DRIVING GLOBAL COMMERCIALIZATION

CCRM IN REVIEW

CCRM

Centre for Commercialization of
Regenerative Medicine

REMARKABLE. REGENERATIVE. REVOLUTIONARY.

CENTRE FOR COMMERCIALIZATION OF REGENERATIVE MEDICINE (CCRM)

CCRM is a Canadian, not-for-profit organization supporting the development of foundational technologies that accelerate the commercialization of stem cell- and biomaterials-based products and therapies. CCRM is supported by the Centres of Excellence for Commercialization and Research (CECR) program.

Regenerative medicine, which aims to harness the power of stem cells, biomaterials and molecules to repair, regenerate or replace diseased cells, tissues and organs, has the promise to treat, manage and perhaps cure some of the most devastating and costly diseases in the world today.

Many new and potentially life-changing regenerative medicine-based treatments never reach patients because they are not successfully moved from the laboratory to the clinic. In order to fulfill regenerative medicine's promise to treat the many diseases affecting our population, a world-renowned group of stem cell scientists and bioengineers have come together to form the Centre for Commercialization of Regenerative Medicine (CCRM).

CONTENTS

CCRM is a network that bridges the regenerative medicine commercialization gap by leveraging funding and infrastructure, and mobilizing business and scientific expertise to translate technologies into commercial products and therapies. CCRM's mission is to create and sustain a global nexus for company creation, technology and cell therapy development, and clinical trials in regenerative medicine.

We ENABLE
product development through unique translational platforms that address the key bottlenecks in regenerative medicine commercialization.

We INTEGRATE
Canada's strength in stem cell and biomaterials sciences with dynamic business leadership.

We ENGAGE
through a consortium of leading companies that provide market pull and act as receptors.

CCRM IN REVIEW
EXECUTIVE MESSAGE

Left to Right:

Peter Zandstra
Chief Scientific Officer
Centre for Commercialization of Regenerative Medicine

Greg Bonfiglio
Chair, Board of Directors
Centre for Commercialization of Regenerative Medicine

Michael May
President and CEO
Centre for Commercialization of Regenerative Medicine

Canada is recognized as a leader in stem cell and bioengineering science. Across the country, there are over 400 stem cell scientists working in 68 research centres within, or affiliated with, 25 of Canada's universities where stem cell or regenerative medicine research is conducted[1]. Within these institutions, there are thousands of trainees working in the field. With so many people engaged in Canada's regenerative medicine community, the output is tremendous. In this prolific environment, founding the Centre for Commercialization of Regenerative Medicine (CCRM) was a logical next step to help move discoveries from the bench into the marketplace.

Back in 2010, the academic leaders in the field, coordinated by the success of Canada's Stem Cell Network, applied to the Government of Canada to become a Centre of Excellence for Commercialization and Research (CECR), a program of the Networks of Centres of Excellence. In 2011, CCRM was awarded $15 million for five years to launch a global hub of regenerative medicine commercialization to coordinate the sourcing and diligence of intellectual property, accelerate technology development, support clinical translation and incubate new companies built around strong bundles of technologies. Our plan involved unifying dynamic business leadership with high value innovative translational technology platforms based on demonstrated excellence in fundamental stem cell and bioengineering science. *Enabling* product development with dedicated personnel and facilities, *Integrating* business and scientific leadership, and *Engaging* partners to create a vibrant ecosystem for commercialization has become CCRM's mantra.

This report captures the first two years of CCRM. It was produced at the same time that the organization was conducting a mid-term strategic review. By reflecting on our accomplishments to-date and refining our strategic focus, we aim to maintain our momentum, carving a pathway to success and sustainability in the future.

Our first year, dating back to our launch in June 2011, was focused on hiring personnel, equipping our development facility, forging national and international networks of regenerative medicine business and scientific leaders, and implementing operational and financial processes to build a viable, well-governed centre.

Fast forward to year two when our focus changed to deal flow: commencing co-development projects with industry partners, conducting due diligence on more than 100 discoveries funneled through our institutional partners, funding research grants with partners – like the McEwen Centre for Regenerative Medicine – and building international awareness of CCRM.

At the end of year two, we prioritized six company creations around international bundles of technologies and we are actively engaging with a growing consortium of leading regenerative medicine companies.

Whether you are learning about CCRM for the first time or you have been following our achievements since day one, we hope you enjoy this report as it attempts to capture our significant moments and the opportunities that we feel lie ahead. In the coming months we will launch companies, announce new (funding) partnerships and help the community coordinate clinical capacity so that some of our most promising therapies will move to patients more quickly.

We are proud of the team that we have assembled and grateful to the world-renowned experts who advise CCRM through the Board of Directors, Strategic Advisory Board, Commercialization Review Committee and Founders Advisory Board.

Finally, we would like to acknowledge the support of our institutional partners, our Industry Consortium and the international regenerative medicine community, which has embraced our unique commercialization model with enthusiasm. In particular, we would like to acknowledge our host institution, the University of Toronto, and the Networks of Centres of Excellence.

