2017 Community Dissemination Report

BioCanRx-Cancer Stakeholder Alliance Learning Institute

BioCanRx
Biotherapeutics for Cancer Treatment
Biothérapies pour le traitement du cancer

November 2017

This is the **Community Dissemination Report of the 2017 BioCanRx-Cancer Stakeholder Alliance Learning Institute**.

It is a public document written by the participants of the 2017 BioCanRx-Cancer Stakeholder Alliance Learning Institute that was held at the 2017 Summit for Cancer Immunotherapy (Summit4CI) from June 25 to June 28, in Gatineau, Quebec.

This report serves to share the key research take-away messages presented at the Summit4CI as well as the group reflections of The Learning Institute with the oncology patient and researcher community, BioCanRx, the Cancer Stakeholder Alliance, and the general public.

Welcome Messages

From BioCanRx

We are very proud to share this Community Dissemination Report of the inaugural Learning Institute that was piloted at the 2017 Summit for Cancer Immunotherapy.

The Learning Institute was developed in partnership with the Cancer Stakeholder Alliance, through the members of its working group. We are deeply grateful for this partnership and of the invaluable time and focus participants dedicated to developing this important patient engagement initiative.

Based on the overwhelmingly positive feedback, the Learning Institute has become a permanent component of our annual Summit for Cancer Immunotherapy. We are looking forward to hosting the second event at the next Summit in October 2018.

This report, by the Learning Institute, was written for the Canadian community of cancer patients and researchers. It includes key take-away messages from each panel discussion, the Learning Institute's reflections on these key take-away messages, and suggestions on how to give an accessible presentation.

We hope you will find this informative report as enlightening as we do.

John C. Bell, Ph.D.
Scientific Director
BioCanRx

Stéphanie Michaud, Ph.D.
President and CEO
BioCanR

From the Cancer Stakeholder Alliance

Sometimes someone has an idea that is really really good.

Sometimes that person is a scientist. Sometimes they aren't.

BioCanRx created the Cancer Stakeholder Alliance because they (rightly) recognized that patients have an important and powerful voice that is critically important to advancing cancer immunotherapies.

As part of the Cancer Stakeholder Alliance, Louise Binder made a simple but powerful suggestion. Relying on her background in cancer policy and her experience on the front lines of AIDs advocacy, Louise suggested that we establish a Learning Institute.

So we did.

And ultimately it was successful beyond what all of us (except perhaps Louise) could have imagined.

Conceptually, the idea was that young investigators would adopt advocates as part of the BioCanRx annual meeting and help walk them through the science. And that worked.

The unexpected benefit (by the scientists at least) was how much the advocates taught these young scientists (just ask them).

I believe we have created something special here. Something worth building on. Something that will change the culture of cancer research and improve the scientific enterprise.

I both thank and commend BioCanRx for taking a good suggestion and giving it life.

I also issue a challenge to all reading this. I challenge you to build on what we have started.

Patrick Sullivan
Chair of the Cancer Stakeholder Alliance Working Group
President, Team Finn Foundation
A Founder and Chairman, Ac2orn

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Overview

The BioCanRx-Cancer Stakeholder Alliance Learning Institute (The Learning Institute) is a patient engagement program that brings cancer patients and researchers together at the Summit for Cancer Immunotherapy (Summit4CI) to translate scientific knowledge from researcher to patient, and to integrate the patient perspective and voice in the conference.

The objectives are:

- to create a model of learning that encourages, supports and creates the integration of patient leaders into the scientific conference, and
- to ensure that scientific research presented at the conference is translated to patient participants in an understandable way so that it can be shared with interested partners.

The Learning Institute consists of:

- a series of high-energy knowledge translation and exchange sessions,
- a "buddy system", where patient leaders are paired with academic scholars, and
- writing a report that includes the key research take-away messages presented at the Summit4CI, group reflections about the research, and suggestions for giving accessible presentations.

The Learning Institute exposes researchers to the realities of the cancer patient experience, and familiarizes patients with research concepts in immuno-oncology. Patients and researchers develop their skills in knowledge exchange and translation, networking, and in building and strengthening their connections. The Learning Institute nurtures the growing culture around patient engagement in research.

Development

In 2016, the Cancer Stakeholder Alliance (CSA) and BioCanRx identified the Learning Institute as a joint priority and made it part of their Joint Action Plan. Shortly afterwards, members of the 2017 CSA Working Group partnered with BioCanRx staff and Highly Qualified Personnel (HQP) to form The Learning Institute Developers and Organizers Group (Table 1). They developed the inaugural Learning Institute, which was piloted at the 2017 Summit for Cancer Immunotherapy.

Table 1 Members of The Learning Institute Developers and Organizers Group

CSA Working Group Members:
Louise Binder Health Policy Consultant, Save Your Skin Foundation **Kathy Brodeur-Robb** Executive Director, C17 – Children's Cancer and Blood Disorders **Linda Eagen** President & CEO, Ottawa Regional Cancer Foundation **Patrick Sullivan (Chair)** President, Team Finn and a Founder & Chairman of Ac2orn
BioCanRx HQP:
Nicole Forbes Postdoctoral Fellow, Jean-Simon Diallo Lab, Ottawa Hospital Research Institute **Brittany Umer** PhD Candidate, David Evans Lab, University of Alberta
BioCanRx Staff:
Renée Leduc Manager, Knowledge Mobilization, BioCanRx **Jovian Tsang** Former Manager of HQP Training Programs, BioCanRx

Thank You

BioCanRx and the members of The Learning Institute Developers and Organizers groups wish to thank the CATIE-CAHR Learning Institute for the inspiration and for setting the bar of excellence. They also wish to thank the participants who piloted the 2017 BioCanRx-Cancer Stakeholder Alliance Learning Institute

BioCanRx wishes to give a special thank you to the members of The Learning Institute Developers and Organizers Group for the dedication of their time, energy, focus and work in making The Learning Institute a success.

