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
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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 13th 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)
It is my great pleasure that Royan 13th 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 13th 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 13th 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 Ashlani, 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.
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.
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
The Third Royan International Research Award | September 2002 | Received Papers: 212

International Winners:
- **First Place:** Marco Filicori, Italy
  Novel Approaches to Ovulation Induction: The Critical Role of Luteinizing Hormone Activity in Regulating Folliculogenesis

- **Second Place:** Klaus G. Steger, Canada
  Influence of Histone-Protmine-Exchange on Male Infertility

- **Third Place:** Franck Pellestor, France
  Chromosomal Investigations in Human Gametes: Study of the Interchromosomal Effect in Sperm of Chromosomal Rearrangement Carriers and Mechanisms of Non Disjunction in Oocytes

- **Fourth Place:** Ghazala S. Basir, Hong Kong
  The Effect of High Estradiol Levels on Endometrial Development in Assisted Reproduction Technology: Evaluation of Sonographic Doppler Haemodynamic and Morphometric Parameters

- **Fifth Place:** Mohamed Ali Bedaiwy, USA
  Transplantation of Intact Frozen-Thawed Mammalian Ovary with Vascular Anastomosis: A Novel Approach

Iranian Winners:
- **Saeed Alborzi**
  Laparoscopic Salpingooovolysis. Is There Any Place for Second Look Laparoscopy?

- **Saeed Rahbar**
  Laser Assisted Hatching in Young Women Significantly Increases Pregnancy and Implantation Rates

- **Shir Ahmad Sarani**
  Morphological Evidence for the Implantation Window in Human Luminal Endometrium
  Special Winner in Reproductive Health

- **V. I. Sodestrom-Anttila,** Finland
  Embryo Donation-Outcome & Attitude Among Embryo Donors & Recipient
The Fourth Royan International Research Award | September 2003 | Received Papers: 222

International Winners:

- **First Place:** Yong-Mahn Han, South Korea
  Abnormal Structural Integrity and Reprogramming in the Cloned Embryos

- **Second Place:** Lucille E. Voullaire, Australia
  Chromosome Abnormality In Human Embryos Diagnosed Using Comparative Genomic Hybridization: Its Relationship to Infertility

- **Third Place:** Mauro Maccarrone, Italy
  Low Fatty Acid Amide Hyrolase and Anandamide Levels Are Associated with Failure to Achieve an Ongoing Pregnancy after IVF and Embryo Transfer

- **Fourth Place:** Ali Honaramooz, USA
  Sperm from Neonatal Mammalian Testes Grafted in Mice

- **Fifth Place:** Jan M.R. Gerris, Belgium
  Elective Single Embryo Transfer Halves the Twinning Rate without Decrease in the Total Ongoing Pregnancy Rate of an AVF/ICSI Program

Iranian Winners:

- Mohammad Ebrahim Parsanezhad
  Ovarian Stromal Blood Flow Changes After Laparoscopic Ovarian Cauterization in Women with Polycystic Ovary Syndrome

- Mojdeh Salehnia
  Vitrification of Ovarian Tissue

- Jaleh Zolghadri
  Successful Pregnancy Outcome with IUI in Patients with Unexplained Recurrent Miscarriage, Whose Male Partners Have Low Score Hypo-Osmotic Swelling Test
International Winners:

- **Second Place: Alfonso Guiterrez-Adan, Spain**
  Long Term Effect of in vitro Culture of Mouse Embryos with Serum on mRNA Expression of Imprinting Genes, Development and Behavior

- **Second Place: Maciej K. Kurpisz, Poland**
  Reactive Oxygen Species and “Male Factor” of Infertility

- **Third Place: Michel von Wolf, Germany**
  Glucose Transporter Proteins (GLUT) in Human Endometrial-Expression, Regulation and Function through out the Menstrual Cycle and in Early Pregnancy

- **Fourth Place: Sophie Lambard, France**
  Human Male Gamete Quality: Place of Aromatase and Estrogens

- **Fifth Place: Naojiro Minami, Japan**
  A Novel Maternal Effect Gene, Oogenesin: Involvement in Zygotic Gene Activation and Early Embryonic Development in the Mouse

Iranian Winners:

- **Seyed Javad Mowla**
  Catser 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 α, β, and α, β 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.
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 Trophoderm Cells