[1] *Canadian Asset Map for Stem Cell and Regenerative Medicine*, Industry Canada, 2012

CCRM: THE NETWORK

INSTITUTIONAL PARTNERS

CCRM, with its partners, will deliver on the promise to make Canada a global leader in regenerative medicine discovery, translation and commercialization.

CCRM

IP In-licensing

Cell Therapeutics

EXTERNAL IP

CCRM is collaborating with translation centres around the globe to source the best intellectual property (IP) to develop for our industry partners and to bundle into new companies.

CLINICAL VALIDATION

SCIENTIFIC LEADERSHIP

CCRM is fortunate to have some of Canada's and the world's best academic minds guiding CCRM's operations and vision. (See page 21 for complete list.)

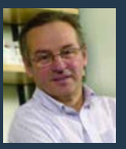
Local Leadership – Founders Advisory Board


Bhatia


Ellis


Keller


Rossant


Nagy


Keating


Shoichet


Stanford


Zandstra


Rudnicki


Sefton

BUSINESS LEADERSHIP

CCRM has access to some of the best business minds in regenerative medicine – leaders with proven track records in regenerative medicine commercialization. (See page 21 for complete list.)

DEDICATED COMMERCIALIZATION TEAM

- IP diligence and bundling
- Core development and manufacturing facilities
- Company incubation
- Contract research services

Technology pull & Co-development $$

Complementary resources, Analytical support

Out-licensing

High value technologies

INDUSTRY CONSORTIUM

CCRM's industry consortium is composed of leading companies that represent key sectors of the regenerative medicine industry – pharmaceutical, devices, reagents, tools, biomaterials and cell therapies. (See page 20 for complete list.)

NEW RM COMPANY CREATION

HIGHLIGHTS 2011–2013

CCRM is Funded

June 14, 2011 – CCRM formally launches after receiving $15M from the Government of Canada's Networks of Centres of Excellence (NCE) Secretariat to operate as a Centre of Excellence for the Commercialization of Research (CECR). Five CECRs are funded in the 2010 competition.

Industry Consortium & 1st Project

March 9, 2012 – CCRM announces that it has created an industry consortium that will work together to address real-life regenerative medicine bottlenecks, provide market pull and be ready receptors for new technologies. The 20 companies have since grown to 29. This is a crucial milestone for CCRM as it fulfills the "Engage" pillar of its strategy. A few days later, CCRM announces its first industry project with EMD Millipore, the Life Sciences division of Merck KGaA. The joint project involves translating 2D tissue culture vessels into 3D tissue bioreactors in order to facilitate large-scale cultivation of stem cells to accelerate the progress of therapies into the clinic. Today CCRM has eight projects in development, not counting those that have been completed.

Innovation Fund

April 30, 2012 – Industry consortium member Pfizer Canada establishes a new $1.5M fund with CCRM to stimulate product development and open innovation in the regenerative medicine industry. The Pfizer-CCRM Innovation Fund, financed by both partners, is designed to accelerate regenerative medicine technologies for drug screening and therapeutic applications of mutual interest.

Inaugural Till & McCulloch Meetings

April 30, 2012 – The Stem Cell Network (SCN) and CCRM rebrand SCN's annual general meeting to become the Till & McCulloch Meetings (T&MM), a conference that maintains the excellence of the original event, but broadens its scope to include biomaterials and commercialization. ThéCell and the Ontario Stem Cell Initiative also support the first T&MM. In 2013, SCN and CCRM are co-organizers. CCRM will host the Meetings beginning in 2015.

International Translation Consortium

May 29, 2012 – CCRM leads the creation of the "Regenerative Medicine Coalition (RMC)," a consortium of centres from Europe and North America working together to support global cooperation in translation and commercialization in the field. The launch of the RMC triggers a number of international partnerships, and the promotion of Canadian discovery and commercialization globally.

Love Toronto List

June 2012 – Only a year after its launch, CCRM is included in a top 30 "list of reasons to love Toronto," by the Toronto-centric magazine *Toronto Life*. Coming in at #18, Toronto's stellar stem cell research institutes are referenced and CCRM is named alongside the McEwen Centre for Regenerative Medicine and SickKids' Transplant and Regenerative Medicine Centre.

Commercialization Impact Prize

August 23, 2012 – The McEwen Centre for Regenerative Medicine and CCRM launch the McEwen-CCRM Commercialization Impact Prize to address the challenges of scaling the production of stem cell-based products for clinical use and high throughput drug screening. In 2013, four winning research projects are chosen to share equally in $1.2 million over two years. They are led by Gordon Keller, Peter Zandstra and Andras Nagy, Thomas Waddell, and Derek van der Kooy.

Fee-for-Service Launches

September 2012 – CCRM launches its first fee-for-service offering: reprogramming of somatic cell types to induced pluripotent stem cell (iPSC) lines and a variety of additional services. Subsidies are offered to investigators affiliated with CCRM's member institutions.

