

INTRODUCTION

The Stem Cell Network (SCN), now in its 20th year, is arguably one of Canada's most successful national research and training networks. Throughout its 20 years, SCN has been guided by strategic plans focused on research, training and outreach and engagement. Today, with the acceleration of activity in regenerative medicine, a field largely fueled by stem cells, the timing is right to consider how we can build and grow SCN and Canada's regenerative medicine research ecosystem to ensure its continued impact. To that end, SCN is developing its new strategic plan for the period 2022 to 2025. It will focus on growing the network to embrace the challenges of regenerative medicine and will fuel the innovative, translational, and entrepreneurial spirit of Canada's research community. As part of the process of developing its new strategic growth plan, SCN conducted consultations between December 2020 and March 2021 with the research and training community to seek input and ideas. This document summarizes the content and themes raised during those cross-country consultations.

An SCN growth strategy

Consultations were based on SCN's conceptual vision for the future of stem cell research in Canada:

To deliver innovative "Made in Canada" regenerative medicine solutions by growing Canada's Stem Cell Network to include emerging disciplines that will power regenerative medicine for generations.

Such a strategy would allow SCN to strategically fund research that starts with stem cells but branches out to other areas such as immunotherapy for regenerative purposes; synthetic biology, tissue engineering; and gene therapy; to develop state-of-the-art approaches to treat chronic disease and illness; and further therapeutic and transplant practices to cure illnesses such as neurodegenerative diseases, blindness, blood cancers and organ and wound repair.

The initial objectives for this growth strategy would be:

- To lead in the development and translation of regenerative medicine therapies and technologies from bench, to bedside, to marketplace for the benefit of Canada;
- To further enhance Canada's regenerative medicine community through networking, research, training and outreach; and
- To provide national leadership in regenerative medicine by enabling research collaborations that will ultimately deliver health and economic benefits for all.

Between December and March 2021, SCN held eight roundtable sessions with trainees, early, mid and senior career investigators, clinicians and biotech and community leaders. Overall, approximately 100 people from across Canada took part in the sessions. Participants were asked to consider the following questions:

- Is there value in growing the Network at this time? Can an expanded Network be of benefit for you and your research team? If yes, how?
- 2. What are the grand challenges that need to be addressed to propel the RM field forward? Should the Network focus its funding to address those challenges?
- 3. SCN currently runs four core funding programs (clinical trials, accelerating clinical translation, fueling biotechs, translation and society). SCN also introduced a new program for early-career investigators in 2020. Do you believe these types of programs to be targeted correctly or are there other options/approaches that should be considered?

COMBINING IMMUNOTHERAPY & STEM CELL RESEARCH FOR REGENERATIVE MEDICINE

Targeted cell-based immunotherapies, which use genetically modified cytotoxic T cells or natural killer (NK) immune cells, are showing great promise as next-generation therapeutics for treating cancer. Immunotherapies also have the potential to treat other conditions, such as degenerative diseases like muscular dystrophy, or cardiac infarcts.

Immunotherapies sourced from patients yield limited numbers of cells, making the scaling of treatments difficult. However, pluripotent stem cells have unlimited expansion capacity and can be generated from adult patients. They are easy to genetically modify and are a scalable source of both T cells and NK cells. Combining these advances with new regenerative applications will drive an upsurge in research, development and commercialization of immunotherapies for regenerative medicine.

This document provides a summary of the feedback that was received during the consultations. It is important to note that not all comments are reflected within this document. Rather, it outlines the major themes and issues that arose across the sessions. These are:

- growing SCN;
- value and niche of SCN;
- extending research support across the research continuum; and
- supporting trainees for career success.

GROWING THE NETWORK

The key conclusion to arise from these consultations was a consensus for growing the Stem Cell Network to be more encompassing of regenerative medicine (RM). This was viewed as a positive step that will give more room to develop strategic partnerships with other investigators and organizations in the broader field of RM. It would also allow the Network to attract early-career researchers into the community, especially those from different disciplines. For the ethical, legal and social implications (ELSI) research community, it was felt that a broadened Network would allow investigators to take on research that goes beyond stem cells

but is still relevant to stem cell research. At the same time, though, participants highlighted that stem cell research is at the heart of the Network and in the process of growing the Network, this should not be lost, forgotten or misplaced.

