



# NORTHERN NEW ENGLAND CLINICAL & TRANSLATIONAL RESEARCH NETWORK

*Health Equity through Innovative Research*

## Special Edition

### ***The NNE-CTR is renewed!!***

Thanks to the amazing contributions of our core leadership, members, and collaborators, the NNE-CTR has received official notification for NIH funding for another 5 years! See the letter from the PIs for details on the next page.

As we look to our next five years here at the NNE-CTR, we would like to share some leadership changes with you. In Vermont, Dr. Gordon Jenson has retired, and Dr. Renee Stapleton has taken his seat on our Administrative Core. Dr. Bernard Cole has stepped down as our BERD Core lead, and Dr. Peter Callas has taken up that role.

In Maine, Dr. Robert Fiesel has stepped down as the TRT Core lead, and Dr. Aaron Brown is now the TRT Core lead at MaineHealth.

Thank you Gordon, Chip, and Bob for the many contributions you made in the formative years of the NNE-CTR. Your guidance and expertise has proven invaluable, and you will always be a part of the CTR.

Welcome to the team Renee, Peter, and Aaron. We are honored to have you join us, and look forward to working with you over the next five years as we continue our work in northern New England.

Visit our website for updated information on our Core Teams!

### IN THIS ISSUE:

#### ***Updates from the Renewal!***

- New Core Services
- Round 7 of Pilot Projects Program

#### ***Tech Spotlights***

- People Spotlight, Dr. Aaron Brown
- TRTC's Tech
- Project Spotlight, Genetic Profile of Breast Cancer

#### ***Connect with Us***

#### ***Upcoming Events***

### AUGUST 2022

#### **NNE-CTR**

#### **Quarterly Newsletter**

**ACTIV-6**

[activ6study.org](https://activ6study.org)



@ACTIV6study  
#feelbetterfaster

Can we find medications that can be easily given at home to treat people with COVID19? The NIH ACTIV-6 study aims to provide answers to help people feel better faster.

Find out more at  
<https://activ6study.org>

# A message from the PIs

*Dear members,*

Our NNE-CTR has been renewed for five years reflecting effectiveness of our members and leadership. The review panel recognized the approaches that our program has developed to address the health and healthcare challenges in our predominantly rural northern New England population. There was appreciation for the contributions that the NNE-CTR has made to increase capabilities in addressing the prevention, early detection, treatment, and survivorship with chronic diseases that include cancer, substance abuse disorders, food insecurity, obesity, diabetes, and cardiovascular disease. The pivotal role of the NNE-CTR in maximizing accessibility to health and healthcare during the Covid-19 pandemic was considered exemplary with practices and policies that provided broad-based benefits.

Moving forward, we are committed to strengthening our partnerships with the Northern New England Practice-Based Research Network Co-Op to reinforce collaborations of primary care colleagues with scientists and physician-investigators in academic medical centers for engagement in health and healthcare initiatives in Vermont, Maine, and New Hampshire. We are expanding our resources for guidance, education, and training in clinical and translational investigation with emphasis on support for professional development and research at all stages of the career continuum. We are enhancing our capabilities for mechanistic, translational, clinical, health services, and implementation investigation, as well as clinical trials. The NNE-CTR community outreach and engagement programs, with resources that focus on bidirectional communication with regional stakeholders, will be a centerpiece as we move forward. A priority of the NNE-CTR will be responsiveness to disparities in both health and healthcare access for New Englanders that leverage capabilities for maximizing health equity, diversity, and inclusion. It was acknowledged by the reviewers that our NNE-CTR provides state-of-the-art instrumentation and technical support with guidance in genomics, proteomics, multispectral cellular imaging, metabolomics, and bioinformatics to support advances in precision/genomic medicine.

We have valued collaborations with our State Departments of Health that are increasingly important for integration of public health strategies and resources for regionally relevant programs that are responsive to the requirements of underserved populations. These collaborations were essential for NNE-CTR effectiveness during the Covid-19 pandemic and will be all the more important as we emerge from the pandemic and reestablish momentum in the prevention, early detection, treatment, and survivorship with chronic diseases.

We are very appreciative of the contributions from our NNE-CTR members and the dedication of our exceptionally competent leadership and administrative support team. Gordon Jensen, and now Renee Stapleton, with Tom Gridley have been instrumental as our partners for strategic planning and program development. Our core leadership have provided incredibly valuable support for NNE-CTR members to develop clinical and translational research initiatives that include pilot projects and programs supported by NIH, USDA, HRSA, and PCORI. Meredith Oestreicher and Michele Locker, initially with Jennifer Smith and recently with Sheila Clifford-Bova, round out the team providing essential program operation expertise.

