

1st Royan Institute International Summer School on Developmental Biology and Stem Cells

Tehran, 12-15 July 2010

From July 12 until July 15 2010, the 1st Royan Institute International Summer School on Developmental Biology and Stem Cells was held at the Royan Institute in Tehran, Iran (Figure 1). This extensive Summer School was devoted to the germ cell cycle and epigenetics and covered subjects such as mammalian preimplantation development, gastrulation, formation of the germ lineage in mammals and the accompanying epigenetic programming. This first Summer School was a great success with around 200 students (MSc and PhD), mostly from Iran. It was enjoyable for students, teachers and organizing staff alike, and the idea is to have an annual follow-up focused on other themes in developmental biology.

In reality, the organizing committee experienced difficulty in finding international lecturers. Indeed, when we [B.R. and S.C.] were invited to lecture at this Summer School, our emotions were mixed between being honored, curiosity and admittedly also some form of anxiety. After all, there are certain laws or religious customs in Iran that westerners are not used to or disagree with. Other customs can be rather uncomfortable, such as wearing a head scarf and long-sleeved manteau (a kind of trenchcoat) which is compulsory for women. Colleagues replied in a similar fashion when we spoke about the Summer School. "Iran, but isn't that dangerous!?" and "Are you sure you want to go there?" were the most heard comments. Before our visit to Iran, we also visited the website of the Dutch Ministry of Foreign Affairs for travelling tips. The advice was clear: "code 5" meaning "only visit the country when strictly necessary" which made us seriously consider cancelling the visit. Our families and friends were also apprehensive regarding our decision to accept the invitation. But we were determined to go and we were looking forward to spending time teaching and discussing our favorite themes: germ cell development, stem cells, epigenetics and early embryonic development. And this we found was the right decision; we encountered a hospitable and modern institute that hosted the Summer School, and the participating students were all highly motivated and enthusiastic. To our relief, both men and women were part of the organizing staff, and both male and female students participated. Men and women contributed equally to the discussions between each other and with the teachers. As a bonus, the cultural heritage of Iran is of jaw-dropping beauty and we had the opportunity to



Fig. 1. The announcement for the 1st Royan Institute International Summer School on Developmental Biology and Stem Cells.

experience at least some of the highlights. We hope that in the near future more scientists accept the invitation to visit and participate in scientific events in Iran.

Day one: introductory day

We flew to Iran on Sunday July 11th and when the plane was descending towards Tehran a transformation took place when women were told to cover their hair and hips. There was a stressful atmosphere in the air. Co-author Susana Chuva de Sousa Lopes (S.C.) was approached by several women who gave advice on how to properly cover her hair and deeply apologized for the inconvenience. When we arrived at Imam Khomeini airport

Abbreviations used in this paper: AP, alkaline phosphatase; ART, artificial reproductive technology; IVF, in vitro fertilization.

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in Tehran, with S.C. decently covered, a student from the Royan Institute was there to welcome us. It was 03.00 AM; we arrived at our hotel an hour or so later. At noon, another student from the Royan Institute and a driver came to pick us up from the hotel. We arrived at the Royan Institute, a modern complex in the North of Tehran and installed ourselves in a spacious office which was to be our own private quarters during our stay. There we met Hossein Baharvand, the scientific director of the Department of Stem Cells and Developmental Biology of the Royan Institute and head organizer of the Summer School who gave us his vision for the course. The Royan Institute is a non-governmental organization that was established in 1991 as an infertility clinic. The Persian word 'royan' can be translated as 'embryo' or 'growing' and is aptly chosen as the name for an institute that is devoted to reproduction and embryology and is successfully expanding. The vision of the Institute is to gain fundamental knowledge regarding development biology and stem cells needed to develop novel "bench to bedside" applications. The Royan Institute believes that educating their scientists by exposing them to international scientists will increase their motivation and knowledge and ultimately will make them "better flowers". Therefore, the idea of a Summer School to provide a hands-on opportunity for students to learn more about the interface between stem cells, germ cells and epigenetics fitted perfectly in their research program. Apart from this International Summer School, the Royan Institute also organizes an annual international twin congress on Reproductive Biomedicine and on Stem Cells Biology and Technology, a joint venture of two separate congresses with different themes coordi-

nated by the Reproductive Biomedicine and Stem Cells Research Centers of the Royan Institute (http://www.royaninstitute.org/cmsen/index.php?option=com_content&task=view&id=157&Itemid=161). Internationally respected scientists, such as Rudolf Jaenisch have participated in these congresses (Jaenisch, 2007) and this year, the congresses are held already for the 6th and 11th times, respectively.

On this first day of the course, introductory talks in Persian were given by Royan PhD students on the topics to be discussed the following days. In this way it was ensured that all participants had sufficient background knowledge to follow the rest of the course in English. Later that day, we prepared the practical work, tested the equipment, the instruments and reagents and prepared several E7.5 mouse embryos and gonads from E13.5 embryos to stain for alkaline phosphatase (AP) activity the following days with the students. A legion of students was behind us when we were making the preparations, already trying to learn as much as possible.