VALUE & NICHE OF THE NETWORK

When asked to consider the value of the Network, several themes emerged, including collaboration, unique funding environment and support for high-risk research, training and support for early-stage investigators, and the opportunities it provides for networking and engagement.

Collaboration

Enabling research collaborations was seen as one of the key benefits of the Network. Participants believed that the Network fosters these collaborations by using a multi-disciplinary team approach that allows those with different skills and expertise to come together on specific projects. SCN collaborations are thought to be productive and are useful for conceptualizing, designing and conducting key experiments for the overall project. It was also noted that these collaborations result in useful sharing of data and

SCN'S NICHE -AS DESCRIBED BY PARTICIPANTS

- Strategic focus on stem cells for regenerative medicine
- A national perspective/focus that has created a Canadian community
- Enabling collaborative research teams
- Convening power to bring today and tomorrow's stem cell leaders together
- Unique training support that gives HQP access to skills, people and resources.

joint publishing of high-quality papers. The value of collaboration was reinforced by participants who noted that they have used other lab teams from across SCN to help validate research findings to support translation and attract investment. In addition, by utilizing teams in other research institutions to conduct validation work, publication outputs have been enhanced.

Unique funding environment

Participants noted that SCN's targeted focus on stem cell science for RM has been of importance, as the large funding agencies do not have a strategic focus in this space; nor do they have peer review panels to assess stem cell-centric applications. It was strongly felt that SCN funding helps to create momentum for innovative research programs and supports them as they develop and move across the research pipeline. SCN's support of hemopoietic stem cell research was referenced as an example of a program that has benefitted from this approach. Community members are interested in seeing this method continue to be employed in the coming years.

Participants also acknowledged SCN support for high-risk research projects that would not likely be funded elsewhere because preliminary data are not available. For instance, this support led to the spinoff of a Quebec-based company, Morphocell, that is now planning on conducting clinical trials to treat liver disease with advanced tissue engineering. SCN funding support has also helped to spur pre-clinical and clinical research as it offsets costs for large animal studies,

biomanufacturing and regulatory prep work. Without this support, it would be difficult to move an academic research program into translation.

Training

The unique value of SCN for both trainees and early career researchers is that it provides a base from which they can develop skills, professional networks and research programs that set them on track to becoming fully immersed in the stem cell and regenerative medicine field. Some stressed that if it were not for SCN, they would have looked to other countries and fields of study that are better funded. However, because SCN has provided them with key supports, including training, mentors and access to resources, they have chosen to focus on regenerative medicine. Principal Investigators (PIs), for their part, indicated SCN has been an effective and efficient way to identify new recruits for their labs. They hope SCN will be able to further enhance its supports for identifying and recruiting HQP for their labs in the future.

Networking and engagement

The annual scientific Till & McCulloch Meetings (TMM) is seen as a highlight of each year, providing Canada's stem cell community the opportunity to come together to share and learn from each other about the opportunities, trends and challenges in the field. Participants noted its importance for kickstarting new research partnerships and projects.

The TMM also provides important opportunities for trainees to present their research through talks and poster presentations. Trainees are able to interact with Canadian and international experts and develop professional networks with peers and others. In addition, the meetings attract high-profile scientific speakers, industry participation and patients who have been part of a stem cell trial. Some consultation participants noted appreciation for these elements along with new initiatives that have been introduced on equity, diversity and inclusion. Overall, the consultation process highlighted the importance of TMM and the unique convening power of the Network.

EXTENDING RESEARCH SUPPORT ACROSS THE CONTINUUM

The message across all consultation groups was clear – stable and strategic funding of research across the research continuum, from innovation to translation, is essential. Such support will better position Canada to compete internationally and bring forward the therapies and technologies that will see Canada's regenerative medicine sector flourish over the coming decade. SCN is the only national network that provides strategic support for stem cell research and as such it should provide for innovative, pre-clinical, clinical and commercially focused research.