To us, addressing the northern New England health and healthcare challenges is not an option but a responsibility. And we are appreciative for the resources and the opportunity we have collaboratively work towards making a difference in regional health and healthcare over the next five years.

*Thank you for your engagement,*

*Cliff & Gary*

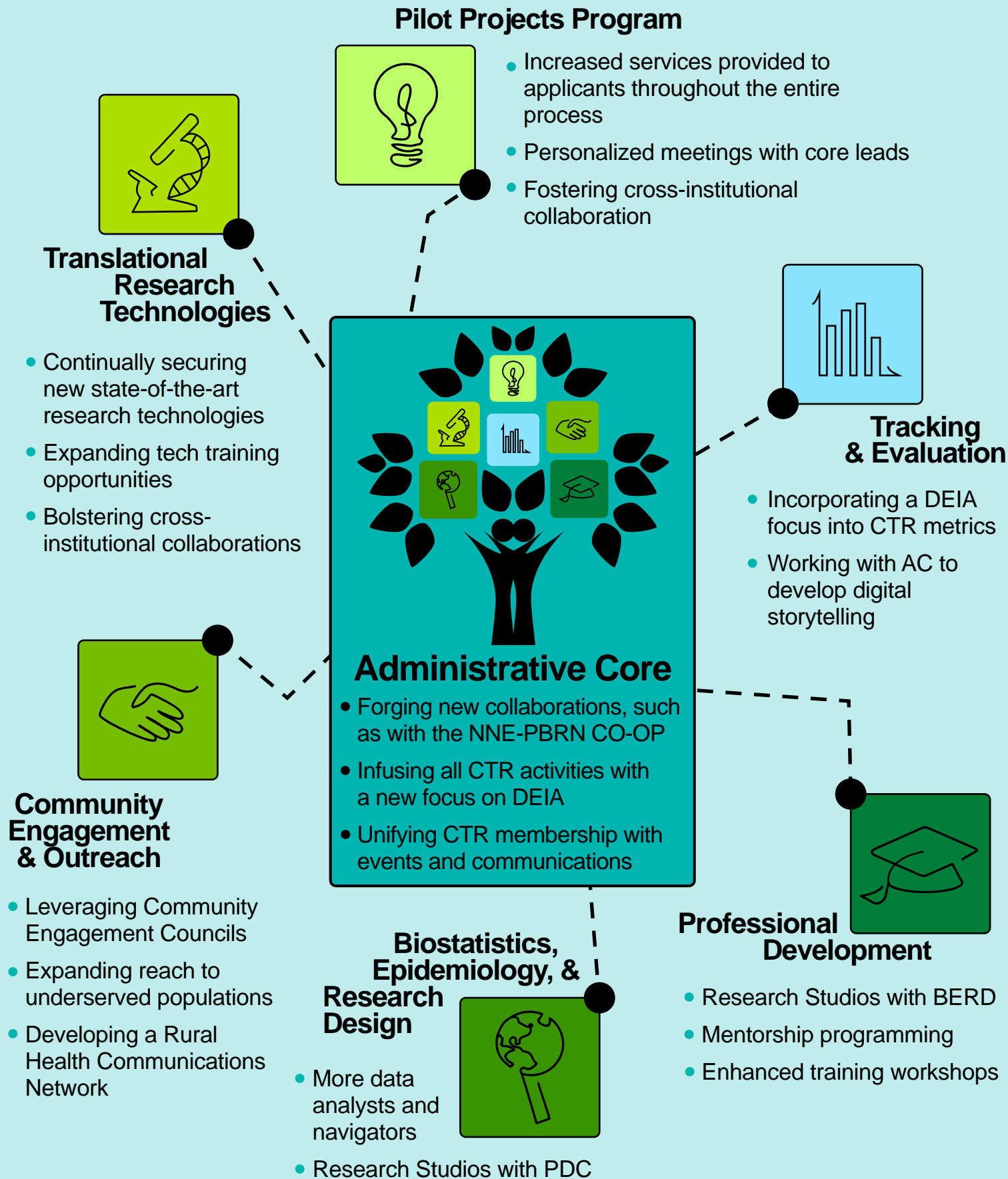


Dr. Clifford Rosen, MD



Dr. Gary Stein, PhD

# Check out the new things coming to NNE-CTR Cores & services!



# PEOPLE SPOTLIGHT

## Dr. Aaron Brown, PhD: NNE-CTR Mentee to Core Co-Lead

Shortly after becoming a faculty scientist at MaineHealth, Dr. Aaron Brown was selected as one of four project leads in the Mesenchymal and Neural Regulation of Metabolic Networks COBRE. His project focused on a special type of fat cell that could be relevant in obesity and associated diseases, and it was a relatively new field to him. *“I was working on a special type of fat called brown adipose tissue,”* explains Aaron. *“This fat tissue actually burns energy rather than storing it like most fats, so it’s kind of like an anti-obesity type of fat. If we can find ways to turn this fat on, we can potentially burn calories and people will be less susceptible to diabetes and heart disease.”*

As part of his project within the COBRE, he had to have three mentors. It was at this point that he met Dr. Irwin Brodsky of MaineHealth and was introduced to the NNE-CTR. Serving as Aaron’s clinical mentor and as a mentor through the NNE-CTR, Irwin connected him with a whole team of clinicians and support personnel who helped with different stages throughout the project.

Aaron also worked alongside Dr. Ivette Emery, a research navigator with the NNE-CTR at the time, to design and develop several clinical projects and write up protocols. Over three to four years, he worked with alongside Irwin and Ivette through both MaineHealth and the NNE-CTR to conduct his COBRE project. At this same time, he started taking on more roles at MaineHealth. At first, he was asked to direct the Molecular Phenotyping Core, then the Flow Cytometry Core, followed by the Viral Vector Core.

It was these experiences with so many core facilities at MaineHealth, as well as his experience running a molecular biology core at Jackson Laboratories earlier in his career, that the CTR administrative core leaders asked if Aaron would consider serving as the Co-Lead of the Translational Research Technologies Core. *“I’m still in the learning phase.,”* says Aaron. *“I’m trying to figure out how we can make all the core facilities work better together. ... I think one thing would be to make the CTR Cores more accessible to people in our network. Get our Cores out there, let people know what we have, that we can train people or help people who’ve never done this type of project before.”* In the end, Aaron is a researcher who wants to see the best research done.



