# 2018 Community Dissemination Report

## BioCanRx-Cancer Stakeholder Alliance Learning Institute

*Cancer Immunotherapy Research - An Outline of Current Work as Discussed at the 2018 BioCanRx Summit4CI written by the Patients and Caregivers Who Were There in Collaboration with Junior Researchers Working in the Field*


BioCanRx
Biotherapeutics for Cancer Treatment
Biothérapies pour le traitement du cancer

December 2018

This is the **Community Dissemination Report of the 2018 BioCanRx-Cancer Stakeholder Alliance Learning Institute**.

It is a public document written by the participants of the 2018 BioCanRx-Cancer Stakeholder Alliance Learning Institute that was held at the 2018 Summit for Cancer Immunotherapy (Summit4CI) from October 27 to October 30, in Banff, Alberta.

This report serves to highlight and 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 coming out of the second iteration of the Learning Institute that was delivered at the 2018 Summit for Cancer Immunotherapy.

The Learning Institute piloted at the 2017 Summit for Cancer Immunotherapy and has become a permanent component of the annual Summit. This initiative 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 that/which participants dedicated to developing this important patient engagement initiative.

We are looking forward to hosting another successful event at the next Summit in October 2019. You can learn more about the Summit4CI at cancersummit.ca

This report was produced by the Learning Institute, and is written for the community of cancer patients and researchers in Canada; it includes key take-away messages from each plenary session presentation and the Learning Institute's reflections on these messages.

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
BioCanRx

## From the Cancer Stakeholder Alliance

In 2017, on the advice of the Cancer Stakeholder Alliance, BioCanRx created the Learning Institute. The Learning Institute was built on the following propositions:

1. Patients have an important and powerful voice that is critically important to advancing cancer immunotherapies;
2. Patients have a lot to learn;
3. Patients have a lot to teach.

As part of the Learning Institute, young investigators adopt advocates and advocates adopt young investigators. They attend the conference as partners and learn from each other throughout the conference.

Young investigators are able to help patients understand science and the scientific process and advocates are able to help young investigators understand the importance of their work in the real world. Patients are able to pass on both their lived experience and their life experience beyond cancer.

I believe we have created the start of something very important. Something that we should continue building on because it has the prospect of changing the culture of cancer research while improving the scientific enterprise.

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


**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 initiative that brings cancer patients/caregivers 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:

- facilitate a model of learning that encourages, supports and creates the integration of patient/public leaders into the scientific conference
- ensure that scientific research presented at the conference is accessible to the cancer patient community
- highlight the patient/caregiver perspective to ensure cancer research is well informed by the patient voice and lived experience
- familiarize Highly Qualified Personnel with the concept of patient engagement in research
- highlight the bi-directional model of learning which both participant groups are actively learning from another

The Learning Institute consists of:

- a series of high-energy knowledge translation and exchange sessions,
- a “buddy model”, where patient/caregiver leaders are paired with BioCanRx Highly Qualified Personnel, and
- writing a report that includes the key research take-away messages presented at the Summit4CI and group reflections about the research discussed

The Learning Institute serves to integrate the cancer patient voice and perspective into the research environment at the Summit4CI. In turn, researchers are exposed to the realities of the cancer patient experience and understand the patient perspective about the research process. Patients and researchers also develop their skills in knowledge exchange and translation, networking, and in building and strengthening their connections. The Learning Institute aims to nurture the growing culture around patient engagement in research.

## Development

The Learning Institute was inspired by the Community AIDS Treatment Information Exchange (CATIE) – Canadians Association for HIV Research (CAHR) Learning Institute. 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. Members of the 2017 CSA Working Group partnered with BioCanRx staff and Highly Qualified Personnel to develop the inaugural Learning Institute which was piloted at the 2017 Summit4CI. This year’s Learning Institute was designed by the BioCanRx-CSA Learning Institute Working Group and BioCanRx staff using the feedback obtained from last year’s initiative.