SCN BY THE NUMBERS: 2001-2021

- \$118M for research, training & outreach
- \$125M in research partnerships
- 196 research teams
- 3,362 trainees & HQP supported
- 24 clinical trials
- 21 companies created or enhanced
- 115+ Network members & partners

(As of March 31, 2021)

SCN's funding programs require a balance that takes into account the full range of activities needed to support high-quality outputs, from small individual researcher-driven awards to large-scale team awards that address significant scientific challenges and support the translation of regenerative medicine. Participants noted that the multi-disciplinary team approach has always been a success for SCN and helps to spur innovative activity that leads to real translational successes. Many also observed the need to have longer timeframes (five years plus) to conduct their research and build partnerships. This timing, along with an opportunity to have awards renewed, would be transformative and allow Canada's research teams to excel.

Within that broader context, several themes emerged:

- Equipping SCN to respond to the future challenges of RM: Participants suggested that SCN community members are particularly well positioned to identify and address the major hurdles for RM and assemble diverse teams to address them and bring new technologies forward, thereby maintaining the investigator-led approach that has worked for the Network over its 20-year history.
- Awareness of the high costs of translational research: Translational research carries with it associated costs often not considered in project funding, among them such things as biomanufacturing, preparation for regulatory approvals, and working with patients and clinicians on protocol design. Testing in large animal models is often required before bringing a cell therapy or drug to the clinical trial stage. To do this is expensive but also important for validation. As such, participants recommended that SCN consider these factors when developing translational research funding programs, as current SCN awards do not cover these costs and finding partners in the current environment has become increasingly difficult. In addition, participants wanted such translational funding support to be accompanied by more education and resources about the tools and skills needed to carry out translational research.
- Jump start for early-career researchers: Early-career researchers noted a specific need to have opportunities to build their networks and brand their areas of expertise and interest. As such, they are looking to SCN to provide platforms for them to share their research and provide targeted funding that will help to jump start their research programs. They noted that, as they are at the start of their career, their focus is not typically translational but could lead to translational work down the road. As such, what is required are awards that will assist them in assembling preliminary data that can be used to secure larger awards and develop a publication track record from which to build. Providing "jump start" awards would better position these researchers to stay within the regenerative medicine field rather than having to turn elsewhere or leave academia altogether.
- Meeting the specific needs of ELSI research: Members of the ELSI community raised the importance of capacity building through fellowships and/or scholarship programs. They noted that small amounts of funding and short timelines to conduct research serve as disincentives for taking on new research and recruiting the next generation of talent. Team awards with longer timeframes and larger budgets would allow greater flexibility and more

in-depth research to bring to bear on the social, ethical and legal topics relevant to regenerative medicine. Open science, bio-banking, gene-editing and health economics of cell and gene therapies were all noted as areas where ELSI research is required to advance the field of regenerative medicine. Members of this community proposed that a large-scale program award, or platform grant, be made available. Such an approach would lend itself to a hub and spoke model, allowing investigators and research associates to take on different topics associated within the overall main theme.

BUILDING ON TRAINING SUCCESSES

The Stem Cell Network's training program was widely viewed to be one of its most valuable aspects. Over the past two decades, more than 3,300 trainees have participated in SCN workshops, TMM events, hands-on learning and exchanges. Trainees noted the value of being part of a network that allows them to interact and learn directly from established researchers from across the country, interactions that encourage mentoring and support career progression.

Nonetheless, the consultations provided a range of suggestions for areas where SCN could expand its training activities. For instance, during the consultation sessions, trainees noted the high costs of pursuing a career in research – both the financial costs of pursuing PhDs and working as post docs and, once that is done, the uncertainty of being able to maintain their careers in the face of declining funding supports. Some expressed concern that they may not be able to stick with the stem cell and regenerative medicine field, and maybe required to pivot to an area where greater funding opportunities exist.

