Meeting Report

Report on 2nd Royan Institute International Summer School on Developmental Biology and Stem Cells Tehran, Iran, 17–22nd July 2011

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ABSTRACT

The 2nd Royan Institute International Summer School was built around the topic of stem cells and grounding in the discipline of developmental biology. The meeting provided not only direct transfer of technical and intellectual information, the normal process in scientific meetings, but was also a forum for the exchange of personal ideas of science as a creative pursuit. This summer school introduced aspiring young Iranian scientists to international researchers and exposed the latter to a rich culture that highly values learning and education, attested by the confident, intelligent young men and women who asked probing questions and who were eager to participate in the workshops. Hossein Baharvand's dedication and passion for science have led to an impressive record of national and international peer-reviewed publications and an increasing number of students who pursue science in Iran, and shows how the right people can create an environment where good science, good science education and motivation will flourish. This report summarizes some of the activities of the workshop in the Royan Institute and the impressions of the visiting scientists in the wider context of the scientific and cultural heritage of Iran.

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What drives your science? Perhaps this is not a question that working scientists ponder frequently, but reflections on this question, in addition to the more strictly scientific discussions on the biology of stem cells and development, were the inevitable result for both teachers and students at the 2nd Royan Institute International Summer School Program held in Iran in July, 2011.

A combination of fine Iranian lecturers, many of them being Ph.D. students, two Royan Institute Principal Researchers, post-doctoral researchers and five international visitors from Australia, Singapore and the UK formed an engaging group of teachers at the Summer School for Stem Cells and Developmental Biology.

The 300 participants, a wonderful combination of advanced undergraduates, post-graduates and post-doctoral fellows, came from universities and institutes predominately from Tehran but also from other cities throughout Iran. The number of participants was much higher than for the inaugural Summer School in 2010, and over two thirds of this audience were female (see Figs. 1 and 2). This summer school was funded by grants provided from the Royan Institute, Iranian council of Stem Cell Technology, Science and Culture University and Royan Stem Cell Tech.

The ability to maintain and control the expansion and the differentiation of stem cells is based very largely on the understanding of equivalent processes in normal development. With this in mind, in broad terms the workshop covered early development; organogenesis of heart, skeletal muscle, liver, pancreas and nervous system; post-natal muscle regeneration; an overview of stem cell types in human and mouse and the molecular program underpinning pluripotency. Diverse animal model systems were discussed, ranging from mouse, zebrafish and chick to marsupials. The Royan Institute's high level of organization allowed for a seamless program to unfold and a smooth transition between lectures and demonstrations of manipulations in embryos. The latter were conducted by experts in their fields, and provided hands-on experience for the students.

The first two days of the summer school were held in the Persian (Farsi) language and started with welcome addresses by Professor Gourabi, (President, Royan Institute), Dr. Mohammad-Hossein
Imani-Khoshkhoo (President, Science and Culture University) and Dr. Sahar Kiani (Scientific Secretary, International Summer School). The morning session began with presentations by Royan Institute Researchers providing an overview of developmental biology and stem cell research. Topics throughout the two days of lectures in Persian included stem cells and regeneration by Dr. Naser Aghdami (MD, Ph.D.) and covered a range of organ and tissue development: heart (Mr. Mahmood Talkhabi, Ph.D. student), neural tube and neural crest (Mr. Ali Fathi, Ph.D. student), epigenetics during preimplantation in mouse (Mr. Mehdi Totonchi, Ph.D. student), muscle (Mr. Mohsen Moslem, Ph.D. student), pancreas (Mr. Ali Farrokhi, M.Sc.), liver (Mrs. Zahra Farzaneh, M.Sc.) and limb (Mrs. Faezeh Faghihi, Ph.D. student) development; Mrs. Seyedeh-Naffiseh Hassani (Ph.D. student) provided a broad overview on pluripotent stem cells and Mr. Ali Farrokhi explained the generation of transgenic mice from embryonic stem cell manipulation. A final lecture by Associate Professor Hossein Baharvand provided an overview on “Translational Developmental Biology” by focusing on current work within the Royan Institute on differentiation and transplantation of neural lineage cells from pluripotent stem cells (see Fig. 3).

In the afternoon of the first two days, Dr. Hassan Rashidi, from the University of Nottingham, UK who is establishing the chick as a model for stem cells and regeneration, demonstrated in ovo chick manipulations. He microinjected mammalian stem cells into chick neural crest or limb buds, and the injected embryos from both workshops were analyzed following 48 h of incubation, highlighting survival and migration of GFP-labeled injected cells in demonstration sessions held later on the last day of the Summer School (see Fig. 5), and was ably assisted by Ibrahim Shahbazi and Ali Farrokhi. The awards for best lecturers speaking in Farsi, as judged by the Summer School participants, were Mr. Ali Farrokhi and Mrs. Seyedeh-Naffiseh Hassani.

