ISSCR Presidents look back on their presidency, the evolution of the field, and the Society

In celebration of the ISSCR’s 20th anniversary we asked past ISSCR presidents the question, “During your presidential year, what key achievements or issue(s) in the field stood out to you?” The collection of responses provides a glimpse of the evolution of the field and the ISSCR over the past 20 years.

Mobilizing the global stem cell community: the start of the ISSCR

In 2002, scientists had made impressive progress on the basic science of stem cells, and a major aspiration was to create pluripotent stem cells. There were ethical issues associated with embryonic stem cells. A group of us felt the need to have a forum to exchange ideas, present the latest work, and discuss the ethical challenges. President Bush had just set the policy that research on existing embryonic stem cells could be worked on with federal dollars—so-called presidential stem cells—but research on new lines could not be federally funded. In my own lab, we marked equipment that used existing lines with a “P” for presidential and equipment for privately funded lines with an “NP” for non-presidential, which allowed us to track the funding. Additionally, only 20% of Americans were in favor of embryonic stem cell research.

I decided to start the ISSCR. In addition to discussing science, it was clear that we needed to mobilize the global stem cell community to educate the public. In our first board meeting, a few investigators said that we should not talk to the press since it would be misinterpreted. I told them that we needed to do the opposite. Who else should provide the world with accurate information about stem cells? I was on TV and radio many times in the early years of ISSCR educating the public, and many board members did the same. By the end of my tenure as president, 80% of Americans were in favor of embryonic stem cell research. The ISSCR flourished as the global braintrust of stem cell researchers. I couldn’t be more proud of the organization.

The first Annual Meeting outside the USA and the discovery of iPS cells

I had the privilege of serving as ISSCR’s second president at a time when the Society was young and growing and the field of stem cell biology was full of excitement, controversy, debate, and hope. While much happened during that year, two events stand out to me as highlights. The first was the opportunity for me to host the 2006 annual meeting in Toronto. This was the first time it was held outside of the United States, and I was excited that Toronto was chosen, as the city has a large stem cell research community and a strong history in stem cell biology. Also, being Canadian myself, it was great to see the meeting come to my home country. The second was Dr. Shinya Yamanaka’s talk at our Toronto meeting, where he described how to make induced pluripotent stem cells. I have been to many presentations at many meetings since then, but I don’t think any have had as much of an impact on the audience or the field as Shinya’s talk did. The entire meeting was buzzing about the findings, and there was excitement and “reprogramming” discussions at many of the dinners, bars, and parties. It was just one of those times in science, and I am truly grateful that I had the chance to share in it as president of the ISSCR.
The voice of the field: The ISSCR releases Guidelines for the Conduct of Human Embryonic Stem Cell Research

I was ISSCR President from 2007–2008, a time of tremendous excitement, revolutionary discovery, and logarithmic growth in stem cell research and the Society. Ours was the first class of officers who stood for election among a slate of candidates, as the Society prior to that time had been run by an authoritarian tyrant—Len Zon—and a small cabal of handpicked associates ;-). Beyond growing in membership and adopting democratic governance, the Society transitioned to independent management, giving it more control over its finances and strategy. The ISSCR Guidelines for the Conduct of Human Embryonic Stem Cell Research, released in December of 2006, were gaining widespread acceptance as the global standard, and together with the ISSCR Guidelines for the Clinical Translation of Stem Cells, released in December of 2008, established ISSCR as the voice and conscience of the growing field. The most transformative science of the time was certainly Dr. Yamanaka’s startling report of transcription-factor-driven reprogramming, which forever changed the field. The annual meeting in 2008, held in Philadelphia, celebrated the tremendous advances of reprogramming, with the keynote lecture by John Gurdon. Sadly, the sound system malfunctioned, leading John to proclaim in his wry manner, “I seem to be having a devastating effect on the equipment.” Those were heady times.

The ISSCR’s expanding international presence

I was president in 2008. The key achievement of ISSCR was undoubtedly that we managed to hold a successful conference in Barcelona after it became clear that London, the original choice, would not work out. I remember how well the ISSCR staff worked together with ISSCR members in Spain to pull off a great meeting. It was also at a time when Catalan’s investment in science had increased, and there was confidence in the air. Funding for stem cell research via the California Institute for Regenerative Medicine was flowing and attracting a lot of attention. George W. Bush was still president of the United States, and there was a lot of public engagement work on the ethics of working with human embryonic stem cells. Of course, in addition, everyone was excited about the new opportunities available through the development of induced pluripotent stem cells.

Focusing on the translation of stem cell science and educating the public

I came into office with an agenda: to plead for purification of stem cells to enable science-based understanding of how the body is constructed and regenerated and how that could lead to clinical translation. To try to combat fraudulent “stem cell” therapies, we wrote a guide for patients and caregivers on how to discover if the offered therapy was proven.