- **Second Place**: Tian-hua Huang, China
  Detection and Expression of Hepatitis B Virus X Gene in One and Two-Cell Embryos from Golden Hamster Oocytes in-vitro Fertilized with Human Spermatozoa Carrying HBV DNA

- **Third Place**: Adrian Richard Eley, UK
  Opoptosis of Ejaculated Human Sperm Is Induced by Co-Incubation with Chlamydia Trachomatis Lipopolysaccaride

- **Fourth Place**: Lone Schmidt, Denmark
  Does Infertility Cause Marital Benefit? An Epidemiological Study of 2250 Women and Men in Fertility Treatment

- **Fifth Place**: Louis Chukwuemeka Ajonuma, Hong Kong
  Molecular and Cellular Mechanisms Underlying Abnormal Fluid Formation in the Female Reproductive Tract: The Critical Role of Cystic Fibrosis Transmembrane Conductance Regulators

Iranian Winners:

- Mohammadreza Baghban Eslaminejad
  Polarized Culture Systems and Their Effects on Embryo Development

- Mansoureh Movahedin
  New Approaches to Assess the Success and Enhance the Efficiency of Male Germ Cell Transplantation in the Mouse

- Ashraf Alleyassin
  Comparison of Unilateral and Bilateral Transfer of Injected Oocytes into Fallopian Tubes: A Prospective Randomized Clinical Trial
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 Bashamboo, France
  Mutations in NR5A1 Associated with Ovarian Insufficiency

Best research project in embryology field
- Mohammad Hossein Nasr-Esfahani, Iran
  New Era in Sperm Selection for ICSI Procedure

Iranian Winners:
- Serajoddin Vahidi
  Prevalence of Primary Infertility in the Islamic Republic of Iran in 2004-2005

- Tahereh Ma’dani
  Improvement of Pregnancy Rate in ART Cycles

- Mehrdad Noruzinia
  MTHFR Promoter Hypermethylation in Testicular Biopsies of Patients with Non-obstructive Azoospermia: The Role of Epigenetics in Male Infertility

- Abbas Piryaei
  Differentiation Capability of Mouse Bone Marrow-Derived Mesenchymal Stem Cells into Hepatocyte-Like Cells on Artificial Basement Membrane Containing Ultraweb Nanofibers and Their Transplantation into Carbon Tetrachloride Injured Liver Model
**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
- **Hiromitsu Nakauchi**, Japan
  Heterogeneity and Hierarchy Within the Most Primitive Hematopoietic Stem Cell Compartment

Best research project in female infertility field
- **Elizabeth Stewart**, USA
  Safely Extending Focused Ultrasound Surgery for Uterine Leiomyomas to Women Who Desire Future Pregnancies

Best research project in reproductive genetics field
- **Paul Thomas**, Australia
  Identification of SOX3 As an XX Male Sex Reversal Gene in Mice and Humans

Best research project in embryology field
- **Steve Tardif**, UK
  Infertility with Impaired Zona Pellucida Adhesion of Spermatozoa from Mice Lacking TauCstF-64

Best research project in epidemiology & ethics 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
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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) tests, 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

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.
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.

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
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. The 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 (± SD) age was 29.1 ± 3.1 years and the mean duration of infertility 3.3 ± 2.0 years. The mean body mass index (BMI) was 22.9 ± 3.5 kg/m². PCOS was diagnosed referring to the Rotterdam criteria. Serum concentrations of FSH (6.5±1.4 IU/L), LH (13.7±4.6 IU/L) and T (2.9±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 included 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 those of group A (5.00%, 1/20) 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±0.62 nmol/L) and D (2.07±0.42 nmol/L) compared with group A (3.10±0.63 nmol/L) (P<0.001; P<0.001) and B (2.98±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
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 methylthiazoletetrazolium (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 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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Reproductive Genetics

Interactorome 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
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.
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, PDGFRα, 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 immunohistofluorescence 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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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)
- 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)
- Production of insulin producing cells from human embryonic stem cells (2004)
- 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)
- 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
- Ricombinant 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.
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)
- Shahrrokh 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, Mehr, MD (Gynecologist)
- Hoseyni, Roya, MD (Endocrinologist)
- Zangene, Mehrangiz, MD (Physician infectionist)