*Table 1 Members of the 2018 BioCanRx-CSA Learning Institute Working Group.*

| **Members:** |
|---|
| **Louise Binder**<br>Health Policy Consultant, Save Your Skin Foundation<br><br>**Kathy Brodeur-Robb**<br>Executive Director, C17 – Children's Cancer and Blood Disorders<br><br>**Manoj Lalu**<br>Associate Scientist, Blueprint Translational Research Group, Ottawa Hospital Research Institute<br><br>**Patrick Sullivan**<br>President, Team Finn and a Founder & Chairman of Ac2orn |
| **BioCanRx HQP:** |
| **Brittany Umer**<br>PhD Candidate, David Evans Lab, University of Alberta<br><br>**Kathy Matuszewska**<br>PhD Candidate, Jim Petrik Lab, University of Guelph |
| **BioCanRx Staff:** |
| **Stéphanie Michaud**<br>President and CEO, BioCanRx<br><br>**Fozia Mohamed Nur**<br>Knowledge Mobilization Intern, BioCanRx |

## Thank You

BioCanRx and the members of the BioCanRx-CSA Learning Institute Working Group wish to thank the CATIE-CAHR Learning Institute for the inspiration and for setting the bar of excellence.

BioCanRx wishes to give a special thank you to the Learning Institute Mentors for their dedication of their time, energy, focus and work in making the Learning Institute a great success.

We would also like to extend a big thank you to Canadian Institutes of Health Research, Institute of Cancer Research for being a proud supporter of this initiative.

## 2018 Learning Institute

This year's initiative brought together nine members from the cancer patient/caregiver community, in the role of patient scholars, eleven members of the BioCanRx Highly Qualified Personnel (HQP) community, in the role of academic scholars, three members from the Learning Institute Working Group, and two BioCanRx staff as facilitators (Figure 1). HQP are defined as all individuals responsible for the translation of promising cancer biotherapeutics. They include undergraduate and graduate students, post-doctoral fellows, and research and clinical staff.


*Figure 1: 2018 BioCanRx-CSA Learning Institute participants. Back to front row, from left to right: * Kathy Brodeur-Robb, Richard Stephens, Josh Del Papa, Heather Douglas, Jianyin Liu, *Fozia Mohamed Nur, Israel Matos, *Patrick Sullivan, Roberta Casabon, Nathalie Baudais, James Han, Judy Needham, Gabrielle Siegers, *Brittany Umer, Terry Hawrysh, Kathy Brooks, Alyssa Vito, Lauren St-Germain, Samuel Rouleau, Gretta Hutton, Stefany Dupont, Courtney Victoria Mowat, *Louise Binder. Missing from photo: *Kathy Matuszewska, and *Stéphanie Michaud.*

*Members of the BioCanRx-CSA Learning Institute Working Group are indicated by "*".*

Together, they participated in a series of interactive and collaborative “Knowledge Exchange sessions” that served to guide the process of knowledge synthesis, dissemination, and exchange. (Figure 2).

*Figure 2: An early morning Knowledge Exchange session in action. Participants discussed the plenary sessions from the previous each morning over breakfast. These high-energy sessions included an overview of the day ahead provided by the academic scholars, small group discussions followed by a report back to the group on key highlights, scientific content, personal thoughts and overall accessibility of each presentation.*

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

*Table 2 List of the participants in the 2018 Learning Institute.*

| **Patient Leaders/Caregivers who participated as “patient scholars”:** | |
|---|---|
| **Nathalie Baudais**<br><br>**Kathy Brooks**<br>Canadian Partnership Against Cancer<br><br>**Roberta Casabon**<br>Prostate Cancer Canada<br><br>**Stefany Dupont**<br><br>**Heather Douglas** | **Gretta Hutton**<br>Canadian Cancer Clinical Trials Network<br><br>**Terry Hawrysh**<br>Leukemia Lymphoma Society of Canada<br><br>**Judy Needham**<br>Canadian Cancer Trials Group<br><br>**Richard Stephens**<br>England’s independent Cancer Taskforce |