The following four days were mainly in English with a mixture of lectures and workshops delivered by the five international visitors. Dr. Mary Familari from the Department of Zoology at the University of Melbourne kicked off this part of the program with a very well received overview of stem cells and our current understanding of the molecular events involved in pluripotency and reprogramming. Familari also presented a comparison of early development in eutherian and marsupial mammals, having been involved in the study of organ development in a variety of species including frog, mouse, rat and two marsupial species over the last fifteen years. In addition, Mary presented a highly engaging workshop on getting students to train their minds to think in three-dimensions. This workshop incorporated a talented fourth year undergraduate at the University of Tehran, Ms. Zahra Masoumi, who made it possible to conduct the activities in both...
Farsi and English in order that participants received explanation of difficult concepts in their native tongue (see Fig. 7).

Professor Miranda Grounds, a researcher in the field of skeletal muscle damage, regeneration, and cell transplantation therapies for muscle disorders, from the School of Anatomy and Human Biology at the University of Western Australia, provided lectures and stimulated discussion about what is often an overlooked but much needed perspective, the ethics of stem cell research. She also discussed important concerns for cell transplantation therapies based on the long experience for treatment of muscular dystrophies. The issue of a different response of muscle cells that elongate during post-natal growth, compared with the situation in mature animals, and also subsequent changes during ageing are all aspects of development and were addressed in one lecture. Much of the development proceeds by cells engaged in an intimate relationship with the extracellular matrix (ECM), and Prof. Ground’s lecture reminded students of the often overlooked but critical roles of ECM interactions, with an emphasis on the in vivo perspective.
Dr. Donald Newgreen, from the Murdoch Children’s Research Institute, Melbourne, an expert in neural crest cell development, provided a series of lectures, beginning with the development of the initial organizational plan of vertebrate embryos that unfolds during gastrulation, which sees the specification of the ectoderm, mesoderm, endoderm and assemblage of each in the correct spatial relationship. This was followed by lectures on development of the neuroectodermal layer; that is, nervous system development and neural crest cell migration and differentiation, including a brief review of epithelial–mesenchymal transitions that are involved in many developmental processes. In addition, he presented an overview of current understanding of the molecular mechanisms involved in patterning during central nervous system development. The molecular signaling that controls the extension of the body plan by adding mesoderm body segments (somites) was also the subject of his last lecture. Don also conducted several highly successful chick embryo manipulation workshops and the participants eagerly sought hands-on practice in these techniques (see Figs. 4 and 6) and were ably assisted by Hassan Rashidi, Ali Farookhi and Ibrahim Shahbazi.

In particular, Newgreen demonstrated a number of techniques in chick embryos including mechanical neural tube and neural crest cell isolation by enzyme assisted microdissection, followed by cell culture and migration assays involving ECM substrates. In vivo experimental approaches facilitated by the avian embryonic system included in ovo gene transfection by electroporation, intra-embryonic tissue transplantation (grafting) and chorio-allantoic membrane grafting. Each of these techniques has different strengths and weaknesses, and illustrated the often inverse relationship between (1) ability to simplify in order to experimentally isolate and manipulate molecular and cellular variables, and (2) the degree of ‘reality’ of the experimental system versus the true in vivo biological system, which is highly complex. A most useful extension of immunolabeling is when several target molecules can be simultaneously identified in the same specimen. This multi-immunolabeling of cells, microtome sections and whole mounts is in theory simple, but in practice has many pitfalls: these were explored in detail in the last workshop.

The world of zebrafish is fortunate to have Dr. Suresh Jesuthasan, based in the Biomedical Sciences Institutes, Singapore, whose interest lies in brain development and behavior. Suresh provided a unique perspective on brain development and how one assesses fear, anxiety and helplessness using this animal model. He highlighted the techniques that can be performed in zebrafish because of its transparency during embryonic and larval stages that allow imaging or manipulation of very specific brain areas or even single cells in order to address questions in axonal guidance and animal behavior. Jesuthasan also described new tools for manipulating the fish genome. In addition, he provided demonstrations and an opportunity for microinjection of zebrafish embryos. Students were also shown simple behavioral tests in newly hatched larval fish.