Research Assistants:
- Amirchaghmaghi, Elham, MD, PhD (Candidate)
- Kiani, Kiandokht, PhD (Candidate)
- Jahangiri, Nadia, MSc (Midwifery)
- Mohamadi Veganeh, Ladan, MSc (Midwifery)
- Malekzadeh, Farideh, MSc (Nursing)
- Jahanian, Shahideh, PhD (Candidate)
- Arabi Pour, 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


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

**Journal Clubs:**

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<td>1</td>
<td>Dr Reza Aflatoonian</td>
<td>May, 17, 2011</td>
<td>Innate immunity in reproduction</td>
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<td>2</td>
<td>Dr Fariba Ramezanali</td>
<td>November 22, 2011</td>
<td>Premature ovarian failure (POF)</td>
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<td>3</td>
<td>Dr Fereshteh Sabeti</td>
<td>February 28, 2012</td>
<td>Psychological effects of infertility on infertile couples</td>
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</table>
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
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 varicoceles, 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
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


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:
- Hosseinzafar, Hani, MSc (Cellular Molecular Biology)
- Modarresi, Tahereh, MSc (Developmental Biology)

Student Trainees:
- Ghasemzadeh, Mohammad
- Raeisi, Asieh

MSc Students:
- Yazdanikah, Samaneh
- Ahmadian, Zahra

Publications


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.

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<tr>
<td>1</td>
<td>Dr Faramarz Farrahi</td>
<td>August, 24, 2011</td>
<td>Recurrent implantation failure (Male Aspect)</td>
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<td>2</td>
<td>Dr Seyyed Jalal Hosseini</td>
<td>August, 2, 2011</td>
<td>The role of infertility team in providing information for infertile couples at Royan Institute in comparison with other international fertility centers</td>
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**Publication Chart:**

- **2009:** 2 items
- **2010:** 6 items
- **2011:** 8 items

**Andrology Scientific Members During the Past 2 Years**

- **2011:**
  - Staff: 14
  - Students: 2

- **2012:**
  - Staff: 12
  - Students: 6
Department Head: Mojtaba Rezazadeh Valojerdi, PhD
Anatomy and Embryology (Full Professor)
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 Modares 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

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


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, Zienab, 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.
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

Group Leader:
Bahar Movaghar, PhD
b.movaghar@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 Rezaazadeh 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.
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, Afshaneh, 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, Afshaneh, MSc
• Tavana, Somayeh, MSc
• Abtahi, Naeemeh Sadat, MSc
• Aeinehvand, Samaneh, MSc
• Zandevakili, Maryam, MSc

Publications


Journal Clubs:

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

Group Leader:
Hossein Eimani, PhD
h.eimani@royaninstitue.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.
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:


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 17th 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)

Publications


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 Eftekhar-Yazdi
  Executive managers: Azam Dalman and Zeinab Vahabi
  September 3, 2011

Group Leader:
Abdolhossein Shahverdi, PhD

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 Rajabipour 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

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<tbody>
<tr>
<td>1</td>
<td>Azam Dalman</td>
<td>February 6, 2012</td>
<td>Evaluation of epigenetic marks in human embryos derived from IVF and ICSI</td>
</tr>
<tr>
<td>2</td>
<td>Zeinab Vahabi</td>
<td>October 8, 2011</td>
<td>Methods of in vitro maturation of oocytes</td>
</tr>
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</table>
ANNUAL REPORT
Reproductive Genetics Department of RI-RB

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 azosperma, 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.
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, heterochromatination 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 subgroup 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


Abdossamadi, S., Rabbani Chadeegani, A., Shahhoseini, M. Identification of low mobility group protein, Lmg160, in rat liver chromatin. FEBs J. 2011; 278: 91.