| **BioCanRx HQP who participated as "academic scholars":** | |
|---|---|
| **Josh Del Papa**<br>PhD Candidate, Robin Park's Lab,<br>Ottawa Hospital Research Institute<br><br>**James Han**<br>PhD Candidate, Pamela Ohashi's Lab,<br>University of Toronto<br><br>**Jianyin Liu**<br>Undergraduate Candidate, Year 4, David Evan's Lab, University of Alberta<br><br>**Israel Matos**<br>PhD Candidate, Year 1, Kenneth Harder's Lab,<br>University of British Columbia<br><br>**Kathy Matuszewska**<br>PhD Candidate, Jim Petrik's Lab,<br>University of Guelph<br><br>**Courtney Victoria Mowat**<br>MSc Candidate, Year 2, Kristi Baker's Lab,<br>University of Alberta | **Samuel Rouleau**<br>Postdoctoral Fellow, Lee-Hwa Tai's Lab,<br>Université de Sherbrooke<br><br>**Gabrielle Siegers**<br>Research Associate, Lynne Postovit's Lab,<br>University of Alberta<br><br>**Lauren St-Germain**<br>MSc Candidate, Alex Beristain's Lab,<br>University of British Columbia<br><br>**Brittany Umer**<br>PhD Candidate, David Evan's Lab,<br>University of Alberta<br><br>**Brett (Chung-Hsi) Wang**<br>PhD Candidate, Naoto Hirano's Lab,<br>University of Toronto |
| **CSA Working Group members who participated as "mentors":** | |
| **Louise Binder**<br>Health Policy Consultant, Save Your Skin Foundation<br><br>**Kathy Brodeur-Robb**<br>Executive Director, C17 – Children's Cancer and Blood Disorders | **Patrick Sullivan (Chair)**<br>President, Team Finn and a Founder & Chairman of Ac2orn |
| **BioCanRx Staff who participated as "facilitators":** | |
| ***Stéphanie Michaud**<br>President & CEO | ***Fozia Mohamed Nur**<br>Knowledge Mobilization Intern |

## Key Take-Away Messages and Group Reflections

The Learning Institute key take-away messages and group reflections from each plenary session at the 2018 Summit4CI can be found below.

This conference was held from October 27 to October 30, 2018, in Banff, Alberta. A general overview of the program agenda is provided below.

| | |
|---|---|
| **Saturday, October 27 (Day 1)** | • Two (2) opening keynote speakers |
| **Sunday, October 28 (Day 2)** | • Plenary Session 1: Tackling Challenges in CAR T and Engineered T cells<br>• Plenary Session 2: Understanding and Overcoming Resistance Mechanisms in Immunotherapy<br>• Plenary Session 3: The Underdogs: The Other Players in Cancer Immunotherapy |
| **Monday, October 29 (Day 3)** | • Plenary Session 4: The Tumour Microenvironment/Metabolism and Immune Profiling<br>• Plenary Session 5: Emerging approaches to enhancing translational research: Innovative design and patient involvement<br>• Plenary Session 6: Antigen Discovery and Neo-epitopes |
| **Tuesday, October 30 (Day 4)** | • Plenary Session 7: Combination Immunotherapy Strategies<br>• One (1) closing keynote speaker |

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

**SATURDAY, OCTOBER 27, 2018 (DAY 1)**

## Opening Keynotes

### *Stefany Dupont, Patient Representative*

Key Take-Away Messages

- First cohort of CAR treated
- Patients also require psychosocial help or assistance
- Impact of patient engagement on the research process?
- Sense of urgency for moving implantation of research
- Research should focus on innovation, compassion, prevention

Group Reflections

- Stefany did a great job of humanizing the cancer experience by sharing her personal cancer experience (acute lymphoblastic leukemia) and ultimate success with the CAR-T clinical trial treatment that she received in the United States.
- During her presentation, she was able to create a sense of urgency for advancing the implementation of cancer research. Cancer patients cannot afford to wait.