From my own lab, comparing gene expression of purified acute myeloid leukemia (AML) stem cells with normal hematopoietic stem cells (HSCs)/multipotent progenitors (MPP), we discovered that leukemias upregulated CD47, a “don’t eat me” signal that blocked macrophage-mediated programmed cell removal to counteract the eat-me signal we discovered, calreticulin. We showed that rituximab could be a super eat-me signal to opsonize lymphoma cells and synergize with blocking anti-CD47 antibodies. This led us to partner with CIRM to develop and test a therapeutic immunoglobulin G4 (IgG4) anti-CD47.
magrolimab, that 6 years later enabled us to form a company that carried out successful phase II trials in elderly patients with AML and myelodysplastic syndrome (MDS) and relapsed, refractory large-cell lymphomas. We later realized that other clonally expanding pathogenic cells in atherosclerosis (detected in positron emission tomography [PET] scans in the lymphoma trial) were CD47+calreticulin+ and were also in fibrotic diseases. I also celebrated the science of Jim Gowans, who taught me in vivo veritas, the basis for my stem cell work.

**Increasing opportunities and inclusion within the ISSCR**

I entered academia at a time when heavy bias made it challenging and yet critical for women scientists to succeed. As I rose through the ranks, I became ever more devoted toward paving routes for talented younger women to shine. In taking the ISSCR helm in 2010, I wanted to make sure that as an international society, we functioned scientifically, ethically, and morally as a world of scientists from all countries, inclusive of all genders and ethnic backgrounds. My agenda included involving a younger, more international cohort of scientists in the Society and creating more opportunities for their professional development. I also wanted to intensify Society efforts to provide educational tools for students, science writers, policy makers, and the public. As the focus of stem cell research in the world, the ISSCR needed to set an example of inclusiveness and also establish educational resources to convey what stem cell research is all about and what its promise and potential concerns are for regenerative medicine and human disease. A decade later, it is wonderful to see how these initiatives have been further developed and broadened by subsequent leaders and to witness the plethora of new initiatives launched. I’ve long felt that what makes this society special is its cohesiveness, openness, and sense of community. The ISSCR remains in good hands.

**The Annual Meeting in Japan that almost didn’t happen and the maturation of the Society**

When I became president after the 2011 Toronto meeting, there were significant discussions about whether the attendance to the 2012 meeting in Yokohama would be affected by the recovery from the tsunami that devastated Japan’s northeastern coast and triggered meltdowns at the Fukushima nuclear power plant. Shinya Yamanaka was President-elect and emphasized to all of us how important it was to have a good turnout for the annual meeting and not to consider moving it to another location. In the end, the turnout was great, as was the meeting, with help from many including the program chair that year, Larry Goldstein. We even had a gathering in an impressive building where we were honored by a visit and welcome from Emperor Akihito and Empress Michiko of Japan.

During my term, we had many discussions and reviewed bids from various publishing companies regarding having our own society journal, but it was not until 2013 that we finally established *Stem Cell Reports* as the official journal of ISSCR. We also held our first strategic planning sessions in December of 2011 in New York City and subsequently formulated the ISSCR’s priorities for the future. Another major event for the Society was our separation from the managing firm Sherwood Group and the hiring of Nancy Witty as our first independent executive director—a crucial step forward for the ISSCR.
**Stem Cell Reports is launched**

The biggest achievement during my presidency was the launch of *Stem Cell Reports*. I was able to bring then leaders of *Cell Press* back to the discussion with ISSCR regarding the establishment of a new journal. I am glad that the journal has been successful thanks to Christine Mummery, Martin Pera, and other editors and staff members. I am confident that the journal will continue to grow and play even more important roles as the communication tool of ISSCR to the entire scientific society.

**Organoids emerging and controversies challenging the integrity of the field**

The beginning of my year as president of ISSCR coincided with the launch of the Society's journal, *Stem Cell Reports*, which has rapidly become a key part of the ISSCR's mission to promote research excellence and be the trusted voice of stem cell science worldwide. Maintaining the integrity of stem cell science was front and center in 2013/2014, with controversies arising from false claims of novel reprogramming methods and with ongoing issues of clinics promoting unproven stem cell therapies. I was proud to see how ISSCR and its members addressed these issues with rigorous science and public outreach.

On the science side, modeling organogenesis with stem-cell-derived organoids was a hot topic. Madeleine Lancaster, Jurgen Knoblich, and colleagues published their remarkable experiments generating cerebral organoids from human pluripotent stem cells, building upon the foundational work of Yoshiki Sasai. Jeffrey Beekman, Hans Clevers, and colleagues showed how intestinal organoids from patients with cystic fibrosis could be used to assess patient-specific responses to drug treatments. These and other studies presaged the ongoing explosion of interest in stem-cell-derived models of all aspects of human development, from the early embryo, through organ development, to adult tissue homeostasis. Developmental biology has been deeply embedded in ISSCR since its inception, and it is exciting to see the continued importance of this linkage today.
Launching the ISSCR public-policy program
With the advent of embryonic stem cell (ESC) research, debates about stem cell ethics and regulation became front-page news. Some politicians began attempting to undermine the research for political or ideological reasons. Stem cell biologists would have to defend the work if we wanted it to continue.