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
- Ebrahim, Somayeh, MSc
- Elyasi Gorji, Zahra, MSc
- Ghanbari, Maysam, MSc
- Khoshbakt, 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

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
- Bazragar, Masoud, PhD student
- Anissi Hemaseh, Khadijeh, MSc
- Asadpour, Ummolbanin, MSc
- Habibi, Roghayeh, MSc
- Kalantari, Hamid, MSc
- Mansouri, Zahra, MSc
- Masoodi, Najmeh Sadat, MSc student
- Zarli Moradi, Shabnam, MSc
- Borjian, Parnaz, MSc Student
- Mokhtari, Pegah, BSc
- Fakhri, Mostafa, MSc
- Hosseinifar, Hani, MSc
- Vaziri, Hamed, MSc

Student Trainees:
- Moazenchis, Maedeh
- Ghezelayagh, Zeinab
- Eslami, Ali
Award
Anahita Mohseni Meybodi, Award winner of Best Poster Presentation in the 23th 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 Clamydia 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 granulose cells in women with premature ovarian failure.
• Investigation of genetic variation and gene expression in the FSH receptor gene in blood and granulose cells of patients with Premature ovarian Failure, referred to Royan Institute.

Publications


Journal Clubs
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<tbody>
<tr>
<td>1</td>
<td>Anahita Mohseni Meybodi</td>
<td>July 07, 2011</td>
<td>USP genes and their effects in male infertility</td>
</tr>
<tr>
<td>2</td>
<td>Hamid Kalantari</td>
<td>June 08, 2011</td>
<td>Prenatal Diagnosis: progress through plasma nucleic acid</td>
</tr>
<tr>
<td>3</td>
<td>Shabnam Zari Moradi and Roghayyeh Habibi</td>
<td>October 10, 2011</td>
<td>MLPA introduction and application</td>
</tr>
</tbody>
</table>
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:

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<tr>
<td>1</td>
<td>Parvaneh Afsharian</td>
<td>January 3, 2012</td>
<td>Pharmacogenetics aspects of PCOS</td>
</tr>
</tbody>
</table>
News and Events

Workshops

• Workshop: Genetic Engineering & Molecular Cloning.
  Scientific Manager: Amir Amiri Yekta; Executive Manager: Totonchi M. June 7-8, 2011

• Primary Methods in Molecular Biology
  Scientific Manager: Totonchi M; Executive Manager: Amir Amiri Yekta. May 3-4, 2011

• Culture, Harvest and Banding of Human Lymphocyte Chromosomes

• 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 Center
  Scientific Manager: Navid Almadani; Executive Manager: Shabnam Zari Moradi, November 22-23 2011

• FISH (Hands-on workshop on Fluorescent In Situ Hybridization)

• 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
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: Bioethics, Epidemiology and Biostatistics. 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 Chehrazi, MSc
8. ART surveillance, Azadeh Gahshiri, 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 6th symposium of nursing role in infertility
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 Shi’ah Muslims, because in Shi‘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:
- Behnam Manesh, 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

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
- Ghaheri, Azadeh, MSc
- Cheraghi, Rezvan, MSc
- Hesam, Saeed, MSc

Publications


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


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.

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<tr>
<th>No</th>
<th>Organizer</th>
<th>Date</th>
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<tbody>
<tr>
<td>1</td>
<td>Shiva Dibaj</td>
<td>05/07/2011</td>
<td>Bias in clinical trial</td>
</tr>
<tr>
<td>2</td>
<td>Leila Alizadeh</td>
<td>27/09/2011</td>
<td>Post-humus</td>
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**Journal Clubs:**

**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
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 multicentral 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)
- Hodeshenas, 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, Naeemeh 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
Ultrasonography and Sonohysteroscopy

Publications


News and Events

Workshops:

- **Hysterosalpingography**
  This pre-congress was held on September 6th 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 6th 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 6th, 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 10th, 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 28th, 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 4th annual Congress of Women Imaging on February 19th–21st, 2012. They were organized by Gondishapor University in Ahvaz and the speakers were Dr Ahmadi and Dr Salamati from the Department of Reproductive Imaging.

• **Comparative Study of Imaging Findings in Patient with Genital Tract Endometriosis**
  This workshop was held on 3rd of Feb, 2012. The chairman of this workshop was Dr Niknejadi and it was a great success with about 30 radiologists.