### *Crystal Mackall, Stanford University*

Key Take-Away Messages

- People love to fund 'Eureka' moments
- Translational research is incremental and takes a long time
- Decreased money for 'slog' moment, difficult to get recognition for blockbuster, need to fund 'slog'
- Hope vs. hype: how do you balance?
- Knowing when to stop and when to persevere

Group Reflections

- Crystal explained that its often easy to fund the discovery but it is difficult to fund the invention, the on-going 'slog' work
- She made a note of patient involvement in advancing cancer research

**SUNDAY, OCTOBER 28, 2018 (DAY 2)**

## Plenary Session 1: Tackling Challenges in CAR T and Engineered T cells

### *"Enhancing Adoptive Cell Therapies through Exogenous Regulation", Steve Shamah, Obsidian Therapeutics*

Key Take-Away Messages

- It might be possible to control activity of engineered T cells in the patient using drugs (small molecule "ligands")
- Addition of the drug causes proper protein folding to stabilize the ligand that directs T cell activity
- This is designed to be reversible
- The regulation of T cells through the use of these drugs holds great promise for safer and more effective immunotherapy treatments

Group Reflections

- Steve should have used the term "drug" instead of "ligand" to make his presentation more accessible
- Applicable to whole array of cells, so it is a very promising talk
- Concerns about drug availability, biodistribution, and persistence
- Steve should have defined the following terminology: ligand, xenograft, syngeneic, constitutive, and PK (pharmacokinetics)

### *"Engineering T cells with a chimeric receptor that co-opts the native TCR", Jonathan Bramson, McMaster University*

Key Take-Away Messages

- TAC T-cells are more specific than CAR T-cells
- CAR T-cells can have toxicities to the heart and lungs in mouse models because they are always signaling at a low level whether their targets are present or not
- Mice with a high tumour burden actually did better when TAC T-cells had a low proliferation rate
- A clinical trial is scheduled to start in Q2 2019 for diffuse lymphoma

Group Reflections

- A few key words that were used in this presentation should be reflected in the glossary
    - Autologous versus allogeneic
    - TAC → T-cell antigen coupler
    - Endogenous TCR (T-cell receptor)

    - ITAM (in the cytoplasmic tail of the receptor): Immunoreceptor Tyrosine-Based Activation Motif
- The presentation looked beyond CARs and was therefore thought to be innovative
- Jonathan did a good job of explaining the markers that he referred to in the presentation
- He presented a good and logical story through his talk
- This talk was thought to be the most accessible presentation

***"TCR-engineered T cells to treat solid tumors: targeting MAGE-A3 and beyond", Yong-Chen Lu, NIH/NCI***

Key Take-Away Messages

- Yong-Chen's research is exploring the use of MAGE-A3, a cancer germline antigen, as a target for immunotherapy
- It may be an ideal target since it is not normally expressed in adults, except in the testes
- Yong-Chen explained why previous attempts to target MAGE-A3 have failed in clinical trials

Group Reflections

- Presentation was quite jargon heavy, so it was rather hard to decipher at times
- There was a lot of discussion regarding the failures and the wins
- For future presentations, speakers should provide a lay summary of their talk

***"Development of a Lentivirus Manufacturing Process for CAR T-cell therapy", Piriya Yoganathan, Biotherapeutics Manufacturing Centre, OHRI***

Key Take-Away Messages

- Piriya spoke about lentivirus manufacturing in Canada and capacity building for CAR-T cell therapies
- Lentivirus manufacturing: Ottawa (John Bell/ Natasha Kekre)
- CAR-T production: Vancouver/Victoria → BC Cancer Agency
    - To eventually go back to Ottawa to be injected into patient!
- CAR-T cells will now be generated in Canada!
- Challenges:
    - Purification of the virus to avoid contamination
    - Concentrating the material while minimizing loss
    - Scaling up production
    - Establishing shelf-life

Group Reflections

- Piriya had a good presentation structure and provided useful introduction, definitions, and explanations throughout her talk
- Some of the slides had too much content/material
- She should have defined key terms such as GMP (Good Manufacturing Process) and stability as they were referred to many times!
- A conclusion slide should have been included after the acknowledgements to summarize the highlights of this content heavy talk