The international invitees were deeply impressed by the standard of students attending the workshop who dynamically interacted with instructors throughout the week. Many students distinguished themselves by their confidence, good English and probing questions that showed deep understanding and intelligence; this was especially impressive considering that the last few days were conducted almost entirely in English while biology is normally taught in Farsi in Iran. There was ample opportunity for students and lecturers to mingle at the workshops and during breaks where student enthusiasm for lecture topics was evident. The international visitors agreed it was a pleasure to engage with such keen, well informed students.

In Farsi, ‘Royan’ means embryo. The Royan Institute, established in 1991, is the leading Iranian biomedical research center and consists of three institutes: (1) Royan Institute for
Reproductive Biomedicine to not only provide infertility treatments, but also to improve embryo health and to research different aspects of infertility. (2) Royan Institute for Animal Biotechnology to shape biotechnology into a tool of the future for creation of wealth, ensuring social justice and also efficiently bridging science with daily life. (3) Royan Institute for Stem Cell Biology and Technology (RI-SCBT) to provide a comprehensive and coordinated “bench to bedside” approach to regenerative medicine, including the development of cell-therapy approaches that can restore tissue function to patients; there is also research in the fundamental biology of stem cells and developmental biology. RI-SCIT (formerly known as the Department of Stem Cells) was established in 2002 and includes the public Cord Blood Bank. Within this institute, human embryonic stem (ES) cell and induced pluripotent stem (iPS) cell lines have been generated, and various protocols established for feeder free cultures, suspension cultures and differentiation towards cardiomyocytes, pancreatic beta cells, hepatocytes and neural cells. Researchers at the Institute have also developed a model of repair of rat spinal cord injury using human ES cells. The fine facilities at the Institute and the increasing number of publications in national and international peer-reviewed high impact journals are impressive.

Three of the international speakers (Grounds, Jesuthasan and Familari) also had the opportunity to visit the Biotechnology branch of the Royan Institute in Esfahan, where the laboratories for cloning domestic animals and the core facility producing research and therapeutic quality proteins are located. To date, several species have been cloned including goat, cow and sheep and such animal bioreactors are in the early stages of producing therapeutic proteins via milk production. The bustling laboratories and quality of this research was impressive. In addition, the visiting speakers hosted by the Royan Institute, were treated to a wonderful opportunity to visit the many splendors of the cities of Shiraz and Esfahan and experience the great richness of history, tolerance and gentle philosophies permeating Persian culture: focused on learning and education, with many manifestations of their reverence for poets, scientists and learned men and women.

This dedication to learning and teaching is reiterated by Associate Professor Hossein Baharvand, Director of RI-SCIT, who passionately promotes an awareness of science as a creative and exciting pursuit, and with the Royan Summer School introduces visiting researchers to young students on the cusp of decision-making about their future career paths. To enhance the learning experience for the students, Baharvand has translated many useful scientific text books into Persian and has written or edited several books about stem cells. In addition, members of the Royan Institute have established two journals: The International Journal of Fertility & Sterility and Cell Journal (Yakhteh). The seemingly endless energy that drives these pursuits arises from a deep desire to provide graduate students and post-doctoral fellows with the best available resources and also to make Iran a world leader in stem cells and regeneration therapies: the Royan Institute seems well on the way to achieving these goals.

Reflections:

Iran (previously Persia) has a long and very rich cultural history, and is unique because many important Islamic scholars were Persian (such as Ibn Sina, Abu Nasr Farabi and Abu Rayhan Birooni) or lived in Persia during the Golden Age of Islam from the 8th to 13th Centuries. The appreciation of science as a creative pursuit and the celebration of knowledge in the Persian culture continue to shine in Iran and this tradition of scholarship is actively pursued by Hossein Baharvand and his colleagues at the Royan Institute.

There is a proverb ‘Esfahan is half the world’. Until you visit this city, and indeed Iran itself, it is difficult to appreciate how much lies behind this statement. Culturally, Iran maintains a strong and distinctive identity. We found a lively curiosity among the students not only in scientific topics, but also in the life of a scientist abroad, as reflected in a question and answer session at the gala dinner. This was a unique feature of this meeting, hosted by Dr. Massoud Vosough, where the international visitors spoke candidly about why they chose science as a career and what it had to offer. This provided a valuable perspective – the human side of scientists – for potential young scientists.

We are grateful for the opportunity to have participated in this dynamic Summer School and for the privilege to have visited Iran and learned more of the culture and the fine scientific achievements that should attract increasing international recognition. Should you be fortunate to receive an invitation to teach next summer, we can only recommend that you accept!