Aaron Brown, Ph.D. (TRTC co-lead, left) and Michele Karolak, B.A. (manager of the Molecular Phenotyping Core at MMCRI, right), showcase one of two new qPCR machines recently funded by the CTR to upgrade older, unserviceable equipment and to increase sample throughput.

*“I had thought the NNE-CTR was more for clinicians, but I didn’t realize how much help you could get. I’d never done a project where you’d get the samples from a hospital. Irwin was instrumental connecting me with doctors to get samples. ... I never hought I’d do projects like that, and the CTR helped me develop & lead this big project.”*

*~ Dr. Aaron Brown*

*“I’m not just the Co-Lead; I’m also a client. I really had no idea how many core facilities Vermont and Maine have together. Now that I know, I think I’ll be using more of Vermont’s cores more often, too. Because these enabled me to do some projects that I otherwise wouldn’t have done.”*

# Gain access to all the tools & tech across UVM & MH through the TRTC!

Mass spectrometry; Flow cytometry;  
Large-scale quantitative proteomics;  
Cell sorting; Microarray; Parallel  
sequencing; DNA analysis; Bio-  
informatics shared resources; X-Ray  
crystallography; Scanning electron  
microscopy; Transmission electron  
microscopy; Confocal, super  
resolution, & atomic force  
microscopy; Laser capture  
microdissection; Light and  
electron microscopic immuno-  
cytochemistry; Morphometry;  
Laser scanning cytometry;  
Whole slide scanning;  
Whole animal imaging;  
Magnetic Resonance  
Imaging and MRI  
simulator; Bio-  
Bank; Genomic  
medicine testing;  
Biostatistics &  
related services;  
Instrumentation  
& modeling;  
Advanced  
computing;  
Data management

Flow cytometry;  
Cell sorting; Cell  
analysis; Molecular  
phenotyping; mRNA &  
DNA sequencing; qPCR;  
Proteomics & lipidomics  
analysis; Epifluorescence  
microscopy; Viral vector  
design, titration, & testing;  
Spectrophotometry; Immuno-  
histochemistry; Tissue fixation &  
processing; Immunocytochemistry;  
Histology-related services; Multicolor  
confocal colocalization; FRET; Live cell  
confocal microscopy; Small animal imaging  
with MRI, MicroCT, & ultrasound; BioBank;  
Mouse transgenic & genome  
modification services; Physiology  
& metabolic analyses;  
Research laboratory  
services; Assay  
design; Bio-  
specimen  
testing

# PROJECT SPOTLIGHT

## Finding the Genetic Profile of Breast Cancer

Can identifying the genetic profile of a unique cell type within tumors help predict disease outcomes in breast cancer patients?