***"PSMA directed CAR T cells in Prostate Cancer-making a better CAR", Susan Slovin, Memorial Sloan Kettering Cancer Center***

Key Take-Away Messages

- Susan spoke about research with improving CAR T-treatments for prostate cancer using PSMA
- They combined cyclophosphamide with the engineered T-cells
- Incremental improvement in CAR for prostate cancer, dose was safe, but more needs to be done
- Patients predictably experienced cytokine release within 48 hours

Group Reflections

- Susan admitted some of the challenges and successes and highlighted that there is a long way to go
- During the presentation, the speaker used the phrase "make a better patient" which is offensive
- Susan spoke about how imaging staff asked patients to sit so that they could image them
    - The patients were shivering from their fevers
- Susan often used jargon/lingo that was not widely understood by the majority of the audience

## Plenary Session 2: Understanding and Overcoming Resistance Mechanisms in Immunotherapy

### *"Advancing CAR T Cell Therapy for Treatment of Brain Tumors", Christine Brown, City of Hope*

Key Take-Away Messages

- If the cure is worse than the disease, then there is no point of the treatment
- Christine spoke about advancing CAR-T cell therapy for treatment of brain tumours
- She explained some of the challenges in treating solid tumours (tumour heterogeneity) and that they were trying to make tumours "hot" to get a better immunotherapy response
- CD19 CAR-T therapy for glioblastoma proved successful in Phase 1 trials
- Patient quality of life looks to be very positive and promising with this treatment; however, the response was not long-term

Group Reflections

- The concept of CSF should have been explained much earlier in the talk
- She sometimes used a term before she explained its relevance
- Christine mentioned patients and referred to clinical trial participants during her presentation
- She also thanked the patients, so it was definitely a "bravo" moment

### *Immune response in colorectal cancer liver metastasis", Simon Turcotte, Université de Montréal*

Key Take-Away Messages

- The first generation of immunotherapeutic drugs are not effective in colorectal cancer, since they are not directed at the right targets. This is due to:
    - Lack of antigen (identified, tested in cultures, able to incite immune responses)
    - Lack of correct cells (hot vs. cold)
- Identified transcripts of six immune features that predict efficacy (immune cells, antigen presentation, interferon gamma, checkpoints, cytokines and their receptors, chemokines and their receptors)
- Immune reactions do exist in some metastasis
- Higher correlation of checkpoints in hot vs. cold metastasis
- Spontaneous immune response to PAM neo-antigen
- Neoantigens may not be a good predictor of immune response

Group Reflections

- Simon delivered a very technical presentation that was not accessible to the majority of the audience
- The language and jargon used was very technical and the presentation itself was very long therefore leaving very little time for conclusions

***"Granulocyte colony-stimulating factor induces immunosuppression and poses a barrier to immunotherapy", Israel Matos, University of British Columbia***

Key Take-Away Messages

- G-CSF (cytokine) is secreted from tumours and impacts dendritic cells & myeloid cells by impairing function & making them immunosuppressive
- Neutralizing G-CSF induces a protective tumour immunity, which could improve tumour response to immunotherapy
- More G-CSF leads to a worse prognosis in a variety of cancer types

Group Reflections

- If the speaker discussed the relevance of this subject at a higher level and placed the research into context, this might have enhanced the accessibility of the talk
- It would have been very helpful if the speaker explained the clinical context of cytokines in cancer
- Too much data was presented for a short time slot
    - Presentation would have been more effective if he explained the concepts more clearly

***"Single cell RNA sequencing for Simultaneous Analysis of Cancer Clones and Immune Microenvironments", Trevor Pugh, University of Toronto***

Key Take-Away Messages

- Trevor provided an overview of multiple myeloma and explained their clinical trials
- FGFR3 mutation cells may be sensitive to treatment; however, they need shared data to validate
- Loss of chromosome 5 in every mouse, even no disease mice
- ~ 50 genes on mouse chromosome 5 match human chromosome 13
- By flow cytometry, found increasing evidence of T cell exhaustion with myeloma development (in mouse model)
- 14 bone marrow samples from 8 patients for sequencing, analysis of FGFR mutation

