Transplantation.* NazemKh, Safdarian A, Fesharaki M, MoulaviF, MotifardM, Zarezadeh A, Shakibaei M, Esfandiari E, and Nasr-EsfahaniM.H. J Res Med Sci.16(7):855-61. 2011

*Bone Morphogenetic Protein-4 Influences Neural Differentiation of Induced Mouse Mesenchymal Stem Cells.* Rezaei M, KarbalaieKh, S Tanhaie, MadaniH, Nasr-EsfahaniM.H, BaharvandH. Cell Journal(Yakhteh), Vol 12, No 4, Pages: 511-516. 2011.

## Genetics

### Introduction

Understanding molecular mechanisms that are involved in cell differentiation is an interesting research area. In this department, researchers are engaged in locating genetic and molecular factors responsible for neurogenesis at the cellular level. The peroxisome biogenesis factors that are required for the maintenance and integrity of peroxisomes are tested to discover their possible roles for neural cell differentiation. This department is also interested in the role of genes and their related promoters in the neurogenesis process.

### The Main Goals of This Research Department:

- Assessment of peroxin gene expression in development and cell differentiation
- Assessment of recent peroxisomal protein (PEP) gene expression and function
- Implementation of RNAi technique to assess gene functions
- Analysis of promoters of genes responsible for cellular differentiation
- Analysis of protein interactions in cellular differentiation
- Molecular analysis of patients with peroxisomal disorders in our population

The mission of this department is to locate the molecular mechanisms of stem cell proliferation and neural differentiation steps with the purpose of restoring or replacing tissue that has been damaged by disease or injury.

### Research Assistants:

- **Salamian**, Ahmad, MSc
- **Ghochani**, Ali, MSc
- **Kiani**, Gholam Abbas, MSc
- **Peymani**, Maryam, MSc
- **Hashemi**, Motahharez Sadat, MSc

### Lab Technicians:

- **Izadi**, Tayyebeh, BSc
- **Rabiee**, Farzaneh, BSc

### Student Trainees:

- **Mohammadinezhad**, Parisa, PhD
- **Jodeyri**, Mohammad, MSc
- **Hosseini**, Samaneh, MSc
- **Mazaheri**, Neda, MSc
- **Ghazvinizadehgan**, Faezeh, MSc
- **Taheri**, Marjan, MSc
- **Forouzanfar**, Mahboubeh, MSc
- **Modarres**, Parastou, MSc

### Previous Student Trainees:

- **Hashemi**, Motahharez, MSc
- **Seifi**, Tahereh, MSc

### Publications

*The influence of peroxisome proliferator-activated receptor g1 during differentiation of mouse embryonic stem cells to neural cells.* Ghoochani A, ShabaniKh, Peymani M, Ghaedi K, Karamali F, KarbalaieKh, Tanhaie S, Salamian A, EsmaeiliA, Valian-Borujeni S, Hashemi M, Nasr-Esfahani M.H, Baharvand H. Differentiation. 2012; 60-67.

*The expression of peroxisomal protein transcripts increased by retinoic acid during neural differentiation.* Ostadsharif M, Ghaedi K, Nasr-Esfahani MH, Mojbafan M, Tanhaei S Karbalaie KH, Baharvand H. Differentiation. 2011; 127-132.



### Chief Researcher: Kamran Ghaedi, PhD

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### Biography

Dr Kamran Ghaedi graduated with a BSc in Biology from the University of Isfahan (1989), and an MSc in Clinical Biochemistry from Isfahan University of Medical Sciences (1993). He pursued his studies toward a PhD degree from Kyushu University (Fujiki's lab) in the field of Molecular Cell Genetics (1999). Fujiki's lab was recognized as one of the pioneer laboratories in the world working on peroxisome biogenesis. Dr Ghaedi was engaged in the isolation and characterization of several Chinese hamster ovary cells defects in peroxisome assembly and biogenesis. He cloned PEX3 and PEX7 genes and published several highly reputed papers in this regard. After receiving his PhD degree, Dr Ghaedi was hired as a post-doctoral researcher in the field of Molecular Biology by Japan Science and Technology (JST) at Kyushu University (Fujiki's lab) where he worked for two years. He conducted his studies in the same lab as a post-doctoral fellow (Japan Society for Promotion of Science) and as a senior post-doctoral researcher (JST) for four additional years. Dr Ghaedi returned home to Iran after 10 years of working in the field of peroxisome biogenesis in mammals. He then started his academic career as a faculty member in the Biology Department of the University of Isfahan, and his collaboration with Royan Institute for Animal Biotechnology. During his collaboration with Royan Institute, he has established a research group (Department of Cell and Molecular Biology) that is working on the involvement of genetic factors required for peroxisome biogenesis in neural differentiation of embryonic stem cells. In his collaboration with Dr Nasr-Esfahani, he has been involved in the production of recombinant proteins such as t-PA. He has also supervised several projects and has numerous international publications.