Dr. Jonathan Gordon at the University of Vermont recently leveraged NNE-CTR Translational Development Initiative awards to try and explore this idea further. Dr. Gordon studies a specific population of cells that reside in breast tumors called mesenchymal stromal cells, or MSCs. MSCs in the healthy body respond to injury, and they often derive into either cartilage and bone or into fat. These cells are typically rare in the breast tissue, but in the case of breast cancer, something different happens. *“These MSCs can have a pseudo-wound healing response where they target the tumor tissues, and they end up either aiding in the tumor’s growth or helping it evade our natural immune systems,”* explains Jonathan. *“This is because the immune cells will see these normal cells surrounding the tumor, so it doesn’t see the tumor itself.”* As a result, breast cancer patients may have a population of MSCs within their tumors that wouldn’t normally be there. Dr. Gordon’s hypothesis is that some breast cancer patients might have different subpopulations of MSCs within their tumor that influence how they interact compared to other patients or even non-breast cancer patients. The first question, then, is do all these MSCs look the same, or are they different?

To answer this question, Dr. Gordon and his team first used cell sorting to isolate the MSCs and separate them from the rest of the tumor. They then used 10x Genomics Single Cell analysis systems, provided through the NNE-CTR award, to analyze the individual genetic profiles of over 7000 MSCs from breast cancer patients, as well as a population of control MSCs from non-cancer donors. They found that there are 7 different subpopulations of MSCs within these tumors, one of which did not exist in any of the control cells. Instead, this population was only found in the cancer patient samples. This critical finding is currently being prepared for publication alongside their larger project investigating these cells.

### What is the Translational Development Initiative Award?

These awards, or TDIs, provide financial support for NNE-CTR members to use or receive training on any of the state-of-the-art tools and technology within our TRT Core. Check out the extensive list on the [core webpage](#).

*“The TDI 10x genomics was an integral part of the larger project. When we got the 10x, it immediately became available that we could answer this question, and it was fortuitous that there was a very specific result where we have this one population with a defined gene expression different from the whole mix.”*