Group Reflections

- This presentation had beautiful graphics and their context was not thoroughly explained
- The speaker had a relatively good sense of clinical reference e.g. where, how, and why we are going here/there
- To enhance accessibility, speakers should include a slide with a brief lay summary to supplement their presentation

## Plenary Session 3: The Underdogs: The Other Players in Cancer Immunotherapy

***Katharine Hsu, Memorial Sloan Kettering Cancer Centre***

Key Take-Away Messages

- NK cell therapy research is promising
- NK cells are safe and can be stimulated by a variety of cytokines (signaling molecules) to be more effective and overcome exhaustion
- They offer a promising therapy because they are safe and can be stimulated by a variety of cytokines

Group Reflections

- Although the topic was rather complex, the presenter did an excellent job of explaining NK cell immunotherapies
- Katherine provided clear diagrams for visual learners and drew conclusions periodically

***"B cells: the immune system's secret weapon to combat intratumoral heterogeneity?", Brad Nelson, BC Cancer Agency***

Key Take-Away Messages

- Brad explained the difference between T-cells and B-cells: T-cells are assigned to tumour clones whereas B-cells may recognize the original parent tumor cells and all cells with related features
- T-cells and B-cells are the immune "soldiers" that play different but complementary roles in fighting and killing tumour cells
- Patients do better when there is both a T-cell and B-cell immune response
- NK cells are safe and can be stimulated by a variety of cytokines (signaling molecules) to be more effective and overcome exhaustion
- They offer a promising therapy because they are safe and can be stimulated by a variety of cytokines

Group Reflections

- This presentation had beautiful graphics and their context was not thoroughly explained
- The speaker had a relatively good sense of clinical reference e.g. where, how, and why we are going here/there
- To enhance accessibility, speakers should include a slide with a brief lay summary to supplement their presentation

***"AhR and control of immunity in pancreatic cancer", Rahul Shinde, Princess Margaret Cancer Center***

Key Take-Away Messages

- Aryl hydrocarbon receptor (AhR) contributes to Pancreatic Ductal Adenocarcinoma (PDAC) progression
- AhR ligands include apoptotic cells
- Macrophages are critical in PDAC progression
- Macrophages take up apoptotic cells, which leads to activation of AhR responsive genes and M1 polarization, shifting them to an inflammatory phenotype
- The gut microbiome may drive tumour growth and activate the AhR pathway in macrophages

Group Reflections

- The speaker presented a human problem clearly, but then ran through scientific trees in a forest
- Speaker was suggested to define key terms such as downregulate, inhibit, and suppress

***"Restraining DC activation by PCGF6 and PD-L1", Connie Krawczyk, McGill University***

Key Take-Away Messages

- Tumour-derived factors can change the organization of chromatic (DNA structures) to change how they mature and activate dendritic cells
- Dendritic cells need a threat or disruption message (e.g. pathogen, cell death, etc.) to become activated
- There are very few dendritic cells in the tumour
    - If they are working properly, they should be in the lymph system

Group Reflections

- There was a lot to take in from this presentation, but it followed a chronological story line, so it made it much easier to follow

## Plenary Session 4: The Tumour Microenvironment/Metabolism and Immune Profiling

### *"Metabolic regulation through CD73-adenosine", John Stagg, Université de Montréal*

Key Take-Away Messages

- CD-73 is linked to immunosuppression and promotes anthracycline resistance
- CD-73 is regulated by estrogen receptor signaling
- CD-73 is associated with poor prognosis in triple negative breast cancer
- CD-73 and PD-1 show a synergistic combination effect
- Anti CD-73 antibody promotes anti-tumour immunity
- Oleclumab (anti-CD73) Phase I/II clinical trial began in August 2018

Group Reflections

- John should not have used the term "obviously" as some people in the audience may not be familiar with the concept
- Plenty of jargon was used that was not well explained
- Instead he should have used the phrase "as some of you may know" to be more inclusive
- John made the audience feel optimistic in regards to clinical trials