**Chief Researcher:**  
**Kianoush Dormiani, PhD**

dormiani@yahoo.com

#### Biography

Dr Dormiani received his doctorate in Pharmacy (Pharm.D) in 2000 from the faculty of Pharmacy and Pharmaceutical Sciences, at the Isfahan University of Medical Sciences. His interest in molecular biology and biotechnology lead him to become a member of the group involved in recombinant protein production. He has been involved in different projects in the production of recombinant proteins in different hosts, such as eukaryotic and bacterial cells and transgenic animals. He is also working on vector design and production for different applications such as genetic correction in cells isolated from patients with monogenic diseases in vitro.

## Recombinant Protein

### Introduction

Following the production of the first recombinant protein insulin in 1978, extensive research has been undertaken for the purpose of producing other recombinant proteins. Different strategies can be utilized for the production of recombinant proteins, which include proteins produced via bacteria, plants, cell culture, and milk production in transgenic animals. Although the production of recombinant proteins through the former methods might be the easiest and most straight forward procedures, research has shown that the production of recombinant proteins through the latter methods might be more functional due to post-translational modifications, which are very similar to the native protein. One of the main missions of this group is to master and establish efficient methods for producing recombinant proteins through cell culture and animal transgenesis.

### The Main Goals of This Department

- Construction of efficient vectors for producing recombinant proteins with therapeutic or laboratory applications
- Cloning appropriate genes
- Genetic manipulation of the genes for pharmaceutical purposes
- Increasing gene transfection efficiency through non-viral procedures
- Isolation and maintenance of the stable transformants of mammalian cells
- Homologous or site directed recombination of genes into a target genome

### Research Assistant:

- **Lachinani, Liyana, MSc**

### Lab Technician:

- **Forouzanfar, Mahboubeh, BSc**

### Student Trainees:

- **Pirjamali, Leila, MSc**
- **Abootalebi, Fatemeh, MSc**
- **Rezaei, Naeemeh, MSc**
- **Gavanji, Shahin, MSc**

### Previous Student Trainee:

- **Sanei, Nafiseh, MSc**

### Publications

*Creation of Tenectoplase-Producing CHO Cell Line Using Site-Specific Integrase from the Phage  $\phi$ C31.* Dormiani K, Khazaie Y, Forouzanfar M, Ghaedi K, Mofid MR, Karbalaie KH, Karamali F, P. Calos M, Nasr-Esfahani MH, Yakhteh Medical Journal 2010; 12(2): 207-214.

### News and Events

- Establishment of a molecular method for predication of failed fertilization post ICSI
- Establishment of a herd of transgenic animal
- Production of cows with high milk production through technique of IVF/ cryopreservation
- Production of recombinant protein, the TPA, from cell culture technology
- Establishment and full characterization of Dental Palp stem cell line
- Establishment of a diagnostic center for peroxisomal related disease



**Core Facilities:**

- Animal farm
- Viral Transduction
- Gene Targeting
- Flow Cytometry
- Molecular Biology
- Royan Plasmid Bank
- Cell Culture Lab
- Molecular and Genetic Lab

**Awards**

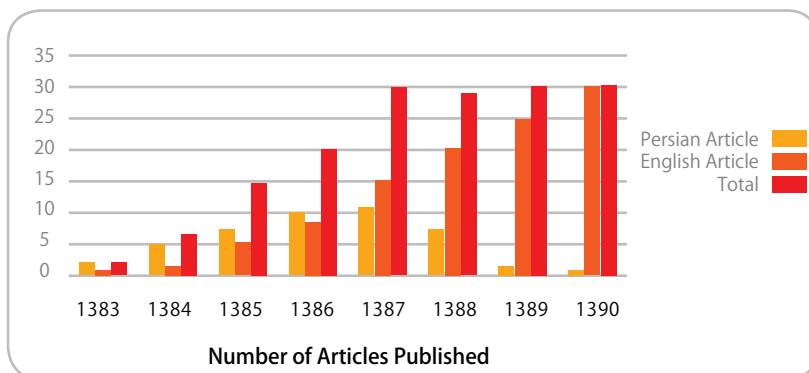
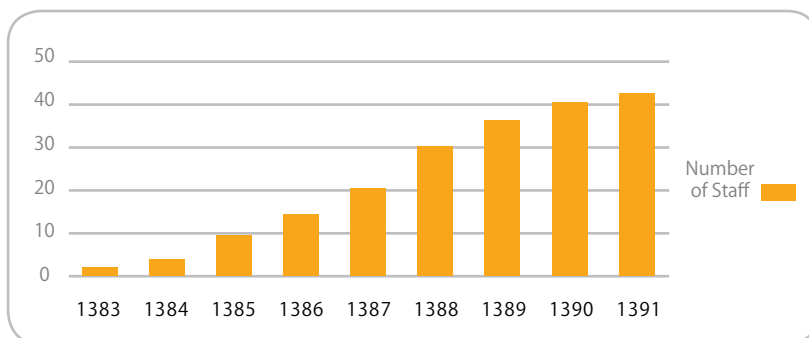
**Grants**

In addition to financial support from Royan Institute, RI-AB received research grants from (1) Stem Cells Development and Technology Council of Science and Technology Deputy of Iran Presidential, (2) Islamic Azad University Marvdasht, and (3) Islamic Azad University Khurasgan to do following projects:

- Construction of a minicircle carrying S/MAR elements and the NURR1 gene, Evaluation of this construct in NURR1 gene expression and dopaminergic neuron differentiation from mouse embryonic stem cells.
- A comparison of Menezos B2 and TCM-199 for in vitro production of bovine embryo on a Vero cell co-culture.
- Enhancement of the milk productivity potential of traditional and semi-developed dairy herds in Isfahan Province through in vitro embryo production and embryo transfer technology.