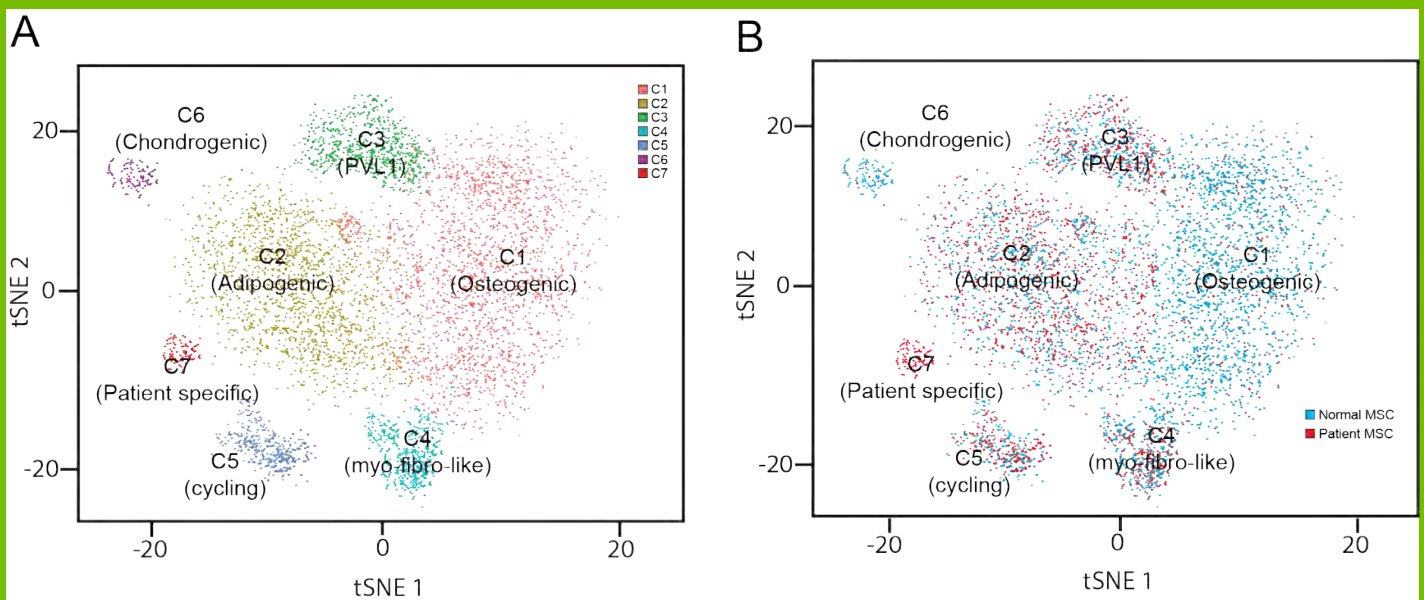
*~ Dr. Jonathan Gordon*

# PROJECT SPOTLIGHT

## Finding the Genetic Profile of Breast Cancer, continued

Due to this finding, Dr. Gordon and his team were able to cement a defined signature of patient specific MSCs. They could then go back to the full data sample and see those very signatures across the larger population of patients. The goal, says Dr. Gordon, is to use that signature, the unique group of genes in these patient MSC cells, to make individual predictions about patient outcomes and disease progression. *“These identified genes would likely be a risk factor at this point,”* Jonathan explains. *“During all of this, we were looking at differences between patients with DCIS and those with invasive breast tumors. With DCIS patients, it’s a low-grade cancer that might not progress to something invasive, so we were trying to find predictive factors for when maybe surgery is or is not necessary. Perhaps our findings here could be part of a gene signature that would help dictate that,”* and this is just the type of hypotheses they are still working towards.

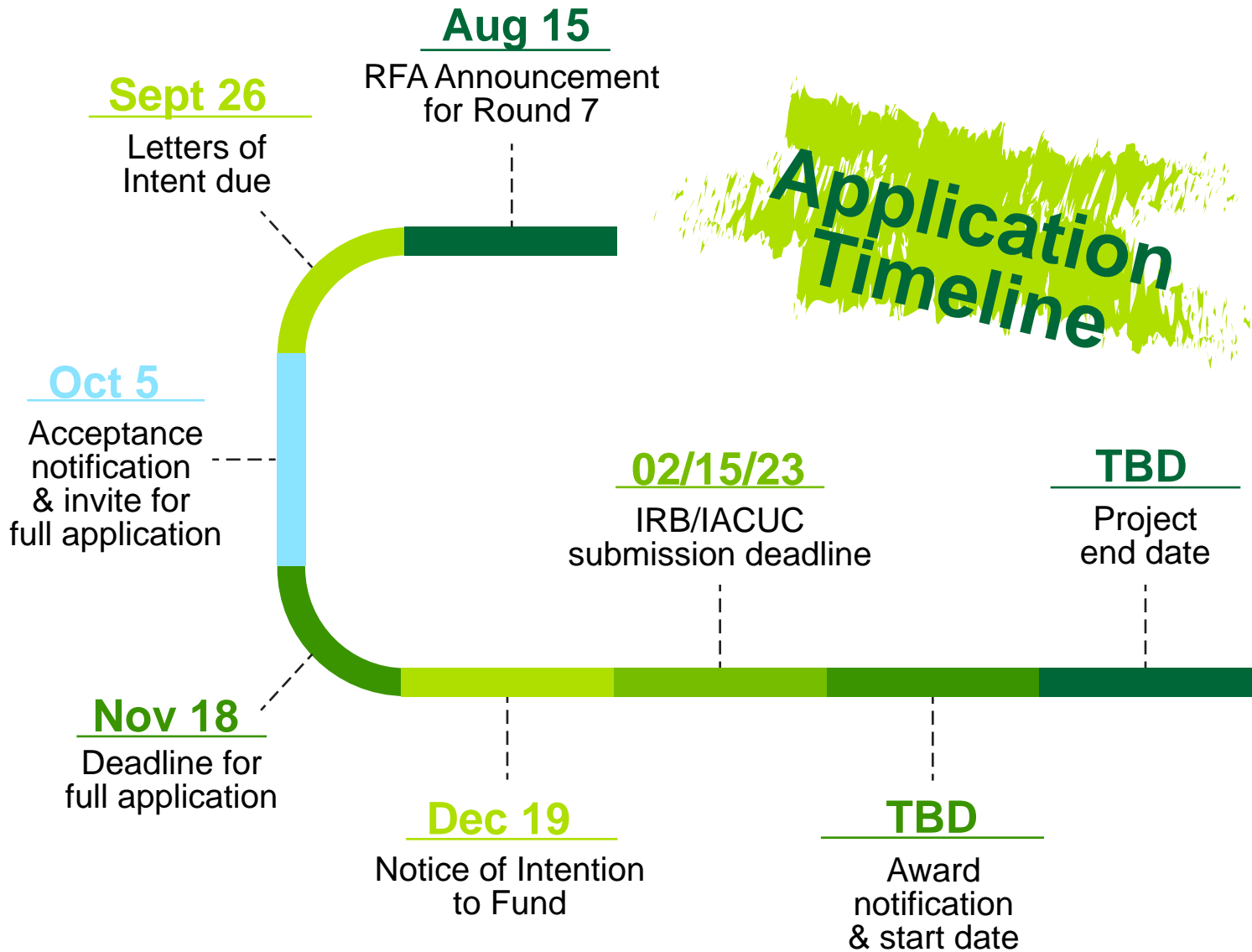
Dr. Gordon has a second NNE-CTR Translational Development Initiative award currently supporting use of another detailed technique to delve even deeper into this unique genetic profile and look at the genes themselves. The NNE-CTR TDIs are provided through the [Translational Research Technologies Core](#).