"CCRM is a global leader in accelerating the translation and commercialisation of cell therapies," says Chris Mason, Professor of Regenerative Medicine, University College London. "It has created and led many important initiatives and collaborations both within Canada and internationally. The impact of CCRM's innovative activities will undoubtedly greatly benefit patients, companies and society for decades."

First Option

October 1, 2012 – Executing on its commercialization model to in-license and develop promising technologies sourced from its academic network, CCRM executes its first option to license on a versatile, bioresorbable hydrogel technology for cell delivery developed in the laboratory of Professor Molly Shoichet, at the University of Toronto.

Ethics Unit with CGP

February 20, 2013 – CCRM introduces an ethics unit to address ethical, legal and social issues (ELSI) that can arise in the development of regenerative medicine products for commercialization. McGill University's Centre of Genomics and Policy (CGP), a partner with CCRM from the outset, will manage CCRM's ELSI needs, producing standard documents and policies for the community.

Ontario-China Partnership

April 2013 – After 18 months of discussions, an agreement is reached to support a new Ontario-China Stem Cell Partnership involving CCRM, the Ontario Stem Cell Initiative, Ontario's Ministry of Economic Development and Innovation (MEDI) and the Ministry of Science and Technology (MOST) in China. The parties will collaborate on research projects in the following areas: pluripotency, reprogramming and stem cell banking; stem cell differentiation to endoderm and pancreatic lineages; and, blood stem cell expansion and transplantation. Funding is being leveraged from MEDI's Ontario China Research and Innovation Fund and MOST. CCRM will act as the commercialization vehicle for opportunities emerging from the partnership.

Collaboration with the UK Cell Therapy Catapult

May 2013 – CCRM signs a collaboration agreement with the Cell Therapy Catapult, a UK government-funded translation centre, to facilitate co-funding of international initiatives in standardization, the co-development of enabling technologies and the co-support of cell therapy clinical trials in Europe and North America.

Award-Winning Blog

Summer 2013 – Signals Blog is a highly regarded regenerative medicine and stem cell blog produced by the Stem Cell Network and CCRM. It was chosen as a finalist in the Best Blog, Business to Business category by the Canadian Online Publishing Awards (COPA). In November, we learned that we won Silver in our category!

Company Creations

September 2013 – CCRM's Board of Directors approves the creation of six company concepts, employing bundled technologies in CCRM's disclosure pipeline. These companies are being incubated as projects within CCRM, using staff and external consultants, and are slated to be rolled out over the next 18 months.

360ip Collaboration

October 11, 2013 – CCRM signs a collaboration agreement with 360ip, a global technology commercialization, investment and fund management company, to source RM technologies in Asia and to invest in the development, at CCRM, of best-in-class regenerative medicine technologies from around the globe.

RM Video Network

November 4, 2013 – CCRM launches a new RM video information channel using content from its substantial network of partners, including the Stem Cell Network and the Ontario Stem Cell Initiative: www.ccrm.ca/rmnetwork.

ENABLE

PRODUCT DEVELOPMENT

Milica Radisic, *PhD is the Canada Research Chair in Functional Cardiovascular Tissue Engineering and Associate Professor, Institute of Biomaterials and Biomedical Engineering at the University of Toronto*

Capitalizing on the foundation laid by distinguished researchers James Till and Ernest McCulloch, Canada has been able to produce excellent research in the fields of stem cells and bioengineering. The challenge for Canada has been to translate those discoveries into products or therapies that can ultimately benefit the patient.

CCRM has been working with researchers across Canada (and abroad) to determine the market-readiness of their technologies. So far, we have evaluated more than 100 disclosures from our institutional partners and identified five to in-license or bundle as company creations.

Milica Radisic has been working with CCRM to promote a drug-screening platform. The platform, developed by graduate student Nimalan Thavandiran who is co-supervised by Peter Zandstra and Radisic, includes a set of human cardiac micro tissues that are three-dimensional in shape and whose cell composition is precisely controlled to enhance cell maturation and improve contractile function. The cells that make up this human cardiac tissue are derived from human pluripotent stem cells.

Dr. Radisic turned to CCRM expecting that we would provide "a clear path for bringing a product to the market." Although Canadian universities and hospitals have their own tech transfer offices – and CCRM works closely with them through the due diligence and patenting process – Dr. Radisic says working with CCRM has given her trainees, like Nimalan, "an additional source of expertise [to] help them enhance their research projects."

INTEGRATE

BUSINESS AND SCIENCE LEADERSHIP

Board of Directors
Left to Right:

Peter Lewis
Allen Eaves
Geoff MacKay
David Smith
Greg Bonfiglio
Michael May
Peter Zandstra
Lisa Drouillard
Rafi Hofstein
Stephen Minger
Christopher Paige
(Absent: Susan L. Solomon, Duncan Stewart)

A key strength of CCRM is its network.