2017 Learning Institute

The 2017 pilot brought together seven members of the CSA Working Group, in the role of patient/public leaders, fifteen members of the BioCanRx HQP community, in the role of academic scholars, and one BioCanRx staff as a facilitator (Figure 1).

*Figure 1 2017 BioCanRx-CSA Learning Institute participants. Back row, from left to right: Israel Matos, Madison Turk, Samantha Burugu, Kathy Matuszewska, Allison McNamara, *Kathy Brodeur-Robb, John-Peter Bradford, Chad Irwin, Tammy Northam, Tim Guo, and John Bell. Front row, from left to right: Rebecca Foley, Rachelle Davis, Xining (Linda) Yang, Ksenia Bezverbnaya, Helene Hutchings, *Nicole Forbes, *Louise Binder, Aditi Sood, Gabrielle M. Siegers, *Brittany Umer, and *Renée Leduc. Missing from photo: *Linda Eagen, *Patrick Sullivan, and *Jovian Tsang. The members of The Learning Institute Developers and Organizers Group are indicated by "*".*

Together, they participated in a series of interactive and collaborative "Knowledge Exchange Sessions" that helped them become familiar with research concepts in immuno-oncology, develop knowledge translation and exchange skills, network and create partnerships (Figure 2).

Figure 2 Early morning Knowledge Exchange Sessions in action. Every morning over breakfast, participants discussed the previous day's plenaries, talks and events. These high-energy sessions included small group discussions followed by a report back to the room on key take-aways, scientific content, personal thoughts and overall accessibility of each plenary.

They also worked together to write this **Community Dissemination Report**, which captures the key take-away messages from each plenary talk at the 2017 Summit for Cancer Immunotherapy and group reflections.

The report serves to inform oncology patients and researchers, BioCanRx and the general public. The report also includes suggestions from The Learning Institute participants on the "DOs" and "DON'Ts" of giving an accessible presentation.

The full list of participants can be found in Table 2 below.

Table 2 List of the participants in the 2017 Learning Institute

CSA Working Group Members who participated as "patient/public leaders":	
***Louise Binder** Health Policy Consultant, Save Your Skin Foundation, previously with the Canadian Cancer Survivor Network **John-Peter Bradford** CEO, Life Saving Therapies Network ***Kathy Brodeur-Robb** Executive Director, C^{17} – Children's Cancer and Blood Disorders ***Linda Eagen** President & CEO, Ottawa Regional Cancer Foundation	**Helene Hutchings** CEO/Founder of Hair Donation Ottawa and CEO/Founder of Anal Cancer-A Bum Rap **Tammy Northam** Executive Director, Bladder Cancer Canada ***Patrick Sullivan (Chair)** President, Team Finn and a Founder & Chairman of Ac2orn
BioCanRx HQP who participated as "academic scholars":	
Ksenia Bezverbnaya PhD Candidate, Jonathan Bramson's Lab, McMaster University **Samantha Burugu** PhD Candidate, Torsten Nielsen's Lab, University of British Columbia **Rachelle Davis** MSc Candidate, Year 1, Craig Jenne's Lab, University of Calgary **Rebecca Foley** PhD Candidate, Year 1, Tania Bubela's Lab, University of Alberta ***Nicole Forbes** Research Associate, Jean-Simon Diallo's Lab, Ottawa Hospital Research Institute	**Kathy Matuszewska** PhD Candidate, Year 2, Jim Petrik's Lab, University of Guelph **Allison McNamara** MSc Candidate, Year 2, Kristi Baker's Lab, University of Alberta **Gabrielle M. Siegers** Research Associate, Year 3, Lynne-Marie Postovit's Lab, University of Alberta **Aditi Sood** Postdoctoral Fellow, Year 2, Heather Melichar's Lab, Hospital Maisonneuve-Rosemont **Madison Turk** MSc Candidate, Doug Mahoney's Lab,

Tim Guo PhD Candidate, Year 5, Naoto Hirano's Lab, University of Toronto **Chad Irwin** Postdoctoral Fellow, David Evans' Lab, University of Alberta **Israel Matos** PhD Candidate, Year 3, Kenneth Harder's Lab, University of British Columbia	University of Calgary ***Brittany Umer** PhD Candidate, David Evans' Lab, University of Alberta **Xining (Linda) Yang** PhD Candidate, Year 4, Mark D. Scott's Lab, University of British Columbia
BioCanRx Staff who participated as "facilitator":	
***Renée Leduc** Manager of Knowledge Mobilization	

How to give an accessible presentation: "DOs" and "DON'Ts"

The participants of The Learning Institute suggest taking into consideration the follow points when preparing for and giving a presentation to a broad audience.