To supplement support already offered by SCN, trainees would like to see SCN able to offer direct stipends, fellowships and targeted awards. They would also like SCN to offer a variety of training programs on topics such as designing a translational research program, the fundamentals of manufacturing and requirements for regulatory approvals – all areas not traditionally covered in academic training. In addition, trainee participants noted that not all trainees will have academic labs and therefore SCN should be assisting them with pursuing alternative career paths, such as in the biotech, policy and science communication fields. Trainees noted they would like greater exposure on how to engage with industry and have the opportunity to learn key skills needed to work within an RM company. Mentoring was also a concern, with trainees asking that SCN develop a formal mentoring program that would help to match them with established researchers from across the network and that SCN provide forums and tools that can be used to facilitate successful and effective mentoring.

Early-career researchers (ECRs) felt that they had benefitted strongly from their time as trainees, but would like to see that support continue, through **a formal training program and committee established specifically to support them** as they work to develop their research focus and programs. A training program could help ECRs deal with the practical side of managing a lab, including human resources, budgets, projects, grant writing and publication

requirements. A committee would be of value for developing networks and building visibility for this generation of talent.

Finally, it is important to note the enthusiasm of both trainees and early career investigators for providing science education for the public and assisting with attracting a new generation to pursue careers in the regenerative medicine field. A number of trainees expressed concern regarding a decline in public trust of science and the increasing level of disinformation that is circulating online and in other public forums. As such, they expressed a desire to work with SCN on developing a robust public outreach program to push back on these trends; as well as to attract a more diverse group of individuals into the field.

OTHER COMMENTS & FEEDBACK

Talent Recruitment

Participants were clearly aware of the intense competition for talent in a dynamic and growing area such as stem cell research and RM. They had several suggestions for ways to make it easier to recruit talent, including:

- Tiered membership that would allow unfunded researchers to participate in SCN events such as TMM without having to absorb expensive registration fees for themselves and trainees. Having access to TMM is one avenue that can be used for recruitment purposes.
- Creation of a mechanism to allow industry or biotech companies to officially be part of the Stem Cell Network in return for access to events and other services.
- Development of an external databank to allow investigators to identify and recruit talent for their labs. Such a databank could also include an industry career recruitment portal.

Outreach

SCN regularly engages with federal and provincial government policy and decision-makers to promote stem cell and regenerative medicine research. Participants encouraged the organization to continue and expand this outreach and also noted that ECRs and trainees could benefit from the opportunity to engage with decision-makers and to provide support to government in advisory capacities.

Participants also considered the question of international outreach to promote Canadian stem cell research. This was an original area of strength for SCN but, due to the instability of the network in recent years, the focus has been diminished. Participants believed SCN requires greater resources to engage at the international level so that Canadians are better positioned to lead and take part in international activities. In addition, participants wanted to see SCN providing support for researchers to participate and speak at international conferences and symposiums. It was recommended that SCN identify approximately three international partners to develop new relationships with; their suggestions included the UK, US, Japan and Germany.

Equity, Diversity & Inclusion

Participants viewed SCN's efforts to support Equity, Diversity and Inclusion (EDI) practices over the past three years as both positive and important first steps for creating greater awareness about both EDI and unconscious bias. They stressed the importance of ensuring EDI is reflected in everything SCN does. This should include:

- requiring that funded research teams are diverse in both make-up and career stages;
- assessing research projects for sex and gender dimensions (e.g., using animal models that are both male & female);
- ensuring membership of panels at SCN events are diverse in terms of both race and gender;
- establishing SCN governance that reflects gender, racial and regional diversity; and
- working to develop partnerships that will engage indigenous communities and assist in communicating with different populations across Canadian society.

CONCLUSION

The timing is right for SCN to further develop and grow. The community sees clear benefit from a growth strategy and an opportunity to further advance the fields of stem cell research and RM. Elements of a growth strategy would include maintaining SCN's national leadership role, driving forward outstanding research and training support and providing the critical funding necessary to remain competitive.

In April 2021, the Government of Canada made a new commitment of \$45M to the Stem Cell Network for the 2022-2025 period. This investment more than doubles SCN's annual budget and is an important first step for growing the Network. Based on the feedback provided by the research community, SCN partners, and the expectations of government a new strategic plan for 2022-2025 period will be developed and released by early 2022.