Business leaders, leading researchers and financiers from Canada and around the world have generously volunteered their time to help us realize our mission.

From the outset, CCRM has been governed by a **Board of Directors** that would be the envy of most not-for-profit organizations. Experienced and engaged, these business and research leaders are committed to finding a better way to advance promising discoveries to the market and to patients. From a venture capitalist who leads the Board to one of Canada's most successful stem cell entrepreneurs to several executives from major Canadian institutions, CCRM's Board is an impressive group.

The business leadership on CCRM's Board is matched by the scientific expertise of CCRM's **Founders Advisory Board**. They are leading Canadian researchers in the field who keep CCRM's development scientists and technicians abreast of the latest scientific trends and help trouble-shoot as needed. Their input is augmented by CCRM's **Strategic Advisory Board**, world-leading experts in stem cells and biomaterials who help us communicate our activities and benchmark us against the best clusters in the world. Our scientific advisors are a "who's who" of stem cell researchers and bioscience engineers in Canada and internationally.

After putting discoveries through a rigorous due diligence process, promising technologies are presented to CCRM's **Commercialization Review Committee**. This committee provides an external perspective from individuals with diverse areas of expertise – business, product development, regulatory and finance, to name a few. The Committee is composed of select individuals from CCRM's Industry Consortium, the Board of Directors, partner technology transfer offices and experts drawn from the wider community. The composition of the committee changes, depending on the technologies being reviewed.

ENGAGE

INDUSTRY PARTNERS

Kim Bure,
North American Business Manager for Regenerative Medicine,
TAP Biosystems

CCRM engages with its industry partners in a number of ways, including co-development projects.

TAP Biosystems is an interdisciplinary engineering company that operates at the interface between life science research and bioprocess development and manufacturing. Although based in the UK, its global reach provides innovative automation systems and consumables worldwide that improve productivity and accelerate time to market.

The ongoing project with TAP involves determining optimal media components and process conditions for culturing natural killer cells and human stem cells in suspension. TAP's ambr™, an advanced parallel micro-bioreactor system that replicates the characteristics of larger bioreactors at a 10-15 mL scale in 24 vessels simultaneously, was installed at CCRM to explore multi-variant design of experiment (DOE) studies.

According to Kim Bure, joining CCRM's industry consortium has yielded many benefits. She is pleased that CCRM has shared real ambr™ data, and quickly, at several conferences, and says this partnership "shines a spotlight on TAP's abilities in the regenerative medicine market [and] has given us great reach into Canada."

Kim also appreciates having access to the academics and industry leaders in CCRM's network. "It would be extremely time consuming for TAP to hunt out IP without the help of CCRM, and there is considerable benefit in the fact that it has been diligently vetted first. At the lightning speed of innovation in this space, there are not enough hours in the day to do this for ourselves."

OUR PEOPLE:

TEAMWORK – MAKING IT HAPPEN

Transitional Catalyst

Nick Timmins
PhD – Director of Product and Process Development

Nick manages the complicated process of turning discoveries into clinically meaningful applications. He leads CCRM's team of scientists and technicians developing research and clinical strategies for new product development. He is more than familiar with this process thanks to a career spent in translational regenerative medicine organizations around the world. Originally from New Zealand, CCRM lured Nick to Canada from Australia.

Brilliant Scientists

Emily Titus
PhD – Project Manager and Scientist

Emily arrived at CCRM with an impressive academic record having received numerous awards and seeing her PhD work result in two *Cell Stem Cell* publications. Since joining CCRM, Emily has continued to excel and has quickly taken on an enormous amount of responsibility managing product development projects and fee-for-service contracts for the Cell Reprogramming and Engineering Platform.

An important element of CCRM's vision is to create new jobs in Canada and to foster a dynamic, exciting environment in which to build a career in regenerative medicine at a unique interface between industry and academia.

Innovative Discoveries

Howard Kim
PhD – Development Scientist

Howard began his professional career at a medical devices company, but knew he wanted to focus on regenerative medicine. Howard's position at CCRM combines his academic background in biomaterials with his industry experience in product development. He was seconded to Cambridge, UK on a co-development project with Pfizer and is now working with Pall to develop a high-sensitivity sensor for measuring protein concentrations.