### *"Understanding the Metabolism of Human TIL for Use in Adoptive T Cell Therapy", Julian Lum, BC Cancer Research Centre*

Key Take-Away Messages

- Julian presented on metabolic engineering strategies for T-cell therapy
- His talk focused on 3 main questions:
    - 1) What is the evidence of metabolic competition between T cells and tumour cells in human cancers?
    - 2) What impact does this have on manufacturing T-cells for adoptive cell therapy?
    - 3) Can we target metabolism to improve T-cell therapy?
- When TIL are high → hypoxia low
- When TIL are low → hypoxia high
- Patients with high TIL had a better prognosis
- There is evidence of metabolic competition in human tumours (T cells and tumour cells competing for resources)
- Autophagy may be a good target to improve T cell therapy

Group Reflections

- Julian presented some rather confusing figures, but he did a good job of explaining them
- His talk was presented in a logical manner as he followed three main points throughout

***"Understanding how a 'fatty' tumour microenvironment can impact oncolytic virus therapy", Abera Surendran, University of Ottawa***

Key Take-Away Messages

- Adipocytes or an increase of fat in tumours lowers the effectiveness of oncolytic virus (OV) therapy
- Tumor cells accumulate lipids (fats), which leads to cellular stress and contributes to lower oncolytic virus infectivity/effectiveness
- She used a lipid removal agent to deplete lipids from media and this reversed resistance
- The resistance was largely a lipid driven effect, not an adipocyte effect
- Local fatty tissue and overall fatty diet seem to contribute to reduced effectiveness of the therapy

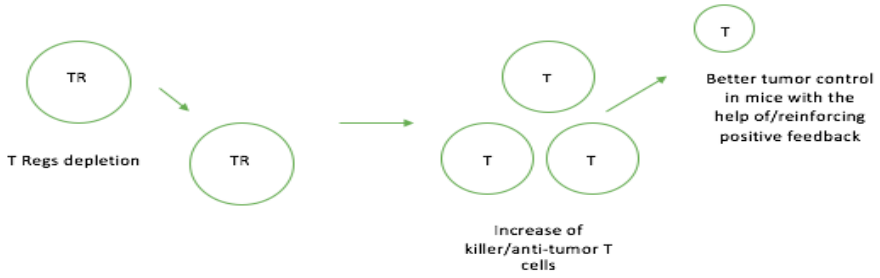
Group Reflections

- Abera was fantastic at describing her work
- She should slow down her talk as she only used half of the allocated time slot

***"Breaking down barriers to effective tumour immunity", Awen Gallimore, Cardiff University***

Key Take-Away Messages/ Group Reflections

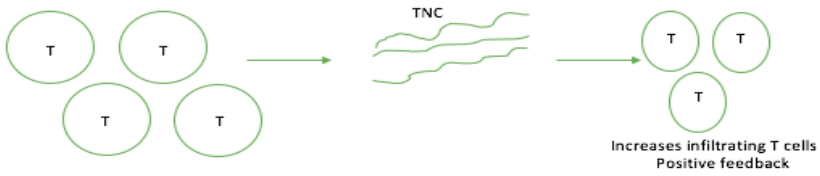
- T-Regs (regulatory T-cells) inhibit the anti-tumour response. Depleting T-Regs may limit progression
- This is shown through the following process:




- TNC (Tenascin C) is an extracellular matrix protein not seen in healthy adult tissues
    - Expressed in inflammation, wound healing and cancer

- Promotes invasiveness and metastasis
- High TNC does not predict resistance
- Low TNC is a consequence of successful immunotherapy, successful immunotherapy is associated with large scale remodeling of the tumor microenvironment

- Challenges:
  - T cell numbers correlate with HEV (high endothelial venules)
  - HEV-negative tumors have low TIL
  - HEV associated with good prognosis




***"Modular and High-Throughput Screening System for Chimeric Antigen Receptor Development", Darin Bloemberg, National Research Council Canada***