- CD90+ cells were isolated from normal donors or patients with invasive breast cancer and subjected to single cell analysis on the 10X Genomics Chromium platform. Gene expression profiles from single cells were clustered using tSNE and 7 distinct cell clusters were observed.
- Comparison of cells derived from healthy donors or breast cancer patients demonstrated proportional changes in number of cells contributing to specific cluster

# Pilot Project Proposals open soon!

Pilot Project Awards provide one year of seed funding for initiation of preclinical, clinical, or translational research that has the potential to impact health or healthcare in our region. Advance your careers with research & professional development support through our Pilot Projects Program!





# Connect With Us

Because we value our members, we will continue to enhance our services and expand our network to better meet your needs.

Want to become a member or update your status?  
Join from our webpage: <http://www.med.uvm.edu/nne-ctr/home>

Click [HERE](#) to Check out our Website!



- Access our membership benefits and sign-up form
- Connect with other researchers, clinicians, and community members in our region
- Explore our services & resources
- Get updates on career opportunities, funding announcements, and events
- Read the latest news or be spotlighted yourself!

## Collaboration Opportunities

Currently recruiting sites for a randomized controlled trial entitled:

### AGGRESSIVE SMOKING CESSATION THERAPY POST-ACUTE CORONARY SYNDROME (ASAP) TRIAL

Join this multi-center trial to assess the efficacy, safety, and tolerability of aggressive smoking cessation therapy initiated in-hospital following acute coronary syndrome.

This study is under the supervision of:

**Dr. Mark J. Eisenberg**

Divisions of Cardiology and Clinical Epidemiology/  
Jewish General Hospital/McGill University



For more information, please contact:

☎ 514-340-8222 extension 2324

✉ [ASAP.Trial@ladydavis.ca](mailto:ASAP.Trial@ladydavis.ca)

Hôpital général juif  
Jewish General Hospital  
Institut Lady Davis / Lady Davis Institute



National  
COVID  
Cohort  
Collaborative

The National COVID Cohort Collaborative (N3C) A National Partnership to Fight COVID-19  
The N3C aims to improve the efficiency and accessibility of analyses using a very large patient-level COVID-19 clinical dataset and demonstrate a novel approach for collaborative pandemic data sharing.  
The N3C Enclave is the largest limited EHR data set in US History:

- Billions of rows of data
- Millions of COVID cases
- Hospitals and Clinics across the Country
- Procedures, visits, and medications go back 2 years before COVID test.

VALUE TO ORGANIZATIONS:

- Access to large scale COVID-19 data from across the nation
- Sample data for grant proposals
- Team science opportunities for new questions and to test informatics methods
- Access to Domain Teams, statistics, machine learning (ML), informatics expertise
- Training on ML analytics, NLP methods, tools, software, additional datasets

[www.ctrnet.org/n3c-data-enclave/](http://www.ctrnet.org/n3c-data-enclave/)