Solid Leadership

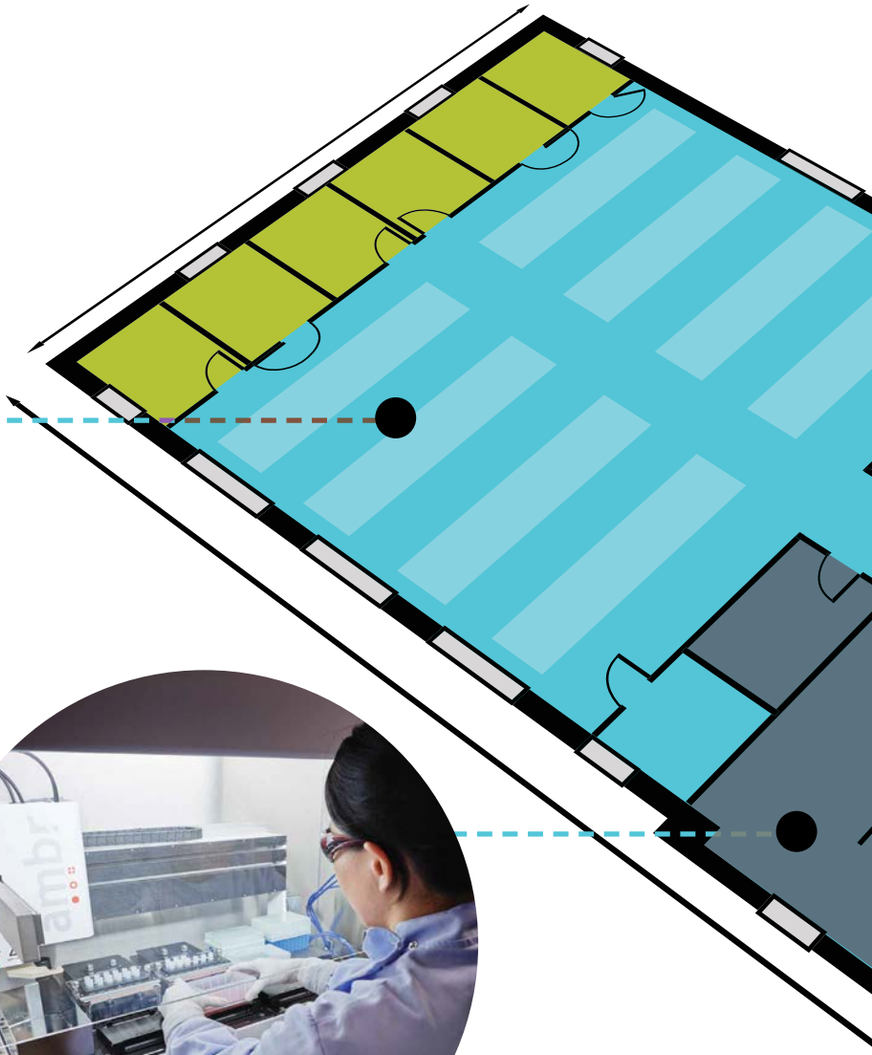
Jennifer Moody
PhD – Director of Operations

Jen cut her teeth in product commercialization at STEMCELL Technologies in Vancouver where she led the R&D team that commercialized pluripotent stem cell products including mTeSR1™. Jen brought her very relevant product development experience to CCRM, first as Manager of Technology Assessment followed by a quick promotion to Director of Operations. When Jen's not managing operational concerns, her industry experience offers valuable insight to CCRM's business development team.

CCRM'S DEVELOPMENT FACILITY

WHERE IT ALL COMES TOGETHER

CCRM's 560 m^2 (6,000 ft^2) facilities feature state-of-the-art technologies operated by knowledgeable staff and supported by world-class scientific leadership. CCRM's development scientists and technologists have expertise in three key areas: cell reprogramming and engineering; cell manufacturing; and, biomaterials.