DO's

- Include a narrative or a story
- Use examples when possible
- Use the specific to prove the general point
- Define terms and explain acronyms
- Explain the methodology used
- Use pictures where appropriate
- Where appropriate, include a demographics slide (usually for presentations about clinical trials)
- Have a logical structure/flow to a presentation like a story (what we wanted to do, here are the methods, here are the people involved, this is what we learned, here are the limitations, conclusions, and what next?
- Focus the presentation on a few key points - keep it tight; better to tell one good story well than 3 stories that are crammed and rushed (that only few can follow)

DON'Ts

- Talk about the people in the trial as subjects
- Tell us that the patients failed; the patients did not fail, the treatment failed (unless it's medical non-adherence)
- Overload your presentation with unnecessary data
- Use busy slides
- Use a lot of jargon and acronyms

Key Take-Away Messages and Group Reflections

The Learning Institute key take-away messages and group reflections for each talk at the Summit4CI can be found below.

The three and a half day Summit4Ci was held from June 25 to June 28, 2017, in Gatineau, Quebec. The program for each day consisted of the following keynote and guest speakers, a panel discussion as well as several speakers linked to a themed plenary session:

Sunday, June 25 (Day 0)	• Two (2) opening keynote speakers
Monday, June 26 (Day 1)	• Plenary Session 1: The Microbiome • Plenary Session 2: Clinical, Social & Economic Impact • Plenary Session 3: Novel preclinical models & in vitro screening platforms
Tuesday, June 27 (Day 2)	• One (1) guest speaker • Plenary Session 4: Antibodies & Antibody-like Molecules • Plenary Session 5: Innate Immunity • Plenary Session 6: Oncolytic Viruses & Viral Vaccines
Wednesday, June 28 (Day 3)	• Plenary Session 7: Adoptive Cell Therapy: Beyond Melanoma • Plenary Session 8: Biomarkers & Immune Profiling • Panel Discussion: Companion Diagnostics Discussion • Two (2) closing keynote speakers

To learn more about the Summit and to view the full program, please visit http://www.cancersummit.ca/.

SUNDAY, JUNE 25, 2017 (DAY 0)

Opening Keynotes

"Oncolytic immunotherapies: making cold tumours hot", Robert Andtbacka, Huntsman Cancer Institute, University of Utah

Key Take-Away Messages

- Immunotherapy is evolving to combination therapy of checkpoint inhibitors and oncolytic viral therapy. When immunotherapies are used in combination with standard care they can be more effective than standard care alone. Immunotherapy toxicities can be very different than standard of care toxicities
- Checkpoint inhibitors are promising, especially in combination with other therapies, but there are still challenges regarding toxicities

- Oncolytic immunotherapy appears to have an excellent safety profile
- Bystander effects are seen in lesions close to the site of viral oncolytic injection, but there is a lower response rate in distant metastatic lesions

Group Reflections

- There have been exciting advancements in oncolytics; complete responses have been documented in some patients! Now the challenge is to determine why some patients respond and others do not, and then improve therapy to increase the number of responders.
- The ongoing issues in sciences were explained, e.g. monotherapy vs combination therapies, higher risks of new treatments. When is monotherapy better than combination therapy?
- Downsides of adverse events, e.g. immune-suppressed people. What is the impact of treatments on highly immunosuppressed people? It's difficult to figure out what's going on in the patient
- Patients need support through this process and through adverse events

"Chimeric antigen receptor modified T cells: killing cancer by design", Stanley Riddell, Fred Hutchinson Cancer Research Center

Key Take-Away Messages

- Working on solid tumours
- CAR T cells show promise in the clinic
- They are learning which T cells will be most effective (combination of CD8+ central memory and CD4+ naive, for example) so as to decrease the number of cells to be infused
- Combination of CAR T and checkpoint blockade will likely be the way of the future
- CAR T's are a living therapy, that can grow/expand in the body to provide long term defense (and why this is both a good and bad thing)

Group Reflections

- Lots of potential, lots of challenges

MONDAY, JUNE 26, 2017 (DAY 1)

Plenary Session 1: The Microbiome

"Oral cancer and the oral microbiome", Donna Albertson, New York University College of Dentistry

Key Take-Away Messages

- Increased fusobacterium/decreased strep associated with cancer
- No causation known

- Challenges in investigating microbiome in cancers including oral cancer
- Dynamic processes, multifactorial

Group Reflections

- Promise in the approach

"An introduction to the microbiome as a driver and modifier of disease", Michael Surette, McMaster University

Key Take-Away Messages

- Good general overview into the importance of the Microbiome and how it impacts disease
- Questions about how this impacts patients long term care, short term treatments, how to manipulate in patients for better care
- Data sensitive to methodology
- Important from bench to bedside
- Leads to further questions, i.e.. What about the impact in childhood cancers and long term care?
- When you treat with immunotherapy what is happening to gut?

Group Reflections

- A lot to learn
- Stimulating, lots of thinking about others areas this may impact

"Fusobacterium nucleatum infection is consistent with the potentiation of tumorigenesis by co-modulation of host and bacterial gene expression", Kyla Cochrane, BC Cancer Agency

Key Take-Away Messages

- Bacteria are involved in a lot of different cancers but we don't really know how
- What comes first?
- New to cancer research: "oncobiotics" affecting outcomes and further tumours

Group Reflections

- Oncobiotic is a new and interesting concept
- Are there parallel to HPV, cervical cancer, stomach cancer?

- Could this be used as a biomarker?