ISSCR had a small staff and little capacity to engage in public policy during its early years. ISSCR members played leadership roles in educating policymakers about stem cell research, but we were organized by the American Society for Cell Biology, which had an established public-policy program and experienced staff.

This taught us a lot about how to influence policy. We learned that the public strongly believed in the potential of stem cell research to cure disease and broadly opposed restrictions. Opponents of the science also knew this, so their strategy was to undermine support by misrepresenting the science to spread fear and confusion. They falsely argued that scores of diseases could already be cured with “adult” stem cells, that ESCs would never yield new treatments, and that the research would lead to human cloning. Of course, none of that was ever true. By reminding policymakers, over and over again, of the truth about the research and its potential to reduce human suffering, we won every public-policy battle we engaged in. Today, derivatives of ESCs are being tested in clinical trials for several major public-health problems.

Recognizing the need for an organization to defend stem cell research internationally, I created the ISSCR Public Policy Program in 2015 when I was elected ISSCR President. It has been one of ISSCR’s most prominent and successful programs. It played a leadership role in defending fetal tissue research and opposing the premature commercialization of unproven stem cell therapies in many countries.

Stem cell research will only deliver on its promise if we explain it to the general public and defend it to policy makers. Working with my ISSCR colleagues to do that has been one of the most rewarding things in my career.

Increasing support for the clinical translation of stem cell science
Along with advances in human stem cell technologies came burgeoning advances and excitement for anticipated stem cell therapies, exemplified by landmark clinical trials of retinal pigment epithelial cell implantation for patients with age-related macular degeneration. This transition of stem cell research to clinical therapies led us to increase support for clinical activities during my presidency in 2016–2017. We asked, how could we help the ISSCR community advance the wealth of discoveries being made in stem cell research labs and bridge efficiently through to clinical studies? To create a roadmap, we initiated key clinical translation training programs and highlighted clinical sessions at the annual meeting. These programs continue to be a hugely successful aspect of ISSCR today. It was clear at that time that stem cell research was diversifying to impact a wider array of disciplines, with an ever-growing international presence. ISSCR embraced this diversity and provided a platform to include scientists working in different disciplines, women and men at all career stages and from different backgrounds and experiences. The program committee worked hard to ensure that the 2017 annual meeting reflected this growing diversity. We were also thrilled to honor the recipients of ISSCR awards: Jayaraj
Rajagopal, George Daley, Elaine Fuchs, John Dick, Adrian Thrasher, Magdalena Zernicka-Goetz, and Margaret Goodell. I am honored to have served the ISSCR community as president.

A groundbreaking proof of principle approach: the use of gene-edited stem cells to treat JEB

Some 40 years ago, Howard Green described the first long-term culture of normal human cells: keratinocytes were cultured on irradiated mouse fibroblast feeders and formed a stratified epidermis. Successive improvements yielded large sheets of epidermis starting from very few primary keratinocytes. These cultured epidermal sheets were successfully used to treat two third-degree-burn patients in 1980. In a particularly dramatic demonstration, the approach was shown to be life saving for the 5-year-old Jamie Selby and his 6-year-old brother Glen, who had both sustained burns over >95% of their skin.

My ISSCR presidency year witnessed another tour de force of the Green approach. Patients with a rare genetic disease called junctional epidermolysis bullosa (JEB) suffer from severe blistering. JEB patients express mutant laminin-332 protein, which normally serves as glue between skin layers. A team led by Michele de Luca isolated skin stem cells from a 7-year-old JEB patient who had lost 80% of his skin. The cultured cells were repaired by introducing the missing gene. Then, sheets of healthy skin were transplanted. Two years later, the transplanted skin remained firmly adhered to the underlying layers. De Luca and his colleagues thus provided a groundbreaking example of combining stem cell therapy with gene therapy. The study argues that restoration of mutated genes may best be accomplished on stem cells in culture—outside a patient’s body—prior to transplantation.

Connecting stakeholders and the start of the virtual meeting

My tenure as president of ISSCR from 2019–2020 began with the recognition that the stem cell and regenerative medicine field had reached an inflection point. After over 20 years of rigorous investigations and seminal discoveries, it was clear the upcoming decade would finally witness the impact of this work for patients suffering from myriad diseases. We therefore prioritized the interface between scientists and the commercial sector to move discoveries faster to clinical trials. We fostered a deeper engagement of scientists with leaders from venture capital, biotech, pharma, and regulatory sectors through activities such as the Nucleus Forum and the direct matching of key stakeholders. We also included disease- or organ-based tracks throughout the programming of the ISSCR Annual Meeting and emphasized translational advancements.