**Journal Clubs:**

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<tr>
<td>1</td>
<td>Dr Maryam Niknejadi</td>
<td>November, 1st 2011</td>
<td>The application of three-dimensional ultrasound in detection of uterine abnormalities</td>
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**Staff Publication Charts**

Members of Reproductive Imaging Department in the past 2 years

Published Items

<table>
<thead>
<tr>
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<th>2008</th>
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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

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 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
  - Dr Baharvand
- Epigenetic Reprogramming
- Dr Baharvand
- Hepatocytes
- Dr Baharvand
- Pancreatic Beta Cells
- Dr Baharvand
- Germ Cells
- Dr Baharvand
- Neural Cells- Developmental Biology
  - Dr Kiani
- 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
  - Dr Aghdami
- Skin Cells
  - Dr Aghdami
- Regenerative Medicine
  - Dr Aghdami
- Molecular Systems Biology
  - Dr Hosseini Salekdeh
- Cancer and Hematopoietic Stem Cells
  - Dr Ebrahim
- Public Cord Blood Bank
- Dr Ebrahim

Core Facilities:
- Royan Stem Cell Bank (RSCB)
- Dr Baghaban Eslaminejad
- Molecular Biology Lab
- Dr Baghaban Eslaminejad
- Electrophysiology Lab
- Dr Baghaban Eslaminejad
- Cytometry and Imaging Lab
- Dr Baghaban Eslaminejad
- History Lab
- Dr Baghaban Eslaminejad
- Gene Targeting Lab
- Dr Baghaban Eslaminejad
- Viral Transduction Lab
- Dr Baghaban Eslaminejad
- Nano/Tissue Engineering Lab
- Dr Baghaban Eslaminejad
- “Stem Cell for All” Lab
- Dr Baghaban Eslaminejad
ANNUAL REPORT
Research Programs of RI-SCBT

Chief Researcher:
Seyyedeh Nafiseh Hassani

Group Leader:
Hossein Baharvand, PhD

snafiseh.hassani@royaninstitute.org

Biography
Seyyedeh 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

Publications


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 pluriotency 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


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:
- Pyriae, 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

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

Chief Researcher:
Behshad Pournasr

Group Leader:
Hossein Baharvand, PhD

pournasr@royaninstitute.org

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.
Publications


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 β-cells. There is a great hope to use renewable sources of cells that could replace pancreatic β-cells.

There are several approaches being considered for the generation of β-cells:
- Differentiation of embryonic stem cells, induced pluripotent stem (iPS) cells, adult pancreatic cells and adult stem cells to the β-cell lineage
- Conversion of other terminally differentiated cells to β-cells in a process called "Transdifferentiation".
- Promote the replication of existing β-cells either in vivo or in vitro.

There are several reports of differentiation of cell populations into β-cells, definitive endoderm, and pancreatic progenitors, using growth factors and small molecules. However, success in final step of directed differentiation to generate functional mature β-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 β-cells.
- Gene manipulation of regulatory networks in pancreas development to enhance the differentiation of mouse embryonic stem cells to β-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
**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).
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**


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 Amirpoura, MD

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.

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

Neural Cells-Neurodegenerative diseases

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.
Publications (of all 3 neural cells research programs)


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

Technical staff:
• Sayyahpour, Forough Azam, MSc

Students:
• Safari, Fatemeh, MSc
• Bagheri, Fatemeh, PhD
• Zaare, Mohammad Ali, PhD
• Faghihi, Faaeze, PhD
• Ghasemzade, Mohammad, PhD
• Karimi, Tahereh, PhD

Publications


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 form 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.

Research Assistant:
• Namiri, Mehrnaz, PhD

Students:
• Ajdari, Manijeh, MSc
• Fatahi, Faranak, MSc
• Fonoudi, Hananeh, MSc
• Ghazizadeh, Xaniar, MD
• Vahdat, Sadaf, MSc
• Khodakarami, Hesam, MSc
• Ranjbar, Fazeleh, MSc
• Shabani, Parisa, PhD
• Rajabi, Sareh, PhD

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±0.5 fold increase in the number of beating colonies. ISL1 also caused a 2.2±0.4 fold increase in the other hESC line (Royan H6; P<0.05).

Publications

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 periostem 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
• Malekmohammadi, Mona, MSc

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.