"Implication of immunogenic commensals on immune checkpoint inhibitors", Bertrand Routy, Institut Gustave Roussy, Paris

Key Take-Away Messages

- Certain species of the microbiome affect responses to immune checkpoint blockade (e.g. anti-PD-1 treatment) - mice obtained from different providers have different responses to anti-PD-L1; anti-PD-1 loses efficacy if mice are treated with antibiotics. PD-1 blockade also alters the microbiome

- Ability to convert tumors not responding to checkpoint blockade into responding tumors using fecal transplantation; increase in tumour infiltrating lymphocytes

- Raised the possibility that administration of probiotics could aid in clinical responses to immune checkpoint blockade-they are moving forward with clinical trials for probiotic supplements (oncobax). Also possibility of using commensals as predictive biomarkers for response to checkpoint blockade.

Group Reflections

- The microbiome field is becoming a hot topic in immunotherapies

- The presentation seemed good itself as a story, but questions were raised about different people in different households or countries having such vastly different microbiomes that perhaps this would not be feasible to use as predictive biomarkers in response to ICI

- Can gut microbiota influence the reaction of the immune system to cancer cells?

Plenary Session 2: Clinical, Social & Economic Impact

"The New Landscape of Patent Eligibility: Empirical Findings", Christi Guerrini, Baylor College of Medicine

Key Take-Away Messages

- Innovation for patent law

- Current US patent law is limiting innovation due to difficulties in getting patents for new creations, which means that companies rely on things as trade secrets rather than going through patent law for protections

- USA issue post "4 horsemen" (4 cases that shifted the way patent law is applied in the USA)

- Research on more common cancer types tend to receive more funding and have more success obtaining patents

- Patents are being rejected in the US based on subject matter, but the same patents are being accepted in other competitive countries -- could cause the US to lose a competitive edge

Group Reflections

- This American data leads us to question the Canadian relevance

"Intellectual Property Trends in CART Development", Katherine Bonter, Clementia Pharmaceuticals

Key Take-Away Messages

- Lots of different CAR-T patents
- Number of patents is likely to increase
- “hard to translate”
- Shift from predominantly academic filing to industry filing
- Low number of industry-academic collaborations

Group Reflections

- *None*

"Educational initiatives to increase validity in preclinical cancer immunotherapy studies", Carly Barron, McMaster University

Key Take-Away Messages

- Reproducibility problem, parallels what’s going on in clinical trials (legal, methodological, social). Clinical trials in oncology have the highest failure rate
- Approximately 5% of drugs that pass preclinical studies get licensed
- Of 53 high impact publications chosen, only 11% could be replicated
- Addressing the reproducibility problem through training and education. Scientific rigour is important, proper randomization and experimental design workshops are helpful
- Thoughts about how this has been observed in other disciplines
- Resources were made available, future training opportunities

Group Reflections

- Eye opening presentation, is working towards a solution to reproducibility in basic science.

- She posed the problem and provided answers through international guides and educational initiatives

Resources:

- NIH core items: Landes et al. Nature 2012
- ARRIVE guidelines: Animal Research Reporting of In Vivo Experiments
- Randomization: www.randomization.com, there are also apps for randomizing clinical trials, stats packages, =RAND in Excel

"More Haste, Less Speed: Could Public Private Partnerships Advance Cellular Immunotherapies?", Tania Bubela, University of Alberta

Key Take-Away Messages

- PPP (public private partnerships) is an interesting model to pursue as it can help expand research opportunities: What does this mean? Who is involved? Don't forget the importance of the contributions of people living with cancer, caregivers, patient representatives, and health economists
- PPP is not linear, but is multi-directional, and it appears we are moving in the right direction overall
- Importance of knowledge exchange; particularly "Tacit knowledge" (flow of expertise through people coming to the lab and showing you techniques for reproducibility)
- Tacit knowledge and PPP is also beneficial for reduction of duplicative research

Group Reflections

- We need to enhance PPP to improve agents at early stages to avoid them failing at later stages in development (translation is highly uncertain - 10 to 15% of drugs entering trials get into the market)
- Clear that she was passionate and open to different participants and stakeholders - creation of inclusive research
- Challenges (treatment development, access, research etc.) need to be addressed, but can PPPs address issues?
- PPP demonstrates an exciting inclusive approach to research which people living with cancer expect . We might be more successful in immunotherapies if there is a shift to PPP models

Plenary Session 3: Novel preclinical models & in vitro screening platforms

"Ultra-deep screening of natural antibody repertoires using high-content single-cell selection assays", Carl Hansen, AbCellera Biologics

Key Take-Away Messages

- Existing technologies make it hard to identify natural antibodies (which have better affinities than synthetic ones)
- Presenter discussed a new high throughput screen of natural antibodies (Abs) which allows for rapid identification of novel targets
- Presented some examples for identifying targets specific for cancer and other diseases

Group Reflections

- impressive, high throughput results in a short amount of time
- Promising technology but requires specific cancer target

"Next Generation Humanized Mouse Models for Cancer Research", Lenny Shultz, The Jackson Laboratory

Key Take-Away Messages

- Lenny has developed – and continues to develop – better and better mouse models with which we can model cancers and now study immunotherapy in a more physiologically relevant setting (closer to human – humanized mice)
- History from nude mice (1960s) award
- Explained different models, methods to humanize mice advantages and drawbacks
- “Storm warning” – test therapeutics in mice before patient
- Humanized mouse avatars
- PDX – orthotopic best for some cancers (e.g. breast)

Group Reflections

- Excellent talk
- Great to hear what goes into making the models we use

"Cytotoxic CD8+ T cell tracking by MRI in response to immunotherapy in a C3 cervical cancer model", Marie-Laurence Tremblay, IWK Health Center, Halifax