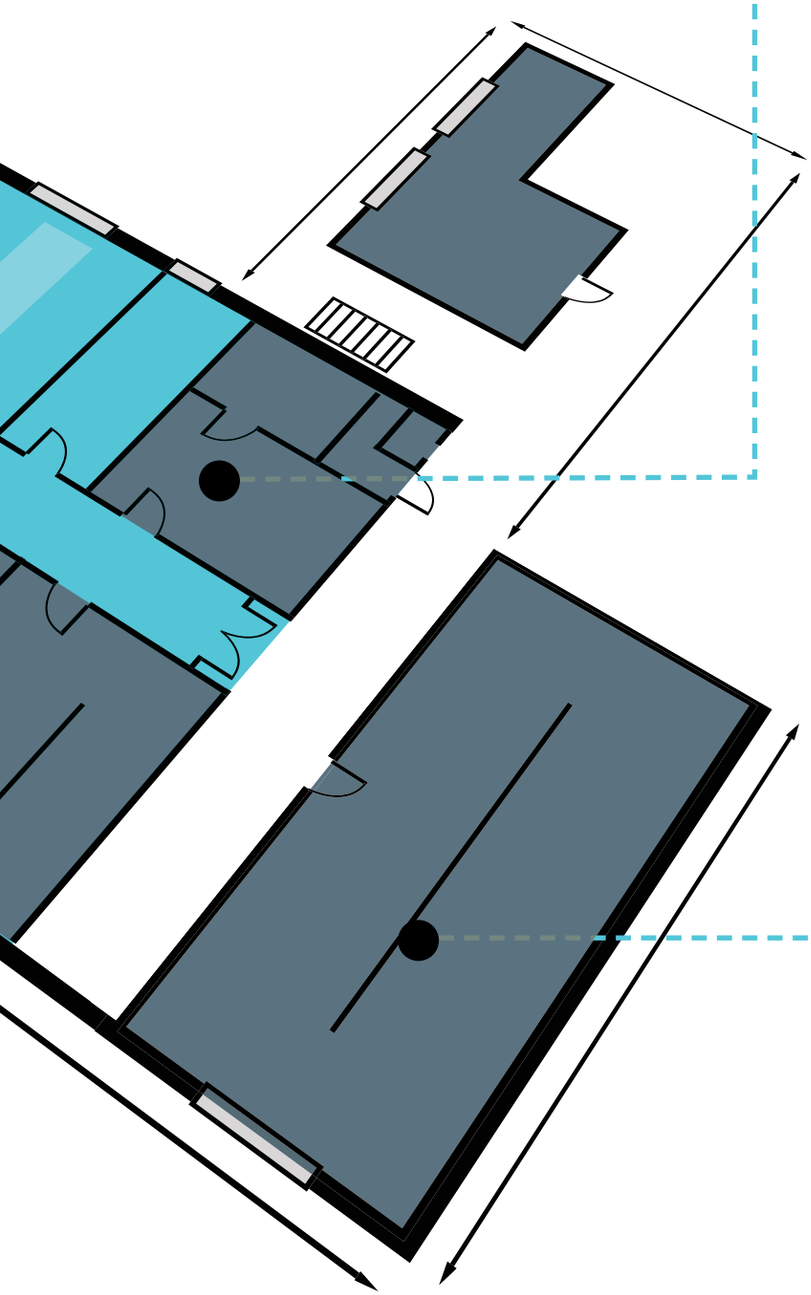


CellScale Microsquisher

The Microsquisher, developed by CellScale (Waterloo, Ontario), is a micro-scale system designed to determine the tensile/compressive moduli of small soft specimens. The system is used to determine the stress-strain properties of various samples such as biomaterial scaffolds, hydrogel microspheres, tissues and cell aggregates in ambient air or submerged in a temperature-controlled aqueous bath.

TAP Biosystems ambr™ system

TAP Biosystems' advanced microscale bioreactor (ambr) workstation controls 24 disposable micro bioreactors for parallel multi-parametric processing and utilizes an automated liquid handler. Currently, CCRM is utilizing the ambr to translate immune cells and stem cells from static cultures into stirred suspension cultures and to determine an optimal bioreactor culture environment.



Nikon BioStation CT

Nikon's BioStation CT consists of a tissue culture incubator fitted with an inverted microscope, enabling observation and recording of live cells in culture. Using advanced analysis algorithms developed by Nikon, numerous measurements on both single images and video sequences can be performed automatically, allowing CCRM's development team to analyze an array of time-dependent events at the cellular scale.

Bioprocess Suite

CCRM uses bioreactors to produce cells in stirred suspension culture with precise and automated control of variables (temperature, pH, dissolved oxygen) critical to achieving robust and consistent cell manufacturing process performance, at different scales of production.

DISCLOSURES - CRC REVIEWED TECHNOLOGIES

More than 100 discoveries have made their way through CCRM's diligent disclosure process. Those listed here are considered to be the most promising to-date and have undergone rigorous scrutiny and evaluation, including being presented to CCRM's Commercialization Review Committee (CRC). Having passed the review, five of the seven successful technologies below are now progressing to the company creation stage.

Cardiac Micro-wire (CMW), PI: Peter Zandstra, Milica Radisic, University of Toronto

D2011-0006: Pluripotent stem cell derived functional cardiac tissue mimetic for drug screening applications

Researchers have developed a self-assembling cardiac micro tissue that offers a potential platform for *in vitro* drug screening. Micro tissues are generated by applying a mixed population of cells in a hydrogel to micro fabricated substrates. Micro scale pockets of cell-laden hydrogel remodel over time to mimic cardiac tissue. The micro tissues contract spontaneously and are responsive to chronotrophic drugs.

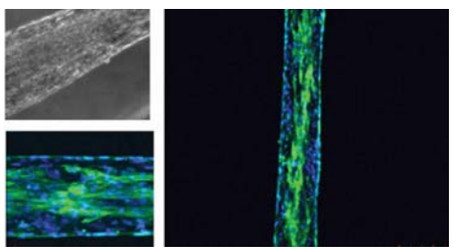


Figure 1: Self-assembling 3D collagen-based construct comprising hPSC-derived cardio-myocytes and non-myocytes.

Advantages:

- Allows for direct force of contraction measurement;
- Can be electrically stimulated but has an intrinsic spontaneous beat frequency and can be stimulated with drugs for alternate contractility rhythms;
- Can be cultured in high-throughput for drug screening platforms; and,
- Compliant with conventional whole mount immunohistochemistry and imaging techniques.