Chief Researcher: Parvaneh Mohammadi

Group Leader: Nasser Aghdami, MD, PhD

mohamadi@royaninstitute.org

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.
Introduction

Although recent advances in medical sciences have made patients’ survival increase in some cases, 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

- Azimian, Vajiheh, MSc
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- Moghaddasali, Reza, MSc
- Shahbazi, Atefeh, BSc
- Taghiabadi, Ehsan, BSc
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- Ghassemi, Masoud, MD (Cardiologist)
- Aghoushi, Abolfazl, MD (Orthopedist)
- Ahmadi, Hossein, MD
- Arab, Leila, MD
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- Emadedin, Mohsen, MD (Orthopedist)
- Madani, Hoda, MD
- Malekzade, Reza, MD (Gastroenterologist)
- Nabavi, Seyyed Masoud, MD (Neurologist)
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- Rafiee, Baradaran, MD (Ophthalmologist)
- Rezvani, Mohammad, MD (Dermatologist)
- Rouhipour, Ramtin, MD (Orthopedist)
- Shafeeyan, Saeed, MD (Dermatologist)
- Sharifeian, Hamid, MD (Dermatologist)
- Vosough, Ahmad, MD (Radiologist)
- Zaali, Ali, 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


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) 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:
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- Rasouli, Hasan, MSc
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- Tale Ahmad, Sarah, MSc
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- Shekari, Faeze, MSc
- Fathi, Ali, MSc

Technical Staffs:
- Parsa Matin, Porya, BSc
- Naghavi, Mostafa, BSc
- Mirshahvaladi, Seyed Shahaboddin, BSc
- Habibi Rezaii, Lida, MSc

Students:
- Shekari, Faeze, PhD
- Fathi, Ali, PhD
- Jangravi, Zohreh, PhD
- Nasrabadi, Davood, PhD
- Arefnejad, Babak, PhD
- Rastgar, Diba, MSc

Molecular Systems Biology

Group Leader:
Ghasem Hosseini Salekdeh, 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.

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

Publications


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
- Khoshchehreh, Reyhaneh, MSc
- Ganji, Fatemeh, MSc

Technical Staff:
- Firouzi, Javad, BSc

Students:
- Rajabi, Motahareh, MSc
- Shokraee, Fatemeh, MSc
- Mohammadi, Maryam, MSc
- Mehdi, Maryam, MSc
- Abdollahi, Pegah, MSc
- Haji Moradi, Bita, 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 endothelia 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


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*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
Royan Stem Cell Bank (RSCB)

Introduction
Today, the Biology of Stem Cells as a growing scientific field, has afford 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, NMR, 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
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
• Sayyahpour, Forough Azam, BSc

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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
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 GS 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

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

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.
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

Generation of human induced pluripotent stem cells
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

Laboratory Head: Hossein Baharvand, PhD
bahravand@royaninstitute.org
**“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

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**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, Azarbaejan, Esfahan, Alborz) have been trained in this laboratory.

**Laboratory Head:**
Hossein Baharvand, PhD
baharvand@royaninstitute.org
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 PPARγ 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, Mehrnoosh, BSc
- Shokouhi, Mostafa, BSc
- Jafari, Ahmad
- Heydari, Homayoun
- Khajeh, Ali Asghar
- Dadgostar, Ahmad Reza
- Shakeri, Maryam
- Shokouhi, Farshad
- Salehi, Hamid
- Nikbakht, Javad
- Yazdekhasti, Javad
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
- Abbasî, Hasan, PhD
- Sekhavati, Mohammad Hadi, PhD
- Jafari, Shahram, PhD
- Esmaeilzadeh, Forouzan, PhD
- Kiani, Maryam, MSc
- Bakhtari, Azzolah, PhD
- Bonakdar, Elham, PhD
- Gharibi, Shahin, MSc
- Hodaei, Mehrdad, MSc
- Rohollahi, Shiva, MSc
- Hosseinia, Pourya, PhD

Chief Researcher:
Sayed Mortaza Hosseini, DVM
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.
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


*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).


Chief Researcher: Marziyeh Tavalaee
tavalaee.m@royaninstitute.org

Biography
Marziyeh Tavalaee 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, Afsoon, MSc
- Bahreinian, Mahsa, MSc
- Barekat, Frouogh Sadat, MSc

Previous Student Trainees:
- Motiei, Marjan, MSc
- Basiri, Farzaneh, MSc
- Bahrami, Soulma, MSc
- Skandari, Marzieh, MSc
- Aghajanpour, Samaneh, MSc
- Shaygannia, Erfaneh, MSc

Publications


Annual Report


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)


Decisive factors in medical tourism destination choice: A case study of Isfahan, Iran and fertility treatments. Moghimehfar F, Nasr-Esfahani MH. Tourism Management 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 Marziyeh Tavalaee. ISBN: 978-964-8115-83-3.