Key Take-Away Messages

- Labelled CD8 T cells migrate to tumors in C3 cervical cancer models
- Follow migration of immune cell subsets. The model allows one to assess how cell numbers change with different immunotherapy protocols
- Looking at other parameters other than tumor volume
- Longitudinal study to monitor immune cells in cancer models

- Nice validations with GFP+ (fluorescent label) cell identification + overlay to prove identity
- Cytotoxic T cell recruitment increases with tumor volume
- This was more of a proof-of-principle study - not meant to test therapy per se

Group Reflections

- The limitations/weaknesses: cell viability, GvHD in mice, where not clearly discussed

"The zebrafish: An emerging model system for cancer immunotherapy", Jason Berman, Dalhousie University

Key Take-Away Messages

- Discussed the use of zebrafish as a model organism for cancer therapies (less expensive than other organisms like mice, similar immune functions as other organism)
- Able to exploit the natural characteristics of a model system (i.e.. zebrafish are transparent) while still being clinically relevant,
- Capacity for screening which allows for identification of rare mutations from patient cancers

Group Reflections

- Zebrafish are more useful as a translational tool than previously thought, and that other organisms (besides mice) can be used in cancer research

TUESDAY, JUNE 27, 2017 (DAY 2)

Invited Speaker

"Reducing bias at the bench and improving reporting of experiments: how you can help improve the quality of our science", Manoj Lalu, University of Ottawa

Key Take-Away Messages

- Need to deal with reproducibility issues
    - Hypothesis is that if we are able to deal with reproducibility issues at the preclinical level there's a better likelihood that the research will lead to better clinical outcomes.
    - If the foundational preclinical research is strong then the subsequent research can be interpreted with more confidence
- Most research studies did not report exact methodology – is that a reporting error or a "cultural" problem in research? Important to understand "how" the research was conducted both for reproducibility and for confidence in the study conclusion

- Are we funding research that has meaningful patient engagement or merely research *on* patients?

Group Reflections

- Want analysis of “good” reports to see if there are increased clinical outcomes
- Was nice to hear a research be recognize the value of meaningful patient engagement, because the patient community believes that it adds value to engagement and retention in clinical trials, as well as knowledge translation

Plenary Session 4: Antibodies & Antibody-like Molecules

"Novel ways to target & activate NK cells to treat cancer", Jeffrey Miller, University of Minnesota

Key Take-Away Messages

- Natural killer (NK) cells are potent and can kill tumor cells; but cancer cells look too similar to self – we can **rationally engineer NK cells** with bi- / tri-specific killer engagers (BiKEs / TriKEs) to increase cancer killing specificity
- Can also rationally engineer NK cells to persist longer in patients by making them resemble Memory NK cells.
- There are some issues with T cell engineering – maybe research with NK cells can improve this
- Cytomegalovirus (CMV) infection of NK cells has some implications on bone marrow transplants – therefore, broad implications

Group Reflections

- Summarized periodically – helped with understanding
- Good science but also accessible to patients
- Brought us along on the story
- Broad implications
- Outside the box/interesting ideas

"Targeting Solid Tumors with Bispecific Antibodies and Drug Conjugates", John Babcook, Zymeworks

Key Take-Away Messages

- Four platforms to exquisitely engineer antibodies that can be 1) bispecific or 2) carry toxins or 3) increase or decrease Fc binding (antibody mediated cellular cytotoxicity) or 4) alter half-life and bind multiple sites

- 2 already in clinical trials, many more in the pipeline
- Can be combined
- “Designer antibodies”
- Explained mutations made to increase specificity
- Low to no toxicity because similar to natural antibodies
- Increased therapeutic window

Group Reflections

- Explained platforms very well
- Stories about patients are very impactful and should be included in some way. His presentation demonstrated this and also showed that he clearly does this for the patients!

"The efficacy of CD133 BiTEs and CAR-T cells in preclinical model of glioblastoma", Parvez Vora, McMaster Stem Cell and Cancer Research Institute

Key Take-Away Messages

- Adapted patient treatment to the mouse model (chemo given to the mouse)
- Since cells expressing CD133 demonstrate resistance, can CD133 be used as a marker to group patients into different risk categories?

Group Reflections

- A good example of scientists having transferable skills that allow them to work/present in different areas of expertise

"Development of single-domain antibody cancer therapeutics at NRC", Kevin Henry, National Research Council Canada

Key Take-Away Messages

- Discussed single chain antibody (Ab): originally from sharks; smaller than human antibodies, which makes them easier for manufacturing and gives them better tissue penetration and stability; and similar targeting affinities as human antibodies
- Can link them to cytotoxic cell-killing agents to target specific cancers
- Can use next generation sequencing to identify antibodies
- Gave an example of one targeting lung-cancer (LDOS-47), which is currently being evaluated in a phase-I safety trial

Group Reflections

- Did a good job explaining the benefits of single-chain antibodies over other technologies
- Real test will be when technology is combined with other treatments
- Good example of made-in-Canada technologies and the role of government agencies in its development

Plenary Session 5: Innate Immunity

"Adoptive immunotherapy with expanded NK cells", Dean Lee, Nationwide Children's Hospital

Key Take-Away Messages

- Natural killer (NK) cells are a hub of the immune system
- NK cell immunotherapy has advantages over T cell therapies, i.e., off-the-shelf potential, broad cancer applicability, lower manufacturing cost, etc.