Fed-batch system, PI: Peter Zandstra, University of Toronto

D2012-0031: Rapid expansion of human hematopoietic stem cells by automated control of inhibitory feedback signaling.

The *ex vivo* expansion of umbilical cord blood (UCB) derived hematopoietic stem cells (HSCs) would enable UCB to be more readily used for transplantation in adult patients by overcoming the limitation of low cell numbers per UCB unit. This HSC expansion technology is built upon a controlled fed-batch media dilution method. The system links cell growth and endogenous factor secretion to a tuneable media dilution algorithm, which results in significant enhancements in stem and progenitor expansion by reducing the inhibitory impact of endogenously produced soluble factors. The fed-batch strategy is integrated into a closed-system bioreactor, amenable to automation and scale-up.

Advantages:

- The system provides significant levels of expansion of stem and progenitor cells in a relatively short culture time (12 days), making it amenable to clinical use;
- The system is semi-automated, enabling ease of manufacturing; and,
- The fed-batch platform can serve as a base technology on which to add other HSC enhancing strategies.

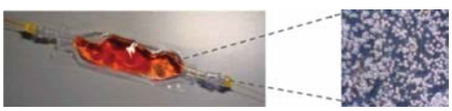


Figure 2: The *ex vivo* expansion of hematopoietic stem cells in a closed-system culture vessel.

Wound healing, PI: Ian Rogers, Mount Sinai Hospital

D2012-0042: Topical, allogeneic cell therapy for the treatment of diabetic skin ulcers

Allogeneic CD34^{+} MPSCs derived from human umbilical cord blood (UCB) deliver potent essential growth factors that encourage tissue regeneration and dermal repair, and potential formation of new blood vessels for treatment of chronic diabetic wounds. Initial proof-of-principle data demonstrate efficacy in a murine diabetic wound model, as well as in murine models for peripheral vascular disease and spinal cord compression repair.

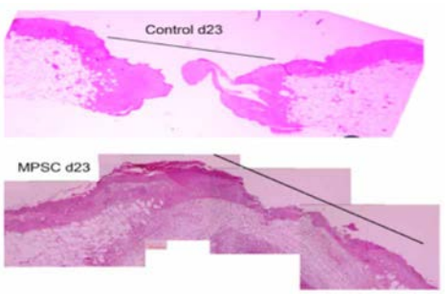


Figure 3: Representative histology of control and MPSC-treated wounds at day 23 of treatment. The black line indicates the size of the wound area. Control mice were treated with DMEM without cells.

Control (top): The wound has not closed and although there is evidence of dermal hyperplasia, there is no evidence of fibrocytes or ECM production. The overall tissue structure is disorganized. Treated (bottom): The wound area contains well-organized tissue that is nearly at full thickness – i.e. healing is almost complete.

Advantages:

- Established intellectual property: Composition of matter patents have been issued in the U.S. and EU;
- High efficacy: MPSCs are more biologically potent than unexpanded CD34+ cells (competitor product);
- Topical application: MPSCs are applied topically for diabetic wound healing, thereby reducing safety and regulatory concerns around this cell therapy;
- Easily obtainable, low-cost supply: MPSCs can be reproducibly expanded *in vitro* up to 10-fold in eight days, and up to 30-fold in 15-20 days, from widely available cell sources such as cord blood units with low cell counts. In addition, several cord blood banks are open to monetizing their low cell count cords for this application at a steep discount (as they would normally discard such units);
- Ease of distribution: Doses can be cryopreserved, and unrelated individuals can receive MPSCs; and,
- Multiple major markets: In addition to diabetic wound healing, MPSCs have also demonstrated efficacy for treatment of peripheral vascular disease and for spinal cord repair.

HAMC, PI: Molly Shoichet, University of Toronto

D2012-0033: A versatile hydrogel technology for cell delivery

This disclosure describes a novel injectable and bio-resorbable polymer for the delivery of cells into diseased tissues. The polymer is a viscous solution, gels at 37°C, liquefies under shear force and re-gels immediately upon extrusion. It also has cell survival properties, aiding in its function as a cell transplantation matrix.

Advantages:

- Issued patent in U.S.;
- Injectable polymer with cell survival properties;
- Tunable features allowing for controlled drug release for prolonged time periods; and,
- Provides uniform distribution of injected cells.