Day two: from zygote to primordial germ cells

At 8.00 am, a group of inquisitive students, women fully covered and most of them wearing the typical chador, a pitch-black sheet, was eager to get started (Figure 2). Their eyes showed excitement and willingness to absorb every detail. The first session on "Preimplantation development" focused on fertilization, cleavage divisions and lineage segregation events. This was followed by a session on "Gastrulation" where the students



Fig. 2. The 1st Royan Institute International Summer School. (A) The auditorium hall at the Royan Institute with the Summer School audience. (B) Participants of the Summer School performing embryo dissections. (C) Bernard Roelen (left) and Susana Chuva de Sousa Lopes (right) preparing one of the presentations. (D) Microscopes in the auditorium enabled all participants of the Summer School to observe mouse embryos.



Fig. 3. Participants and organizing staff of the Summer School.

learned about processes like cavitation, the formation of the anterior visceral endoderm, mesoderm formation and the importance of molecular signaling from the extraembryonic tissues to the epiblast to pattern the embryo. The opportunity was taken to show the diversity of embryo shapes and gastrulation strategies in several mammalian species and the chicken. Then formation of primordial germ cells in the mouse was discussed in detail, focusing on the signaling involved and the molecular markers of primordial germ cells. After lunch, the role of DNA methylation and histone modifications in the development of the preimplantation embryo and germ cells were discussed. Also X chromosome activity during primordial germ cell development and migration was introduced. This presentation was put together by Katsuhiko Hayashi, who unfortunately had to cancel his visit, but kindly prepared several presentations and made sure that SCDSL was in a position to convey his message during the course.

In the late afternoon, about 40 students attended a practical session on “primordial germ cell specification”. The students were taught how to handle mice, remove the uterus, to isolate E7.5 embryos from their decidua, how to remove the Reichert's membrane and perform alkaline phosphatase staining to identify primordial germ cells. Helped with a digital camera connected to a projector, it was possible to demonstrate these procedures before the students tried to perform them themselves.

Day three: aspects of gametogenesis

The third day started with a session on “Folliculogenesis” describing follicle formation, the roles of the different hormones in this process and the importance of the granulosa and cumulus cells for proper functioning of the egg. This was followed by a session on “Sex determination”. The various ways that animals

use for sex determination (genetic, social, environmental) were discussed, followed by introductions to parthenogenesis and genetic imprinting. The role of *Sry* in sex determination was discussed in more detail, as well as the molecular players responsible for the phenomenon known as sex reversal. Furthermore, the roles of somatic tissue and developmental age in sex determination and induction of female/male gametogenesis were discussed.

Before lunch time, thinking was actively stimulated by proposing two conceptual questions which students were asked to answer, on paper. The answers would be collected the next day and the best answers would be rewarded with a prize from the Royan Institute. This created a nice creative buzz among the students; even after the Summer School had ended students were sending in answers and questions in response to the questions, via e-mail.

After lunch, epigenetic modifications that take place during gametogenesis were presented, with specific attention to the enzymes involved, as well as the changes in histone modifications.

Late in the afternoon, during the practical session this time on “sex determination”, the students learned how to isolate E13.5 mouse embryos, recognize the placenta, umbilical cord, visceral yolk sac and amnion. The embryos were subsequently dissected to learn how to recognize and isolate the gonads and discriminate between female and male gonads.

A demonstration was organized for all the students in the auditorium hall where two stereo microscopes were made available and connected to the central projector using material collected during the first day (Figure 2). The students that had not participated in the practical course in this way could still observe the mouse uterus, decidua, whole E13.5 embryos, whole E7.5 embryos stained for AP to visualize the primordial germ cells, as

well as E13.5 male and female gonads.

Day four: cloning, stem cells and pluripotency

The fourth day continued with stem cell epigenetics, focusing on embryonic stem cells versus epiblast stem cells, their epigenetic properties and heterogeneity. This was followed by a session about nuclear reprogramming and cloning by somatic cell nuclear transfer. In the afternoon, the generation of germ cells from stem cells was discussed. The Summer School had a very open character and participants were stimulated to ask questions and pose remarks during and after the presentations. There was for instance an interesting ethical discussion with the audience about ethics and the usage of left-over IVF embryos. It was interesting to hear the student's thoughts on that, in particular because the Royan Institute is the biggest IVF research facility in the Middle East, performing over 6000 ART cycles per year from both Iran and surrounding countries. Despite the government being based on Islam, in Iran it is permitted to use human IVF left-over embryos to generate novel embryonic stem cell lines providing there is patient consent. As in most European countries, it is forbidden to create human embryos from isolated mature gametes for research purposes. The discussion was followed by a session concerning cellular reprogramming and cloning by somatic cell nuclear transfer. Thereafter, an update was given on the efforts to generate both female and male gametes from mouse and human embryonic stem cells.

Later in the afternoon a "Meet the Professors" session was held where we spoke about our careers and gave some academic advice and vision on scientific and personal career moves. Surprisingly, many students attending the Summer School had plans to spend some part of their education abroad and there was interest in the differences between Europe and the USA in term of PhD and MSc degrees.

The Summer School ended by announcing the winners of the contest followed by a group picture where everybody was invited on stage (Figure 3).

Epilogue

The organization of this Summer School was absolutely flawless and the organizing staff extremely motivated and friendly. In addition, the motivation of the participants stimulated us to do our best. For us it was a fantastic experience; in a short time, we have both set-up new collaborations and made new friends. In conclusion, the Summer School was a big success and we hope that other scientists will promote developmental biology in the Middle East region and in particular in Iran, over the coming years. On the other hand, we feel that a summer school on developmental biology, such as that organized by the Royan Institute is practicable, not extremely expensive and an excellent way to motivate post-graduate students to undertake a scientific career in developmental biology.

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Reference

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