WHO laboratory manual for the Examination and processing of human semen, Translated by Dr MH. Nasr-Esfahani and Marziyeh Tavalaee (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”
**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
- Pourveisheh, 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 ES cell-derived neural progenitors to neuronal cells with regional specific identity by co-culturing of notochord and somite.* Salehi H, Karbalaie Kh, Salamian A, Kiani A, Razavi Sh, Nasr-Esfahani M.H, Baharvand H. Stem Cell Research (8), 120–133. 2012


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 peroxisome 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, Motahhareh Sadat, MSc

Lab Technicians:
- Izadi, Tayebeh, BSc
- Rabiee, Farzaneh, BSc

Student Trainees:
- Mohammadinezhad, Parisa, PhD
- Jodeyri, Mohammad, MSc
- Hosseini, Samaneh, MSc
- Mazaheri, Neda, MSc
- Ghavzinizadehgan, Faeezeh, MSc
- Taheri, Marjan, MSc
- Forouzanfar, Mahboubeh, MSc
- Modarres, Parastou, MSc

Previous Student Trainees:
- Hashemi, Motahhareh, MSc
- Seifi, Tahereh, MSc

Publications

Chief Researcher: 
Kamran Ghaedi, PhD
kamranghaedi@royaninstitute.org

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 carrier 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.
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 straightforward 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
- Abootaleb, Fatemeh, MSc
- Rezaei, Nasemeh, MSc
- Gavanji, Shahin, MSc

Previous Student Trainee:
- Sanei, Nafiseh, MSc

Publications

News and Events
- Establishment of a molecular method for prediction 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.
- 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:

<table>
<thead>
<tr>
<th>No</th>
<th>Group</th>
<th>Time</th>
<th>Total Number</th>
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<tbody>
<tr>
<td>1</td>
<td>Embryology</td>
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<td>2</td>
<td>Genetics</td>
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<td>3</td>
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<td>4</td>
<td>Stem Cell</td>
<td>Every Tuesday</td>
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<tr>
<td>5</td>
<td>Recombinant Protein</td>
<td>Every Wednesday</td>
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Number of Staff

Number of Articles Published
ANNUAL REPORT
Laboratory Animal Core Facility

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 an 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
Efficacy of PUREGON

Consistent efficacy in multiple clinical trials in IVF/ICSI and OI/UII^7

Proven efficacy in the world’s largest IVF/ICSI trial^1

- Ongoing pregnancy rate of 38.1% per attempt
- 12.5 oocytes retrieved per cycle
- 4.4 good quality embryos^6

High pregnancy rates regardless of endogenous LH levels^6

Favorable dosing flexibility, easy-to-use device^2

*Grade 1 or 2, median

Please refer to the full SDP test before generating this product. Adverse events should be reported.

Date of revision: 01/18/2001

Always A Step Ahead From The Rest
شرکت زریف خرد
1- مشاور و تامین کننده کلیه تجهیزات IVF و دستگاه‌های مراکز IVF
2- تامین کننده کلیه تجهیزات و مواد مصرفی IVF مراکز
3- تامین کننده انواع مواد شیمیایی از کلیه کمپانی‌های معترض اروپایی و آمریکایی با رعایت زنجیره سرد انگلستان
4- نمایندگی نمایندگی آلمان
5- نمایندگی

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The Coda Tower® is to be used in your laboratories, procedures rooms and other working areas.

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- Unique vehicle;
  - Self-lubricating properties rendering the application neither painful nor messy
  - Controlled slow release of the active hormonal ingredient for easier once or twice daily dose

When to use Cyclogest®?
Whenever progesterone supplementation is needed up to the specialist’s experience...
- Luteal phase support during IVF techniques
- Recurrent miscarriages (RPL) attributed to luteal phase deficiency
- Labeled for the following indications:
  - puerperal depression
  - premenstrual syndrome, including premenstrual tension and depression

Further information is available upon request
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