Reflections

- *None*

"Postoperative left shift: The link between surgical stress, immune dysfunction and metastases", Rebecca Auer, University of Ottawa

Key Take-Away Messages

- Surgical stress leads to immune cell dysfunction: natural killer (NK) cells, T cells leads to high increase in Myeloid-derived suppressor cells (MDSCs), which leads to an increase in metastases. This was seen with ablation of tumour-associated antigens (TAA) vaccination efficacy following surgery
- The perioperative period should be viewed as a window of opportunity for cancer treatment and prevention of future metastases. Even though in itself surgery can be oncogenic, surgical resection of tumors remains a first and often necessary part of many cancer regiments.
- There is an ebb and flow of pro- and anti- inflammatory responses in the postoperative period. Understanding this shift will allow for better perioperative treatments in the context of surgical tumor resection.

Group Reflections

- Nice to hear emphasis on metastasis research
- Revelation surgery should be reconsidered as a go-to cancer treatment

"In vitro differentiated plasmacytoid dendritic cells as a tool to induce anti-leukemic activity of Natural Killer cells", Sabine Herblot, CHU Ste-Justine, Montreal

Key Take-Away Messages

- Potential for plasmacytoid dendritic cells (pDCs) and NK (natural killer) cells to increase anti-leukemia activity

Group Reflections

- Mapping of science to potential application and impact on clinical outcomes
- Interesting and exciting that they found another way to use NK cells

"The role of the innate immune system in cancer metastasis", Donna Senger, University of Calgary

Key Take-Away Messages

- Explained how cancer metastases occur and how her laboratory is interested in whether immune cells (neutrophils) can be used to prevent this from happening
- Researcher explained how Natural Killer (NK) cells are manufactured then infused into patients after which they measure the immune response. The concept is that NK cells recognize the cancer cells and attack them quickly, gave example for acute myeloid leukemia
- Identified a peptide that could potentially be used as a therapeutic to block metastases (trying to develop this further), could potentially be low-cost therapy, which may have be applicable to a wide range of cancers

Group Reflections

- Great diagrams!
- How to prevent metastases “seed and soil” metaphor helped us understand metastasis
- It was interesting to focus on neutrophils; this was appreciated as most cancer immunotherapies focus on the adaptive arm of immunity

Plenary Session 6: Oncolytic Viruses & Viral Vaccines

"Targeted immunotherapy using oncolytic adenoviruses", Len Seymour, Oxford University

Key Take-Away Messages

- Oncovirus can be used to deliver Bi-specific T-cell engagers (BiTEs) and are a great immunotherapy tool
- Expression of the BiTE is linked to virus expression
- BiTE activated T cells will kill tumor cells a lot faster than virus
- BiTEs can activate T cells in immunosuppressive environments
- BiTE: bispecific T-cell engager

- Not major histocompatibility complex (MHC) restricted, they can be targeted to any antigen

Group Reflections

- Immunotherapy is complex and is unlikely that one single treatment will be enough
- Interesting concept of combining different immunotherapies into one treatment

"Oncolytic Viral Vaccines for the Treatment of Solid Tumours", Kyle Stephenson, Turnstone Biologics

Key Take-Away Messages

- Discussed the use of Maraba virus for the treatment of prostate cancer (castrate resistant at prostate specific antigen (PSA) progression). Humans have little prior exposure to this virus, which means less of a pre-existing defense against the virus, which can dampen its ability to grown in, and kill, the cancer.
- Discussed how the virus could be modified to express tumor antigens which would help boost the immune system response (CD8+ T-cells) against the cancer.
- Also discussed how this could be combined with another virus (adenovirus) to improve the anti-tumor response (two viruses may be better than one!)

Group Reflections

- Important to choose the appropriate virus for the patient and cancer
- A good example of really good, made-in-Canada, collaborative research

"A recombinant oncolytic virus expressing the B cell chemokine CXCL13 can induce complete tumour regression, and is associated with intratumoural neutrophil infiltration and massive necrosis", Stephen Redpath, BC Cancer Agency

Key Take-Away Messages

- There is a focus on T cell infiltration and tumour clearance since T cells are what directly cause tumour cell lysis. However, tumour clearance was improved when B cells were also recruited to the tumour microenvironment. A shift in focus may be necessary when trying to manipulate/increase TIL to the tumour to include recruitment of both B and T cells, instead of T cells only
- Neutrophils may have a role in tumor clearing efficacy. Tertiary lymphoid structures are forming in the tumor microenvironment
- Engineering CXCL13 into Vesicular Stomatitis Virus (VSV) lead to better TIL recruitment to the tumor. TIL are important for tumor clearance

Group Reflections

- *None*

"Determinants of efficacy in cancer immunovirotherapy", Christine Engeland, National Center for Tumor Diseases, Heidelberg

Key Take-Away Messages

- Measles encoding granulocyte-macrophage colony-stimulating factor (GM CSF) [have] = good efficacy, but still room for improvement
- Immune cell profiling may determine efficacy (Interleukin 12 (IL-12) or alpha cytotoxic T lymphocyte antigen-4 (αCTLA-4) engineering)
- Using these engineering techniques minimizes toxicity systemically
- Different tumours may need different viruses/vectors
- More Bi-specific T-cell engagers (BiTEs) added to these engineered measles viruses which can increase cancer cell killing by increasing T cell targeting to tumour cells.

Group Reflections

- Good use of patient photos to demonstrate efficacy
- Translational medicine!