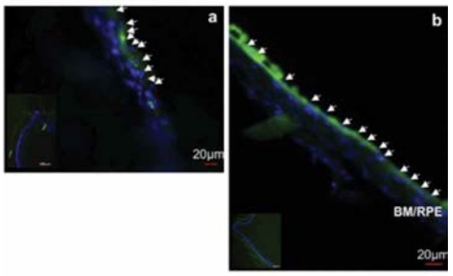


Figure 4: HAMC provides a stable delivery vehicle for cell implantation. In vivo adult sub-retinal transplantation of GFP-RSPCs in HAMC assayed at four weeks post-transplantation. a) Control transplantation in saline, b) HAMC

Hepatic, PI: Gordon Keller, University Health Network

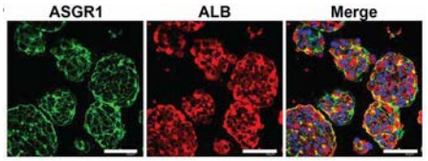
D2013-0022: Scalable production of functional hepatocytes from human pluripotent stem cells

Researchers have devised a simple, reproducible approach to generate functional populations of mature hepatocytes from human pluripotent stem cells (hPSCs). With this protocol, it is possible to routinely generate hESC-derived populations that display measurable levels of Phase I and II metabolic enzymes and gene expression profiles indicative of hepatocyte maturation.

The development of metabolically functional cells is an important endpoint for enabling the routine production of hPSC-derived hepatocyte-like cells for drug metabolism analysis, liver disease modeling, development of bio-artificial liver devices, and cell-based therapies.

Advantages

- High yield derivation of hepatic progenitor cell population from hESCs;
- Generation of mature hepatocytes expressing the two key CYP genes, CYP1A2 and CYP3A4; and,
- Scalable production of mature hepatocytes from hESCs.



Scale bars: 50 µm

Figure 5: Confocal microscope images of hepatic aggregates stained with ASGR1 (green) and ALB (red); Ref. Ogawa S et al. *Development 2013*; 140:3285-3296

Neutrophil, PI: Lars Keld Nielson, University of Queensland

D2013-0023: Improved production of non-activated neutrophils

Despite the routine use of hematopoietic growth factors (e.g., G-CSF) and antibiotic/antifungal therapy to treat chemotherapy-induced neutropenia, neutropenia remains a major contributor to treatment-related mortality and morbidity in cancer patients, and is the single most significant dose-limiting factor for chemotherapy. A cost-effective, fast-acting therapy for the primary prophylaxis of chemotherapy-induced neutropenia would address a significant unmet clinical need, with a potential market size estimated at >US$3 billion. Although neutrophil transfusion has been used to treat neutropenia, supply challenges have previously rendered this impractical for all but the most severely neutropenic. The current technology is a method for efficient expansion of post-mitotic neutrophils from hematopoietic stem and progenitor cells (HSPC), and is the only demonstrated method capable of producing clinically meaningful quantities of mature neutrophils. The envisioned product comprises mature neutrophils for allogeneic transfusion into patients.

Advantages:

- Neutrohils can be manufactured for use as a routine prophylactic;
- Technology has been demonstrated at a clinically relevant scale;
- Technology is readily automated; and,
- Issued patent in the U.S.

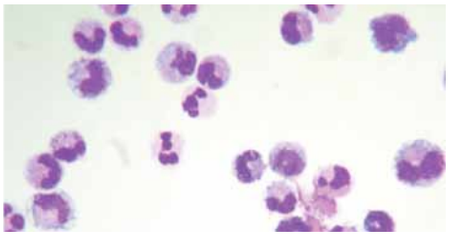


Figure 6: Two neutrophils among many red blood cells. (Ref. GNU Free Documentation License Version 1.2)

SKPs, PI: Freda Miller, SickKids

D2012-0037: Skin Derived Precursor cells (SKPs) for broad applications

The inventors have developed a method for isolating Skin derived Precursor cells (SKPs). SKPs are a novel population of neural crest-related precursor cells that are laid down in the dermis during embryogenesis and persist into adulthood. Injected SKPs have been shown to promote hair re-growth in a nude mouse model. Furthermore, undifferentiated SKPs show capabilities towards wound healing. SKPs are able to differentiate into a host of cell types including: neurons, mesenchymal-like cells such as fibroblasts and myofibroblasts, vascular smooth muscle cells, chondrocytes, osteoblasts, myelinating glia and Schwann cells. Inventors have also identified small molecule compounds that increase SKP proliferation. Technology is relevant to those with a strategic interest in regenerative medicine-based wound care or hair growth.

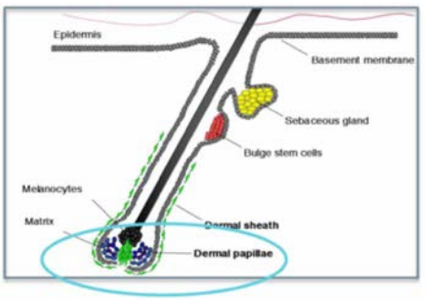


Figure 7: SKPs derived from endogenous Sox-2 positive precursors with a hair follicle niche.

Advantages:

- The technology is well protected, with a large patent portfolio;
- SKPs can be sourced autologously;
- SKPs can be passaged *in vitro* for longer periods compared to existing DP cell-based drug screens; and,
- SKPs differentiate into a variety of cell lineages, which include osteocytes and chondrocytes, Schwann cells and glial cells, vascular smooth muscle cells, dermal fibroblasts and myofibroblasts, adipocytes.

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