Of course, 3 months before the Annual Meeting, the world changed. Coronavirus 2019 (COVID-19) spread across the globe, and we made the difficult decision to hold an entirely virtual meeting. ISSCR leadership executed this admirably and quickly. By June, thousands of meeting participants found themselves engaged in surprisingly stimulating interactions through real-time chats during live talks. Discussions reached a depth and intensity online that had never been seen in an auditorium of 3,000 people. Watching virtual interactions bring scientists closer has been an unexpected reward through this difficult period. I expect and hope this fundamental shift in how we work together will continue to unfold even post-pandemic.
The question of women in science

More than 150 years after the appointment of the first female university professors, why is there still a question about women in science? Why in science, where enquiring minds should open every door, is there not equal representation from all genders and races at every level of academia and industry? Why are women more likely to think that their work is not ready for “prime time” and decline opportunities, including speaking at ISSCR meetings? In 2019, we launched a Women in Science panel at the annual meeting to discuss these issues and more.

Three panels, from 2019–2021, showcased the careers and lives of successful women from a variety of fields, countries, and career stages. Esteemed panelists examined unique communication challenges women face in male-dominated fields, how to achieve career independence, and ways that our community can work together toward solutions. Together, we discussed how we have experienced gender bias, hierarchy, and power, advice for listeners of all genders, and what we can do collectively to mentor and promote women in science. This year, we will continue the conversation with the broader lens of equity, diversity, and inclusion.

Chairing these panels was among my most enriching experiences as ISSCR president: what an amazing group of women we have in the stem cell field! I look forward to our continued progress and the days when our speaker invitations are accepted immediately by all!

Delivering the science and its advances: the challenges now and those that lie ahead

As the current president of ISSCR, I am excited about the diversity of amazing outcomes from our field. The past 18 months has seen everything from the generation of pluripotent-stem-cell-derived models of blastocysts to “first in man” clinical trials for pluripotent stem cell therapies in diabetes. As the current ISSCR President, my presidency saw the release of the 2021 ISSCR Guidelines for Stem Cell Research and Clinical Translation and the initiation of the Standards Initiative as well as our most successful membership survey, from which we hope to deliver a revised strategic plan for the Society. We have also broadened the international reach of our policy work and are working on ways to broaden our engagement with industry to ensure the delivery of stem cell outcomes for the community. It would be impossible not to list dealing with the COVID-19 pandemic as a major challenge, but also as a key achievement, for ISSCR. Our capacity to pivot to an “online” scientific agenda that both enabled continued communication and contact with our members but also enhanced our ability to reach new audiences has sharpened what we can deliver into the future. Moving forward, our focus needs to be on supporting stem cell research across the globe to ensure equitable outcomes for patients into the future.

CONFLICT OF INTERESTS

G.Q.D. holds equity or receives consulting fees from 28/7 Therapeutics, an unnamed subsidiary of Elevate Bio, and MPM Capital, and he is a member of the Cell Stem Cell advisory board. C.L.M. is an associate editor at Stem Cell Reports. S.T. is on the Stem Cell Reports editorial board. G.K. is a founding investigator and a paid advisor for BlueRock Therapeutics LP, a paid consultant for Vistagen Therapeutics, and a member of the board of Anagenesis Biotechnologies. L.Z. is a founder and stockholder of Fate Therapeutics, CAMP4 Therapeutics, Amagma Therapeutics, Scholar Rock, and Branch Biosciences, and he is a consultant.
for Celularity and Cellarity. J.R. is a member of the editorial board of *Stem Cell Reports* and a member of the board of directors for Notch Therapeutics. F.M.W. is on the editorial board of *Cell Stem Cell* and *Stem Cell Reports*, a founder of Fibrodyne, and a trustee of Our Future Health. E.F. is on the editorial board of *Stem Cell Reports*, *Cell*, *Cell Stem Cell*, *Developmental Cell*, and the *Journal of Cell Biology*, has served on the SAB of L’Oreal and Arsenal Biosciences, owns stock in Arsenal Biosciences, and is currently serving on the scientific advisory board (SAB) of Harvard MGH, Cambridge Cancer Center UK, Huntsman Cancer Institute, Northwestern U Skin Center, and the Klarman Observatory at the Broad Institute. D.S. is a co-founder and member of the board of directors of Tenaya Therapeutics and has equity in Tenaya Therapeutics. S.M. is a founder and SAB member for Garuda Therapeutics and Kojin Therapeutics, a SAB member for Ona Therapeutics and Frequency Therapeutics, and a stockholder in G1 Therapeutics.