WEDNESDAY, JUNE 28, 2017 (DAY 3)

Plenary Session 7: Adoptive Cell Therapy: Beyond Melanoma

"Reprogramming T cells and hematopoietic stem cells for adoptive immunotherapy in ovarian cancer", Kunle Odunsi, Roswell Park Cancer Institute

Key Take-Away Messages

- Hematopoietic stem cells (HSCs) can be reprogrammed for a life-long supply of anti-tumor T cells
- cluster of differentiation 4 (CD4) T cell receptor (TCR) transduced HSCs can lead to long-lasting (12m) tumor control in murine models

Group Reflections

- Very interesting and promising work

"Anti-leukemia and –lymphoma T-cell immunotherapy", Denis Claude Roy, Hôpital Maisonneuve-Rosemont, Université de Montréal

Key Take-Away Messages

- Minor histocompatibility antigens (miHAs) are better targets for treatment of hematologic cancers than tissue specific antigens (TSAs)

- Therapeutically relevant: GLIDE strategy (Guided Lymphocyte Immunopeptide Derived Expansion) in vitro expansion of miHA specific T cells under Good Manufacturing Practice (GMP) conditions

- Clinical trials against miHA presented by HLA-A02:01 which is the most common human leukocyte antigen (HLA) type in European Americans allows targeting a large population

- Identification of miHA and their therapeutic targeting in refractory hematological cancers

Group Reflections

- Interesting topic

- Good to see promising clinical trials results

- included great patient story

"Expanding and enriching driver mutation-reactive T cells for adoptive cell therapy of lymphoma", Julie Nielsen, BC Cancer Agency

Key Take-Away Messages

- Tumor driver mutations as the new targets for T-cell based therapy

- Both mutation-specific CD4/CD8 T-cells can be expanded from blood

- Shared driver-mutations can also be recognized by CD4/CD8 T cells

- Proposed clinical trials

- Tumor driver mutations: identified by sequencing methodology

Group Reflections

- Involvement of patients with high relapse rate

- Indicative of personalized treatments

- Easy-to-follow presentation

"Studying and enhancing T-cell mediated anti-tumor immunity to bridge between immunotherapy and personalized medicine", Cyrille Cohen, Bar-Ilan University

Key Take-Away Messages

- Covered different approaches in T cell-based immunotherapy. Described the strategies for precisely isolating T cells specific for the antigen:

    - If we don't isolate melanoma-specific tumor-infiltrating lymphocytes (TILs) and expand bulk TILs, antigen-specific population gets outnumbered by other TILs, therefore it is more effective

    - If T cells do not naturally migrate to the tumor site, they can be modified to express a chemokine receptor that will make them home to the tumor

- Can turn immunosuppressive signals in tumor microenvironment into activating (make T cells express PD1-CD28 fusion protein)

Group Reflections

- Although the field of cancer immunotherapy is growing rapidly, there is still plenty of room for new and exciting ideas

Plenary Session 8: Biomarkers & Immune Profiling

"What can Hematopoietic Cell Transplantation biomarkers teach us about targeted immune therapy studies today?", Kirk Schultz, British Columbia Children's Hospital

Key Take-Away Messages

- Importance of relationship between biomarkers (not just study a single biomarker)
- Toxicity and efficacy cannot be separated!!
- Large collaboration between institutions are needed to find predictive biomarkers
- Link between toxicity and efficacy
- Importance of proper control

Group Reflections

- Made connection with patients: importance of finding biomarkers of response (graft versus host disease)

"Development of methods to assess the state of engineered T cells in clinical trials", Eustache Paramithiotis, Caprion Biosciences

Key Take-Away Messages

- Developing a consistent and standardized, clinical-grade assay to track/measure functional parameters of cellular therapy is challenging
- Incorporating novel technology (e.g. mass cytometry) into these clinical assays is limited by the lack of standardization of practices at different locations, despite the potential of offering more powerful analyses
- The main point of reproducibility and standardizing protocol in clinical monitoring is well emphasized

Group Reflections

- Helps in appreciating much of the work that goes into an cell therapy-based clinical trial behind the scenes

"Assessment of T-cell receptor reactivity by deep sequencing", Govinda Sharma, BC Cancer Agency

Key Take-Away Messages

- Current high throughput methods do not accurately reflect or represent physiological context
- Designed a high throughput functional assay
- FRET-based (fluorescence resonance energy transfer)
- Minigene expression – if granzyme B also expressed see colour change indicating T cell activation
- Sequence to identify minigene
- Proof of principle demonstrated

Group Reflections

- Technically challenging
- The feasibility or the cost of implementation was not fully discussed

"Cytokine Release Syndrome in Cellular Therapy: Making sense in all the noise", David Barrett, University of Pennsylvania

Key Take-Away Messages

- How can we identify when a patient might be at risk of cytokine release syndrome? Monitor the cytokine profile of the patient over time to potentially know when to intervene (with IL-6 blocking)
- Although cytokine release syndrome (CRS) is typically observed in clinical trials with CAR T cells, it is currently defined by a combination of clinical symptoms rather that biological markers. Future clinical and basic scientific research into the types of CRS and its underlying factors will help improve diagnosis and management of this syndrome.
- CARs are not producing IL6. It is host macrophages and antigen presenting cells
- Not every CAR is created equal. Toxicity and functionality depend on everything, including how these T cells were engineered and processed prior to infusion

Group Reflections

- Wonderful story, great clinical implications
- Had such an impact
- Broad implications for all immunotherapies (not just CAR-Ts)

- Neurotoxicity is still a large black box - does not seem to correlate with anything

Panel Discussion: Companion Diagnostics Discussion

Key Take-Away Messages

- Many new precision-based medicines require a companion diagnostic test to identify individuals that are more likely to respond to, or have responded to, these new treatments. The Panelists discussed a white paper report that had been drafted to discuss the issues with establishing these tests.