**Journal Clubs:**

No	Group	Time	Total Number
1	Embryology	Every Saturday	216
2	Genetics	Every Sunday	
3	Andrology	Every Monday	
4	Stem Cell	Every Tuesday	
5	Recombinant Protein	Every Wednesday	



# ANNUAL REPORT

## Laboratory Animal Core Facility



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### Core Facility Head: Mohammad Taghi Daneshzadeh, DVM

[t.daneshzadeh@royaninstitute.org](mailto:t.daneshzadeh@royaninstitute.org)

#### Biography

Educational Background: High School Diploma in Experimental Sciences from Dehkhoda High School, Karaj, Tehran, Iran, 1985

D.V.M from Shahid Chamran (Jondi Shapoor) University, Ahwaz, Iran, 2001

Work experiences:

Working in Laboratory Animal Science Department, Royan Institute, Tehran, Iran  
From: June 2005 to: Present

Working in field of Inbred Mice breeding, Department of Laboratory Animal Science, Pasteur Institute of Iran  
From: Oct. 2001 to: Oct. 2004

#### Introduction

The Laboratory Animal Science Core Facility of Royan Institute consists of the Laboratory Animal Facility, Research Farm and Primate Research Center.

This facility is a service unit that plays a national role in the education of those who work with experimental animals, by arranging courses in all categories within the animal research field.

**In the Laboratory Animal Facility,** Facilities exist for research on rodents (inbred and out-bred mice and rats), rabbits, sheep, goats, cattle, horses and non-human primates. The rodent colonies are housed and maintained under conditional and specified pathogen free (SPF) conditions. The unit provides services for all core facilities and researchers at Royan Institute.

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

- **Replacement:** Replace animal experiments where possible with alternatives
- **Reduction:** Reduce the number of experiments and number of animals in each experiment to an absolute minimum
- **Refinement:** Refine experiments such that 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.

Within this unit, scientists responsible for the design of animal experiments must have graduated from one of the biomedical science fields. Additionally, scientists in this unit must have taken a course on laboratory animal science which concentrates on the human and careful use of animals, and have included information on the alternatives and ethical aspects of animal experimentation.

The mission of the core facility is to discover and disseminate new knowledge about the biology and management of laboratory animals with the vision of expanding knowledge in laboratory animal sciences.

#### Common Goals of the Core Facility

- To provide qualitative care for all animals used at Royan Institute.
- Assist the researchers for researching by the use of laboratory animals.
- To provide researchers with a relevant education, enabling them to achieve scientific pre-eminence in selected areas as well as to produce and support laboratory animals required for research
- To manage the Animal Care and Use Program of the Institute
- To manage a preventive medicine program for disease control
- To advise the research staff on all aspects of the experimental use of animals, including experimental design, surgical, pre- and post-operative care, oocyte and embryo harvesting, and experimental animal modeling.

**Research Farm at Royan Institute,** began their activities on animals (especially sheep and goat) at the Jihad Research Complex in 2006. This center is equipped with laboratory and operating rooms for embryo transfer and other specific operations.

#### The Main Approaches and Accomplishments of This Center Are:

- Transgenic goats carrying human factor IX gene were produced by nuclear transfer in January 2010
- Birth of the first IVM-IVF goat in Iran
- Birth of the first IVM-IVF lamb in Iran

This center is also trying to enhance or improve its technology and equipment to meet the research needs of the Institute.



**Royan primate research center**, was established in 2006 in conjunction with Loghman Hospital. In 2010 a new primate research center was established in Jajroud. Within these centers there are individual and public maintenance rooms, a laboratory and an operation room. These centers are unique habitations for the study of human health and disease, which offer the opportunity to quarantine, keep, breed and assess the cause of disease and new treatment methods in nonhuman primate models that closely resemble humans.

**Specific Objectives:**

- Evaluate and apply modern animal husbandry techniques to ensure optimal care of rhesus monkeys involved in our breeding and research projects
- Maintain a healthy and productive nonhuman primate colony in order to facilitate psychological research at Royan Institute
- Develop animal models for incurable diseases that cannot be treated by routine medical procedures and require further research and advance treatment methods such as stem cell therapy for treating these models
- Provide unique facilities for researchers who are interested in working on nonhuman primates

**Research Assistants:**

- **Asghari**, Hasan, DVM
- **Hajinasrollah**, Mostafa, DVM
- **Kheimeh**, Abolfazl, BSc
- **Mostafaei**, Farhad, BSc
- **Nekookar**, Abdolhosein, DVM
- **Nemati**, Alireza, BSc

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Please refer to the full SPC text before prescribing this product. Adverse events should be reported.

Date of revision of Prescribing Information: January 2009

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