- A number of barriers to implementing these tests exist, including societal, financial, and regulatory

- Challenge of having diagnostics available to patient at the same time as new treatments are approved

Group Reflections

- This highlighted the need for not only new cancer treatments but the need for developing and implementing associated tests which can predict patients who will benefit from such therapies

- Highlighted the complex nature of implementing consistent health-care policies across Canada

Closing Keynotes

"Cancer immunotherapy with oncolytic viruses: Beyond lysis", Dmitriy Zamarin, Memorial Sloan-Kettering Cancer Center

Key Take-Away Messages

- Intratumor Newcastle Disease Vaccine (NDV) treatment caused systemic tumour-specific immune effect; treated tumour and distant tumor. Therapeutic efficacy of NDV is dependent on adaptive immune response. NDV potentiates the efficacy of checkpoint blockade therapy, e.g. CTLA-4, PD-1/PD-L1

- Genetic engineering of NDV enhanced lytic abilities but did not improve therapeutic efficacy. Why? Decreased tumor infiltration with tumor-specific lymphocytes. This shows that NDV was capable of modulating the tumour microenvironment and immune cell infiltration. Manipulating this could either enhance or inhibit antitumour immunity, resulting in different therapeutic outcomes

- Less viral replication correlated with increased anti-tumour immunity. Enhances tumor lysis may not lead to better therapeutic efficacy, what's important is the balance between tumor lysis, anti-viral immunity and anti-tumor immunity

Group Reflections

- An inspiring talk, questions posed along with new findings

- Stimulated people to think
- A lot of data shown, good summary slide in the end

"What healthcare payers wish you knew: Start with cost-effectiveness in mind", Jeffrey Hoch, UC Davis

Key Take-Away Messages

- Decision makers want to spend taxpayers money wisely, thus cost-effectiveness needs to be kept in mind when designing new therapies
- The use of health technology assessment (HTA) involving cost-effectiveness analyses (CEAs) aid their decision-making process (smart shopping).
    - Opportunity costs (having to choose one drug over another)
    - Incremental value within a disease area (is this really making a large enough difference relative to what is already available?)
    - Consider other factors including the type of disease, whether it is an underserved population, and the demographics of the disease population
- As a result researchers should be aware that the questions that decision-makers have additional questions to what are asked by regulators. Researchers should be cognizant of the importance of included HTA focused question in their research to ensure that "good" research outcomes can be made practically accessible to patients.
- Increasing incidence of the prices of new innovative drugs being higher than the incremental population-level health benefits associated with them. Thus, in terms of a cost-benefit ratio public payers will not recognize the value of including high cost drugs that do not demonstrate population-level long term effects
- Actions that researchers should do:
    - 1) Learn more about pan-Canadian Oncology Drug Review (pCODR) and HTA to understand the perspective of decision makers
    - **2) Talk to patients!** Understand their needs, including HTA-relevant questions. During trials, ask about their quality of life and how they feel.
    - 3) Talk to people who work with CEAs to understand how good your drug would need to be to be cost-effective, and therefore funded and implemented in the real world.
    - 4) Consider HTA as part of the research design process including as secondary endpoints

Group Reflections

- Very interesting perspective that we had not previously considered. This information would be good to consider throughout drug/diagnostic research and during clinical trials.

- Very engaging and extremely accessible to all audiences
- As a result of a question, Dr. Hoch agreed that researchers should consider submissions directly to pCODR where appropriate
- Hearing about the history of the development of the HTA process was interesting, and provided an additional perspective about having to fight for the patient voice to be heard.

Helpful Websites

Ac2orn – Advocacy for Canadian Childhood Oncology Research Network
http://www.curesforourkids.com/

Anal Cancer-A Bum Rap http://www.analcancer-abumrap.com/

BioCanRx: https://biocanrx.com/

BioCanRx Cancer Stakeholder Alliance: https://biocanrx.com/about/governance/cancer-stakeholder-alliance

BioCanRx-Cancer Stakeholder Alliance Learning Institute
https://biocanrx.com/about/governance/cancer-stakeholder-alliance/biocanrx-cancer-stakeholder-alliance-learning-institute

Bladder Cancer Canada https://bladdercancercanada.org/en/

Canadian Cancer Society, Research Horizon, Immunotherapy, a promising new field of cancer treatment: http://www.cancer.ca/en/research-horizons/e/c/9/immunotherapy-promising-new-field-treatment/?region=on

C^{17} – Children's Cancer and Blood Disorders http://www.c17.ca/

Hair Donation Ottawa http://hairdonationottawa.com/

Life Saving Therapies Network https://www.lifesavingtherapies.com/

Ottawa Regional Cancer Foundation http://www.ottawacancer.ca/

Save Your Skin Foundation https://saveyourskin.ca/

Society for Immunotherapy of Cancer patient glossary: http://www.sitcancer.org/patient/glossary

Society for Immunotherapy of Cancer patient resource:
http://www.sitcancer.org/patient/resources

Summit for Cancer Immunotherapy: http://www.cancersummit.ca/

Team Finn http://www.teamfinn.com/

The Lung Association – Ontario http://lungontario.ca/