Key Take-Away Messages

- 180,000 new cancer patients are diagnosed each year
- Current CAR-T only works for certain cancer types
- NRC is using CAR-Js to screen for more effective CAR constructs
- J presumably stands for Jurkat cells – a T cell line that they electroporate to insert plasmids coding for CAR constructs and then test for activity via flow cytometry for the activation marker CD69
- Can engineer cells in approximately 3 days!
- NRC's antibody generation team can alter hinge composition and length to improve CARs (example given was modification of an existing antibody versus herceptin)
- Considering Llama single domain antibodies in CARs

Group Reflections

- They can use cellular/genetic coding to create a new toolbox of therapies
- Multiple pre-clinical research avenues

## Plenary Session 5: Emerging approaches to enhancing translational research: Innovative design and patient involvement

### *"UK. Walking The Walk – Consumer Involvement in UK Cancer Research", Richard Stephens, National Cancer Research Institute*

Key Take-Away Messages

- Patients are involved in ALL phases of research: prioritizing, commissioning, designing, and disseminating
    - Patients as PARTNERS
- 35% of UK cancer patients are involved in research and 25% take part in clinical trials
- Patient work is supported by one administrative staff (4 days/week)
    - Patient volunteers are provided with two days of training on how they can "thrive and survive" on academic research committees
- Consumer definition → research is a product; thus we are investors (research is funded by public money). Research should be useful to end users → patients or survivors
- "Dragons Den" – In 2012 first invited industry and lawyers – Astra Zeneca brought lawyers – met three times/year to work through two-page research proposals
- Things take time, but working on shortening processes for practice-changing studies to be implemented
- 'Use my data' citation for posters that recognize patient contributions to research
    - Researchers should thank patients for donating to tissue banks on their posters and in presentations
- NCRI trains 'Cancer Research Consumers' who apply for the role and are selected

Group Reflections

- The speaker included a good mix of humor, excitement, political correctness, and representation in his presentation
- This was one of the best presentations that were delivered during the four days of the Summit!

### *"Discussing trying and dying on Twitter", Rebecca Foley, University of Alberta*

Key Take-Away Messages

- Rebecca summarized her work on terminal patients and how they use Twitter to discuss standard of care
- Her review focused on:
    - Right to try → experimental drugs
    - Right to die → with medical assistance in dying (MAID)
    - Palliative care → aims to improve quality of life (i.e. relieving mental, physical, and emotional pain)

- She used an Application Programming Interface (API) to collect the data over a 6.5-year period
- Rebecca found that palliative care in particular was underfunded and under-discussed

Group Reflections

- Was Twitter the correct vehicle to collect this type of data?
- Word cloud was not clearly defined or explained
    - I.e. she should have explained that the words that appear larger appeared more frequently etc.
- While Rebecca define key terms, she needed to highlight key points more clearly

***"Baskets, Umbrellas and Platforms: Novel Trial Designs in Oncology", Mithat Gönen, Memorial Sloan Kettering Cancer Center***

Key Take-Away Messages

- Mithat provided an overview of novel trial designs in oncology and how they differ from traditional trial designs
- Traditional Phase I: dose escalation to detect maximum tolerated dose
    - They tend to underestimate maximum tolerated dose, leading to under-treating → not representative of potential efficacy and toxicity
- Novel Phase I: CRM (continual reassessment method). Postulate a dose-toxicity curve in advance. Use an algorithm to update curve after each patient is treated. Tend to get better results with dose
- Phase II: Historically set up to answer one question only (e.g. one drug, one cancer). Novel approaches address multiple questions simultaneously:
    - Approach based on nature of drug
    - Basket trial - drug targets a molecular abnormality in multiple cancers; patient selection is based on the expression of a particular marker
    - Umbrella trial - specific to histology, addressed heterogeneity within histology considering different druggable targets, with each treatment considered a trial on its own
    - Platform trial - can be an umbrella trial - single protocol provides platform to evaluate multiple treatments
    - Master Protocol - may not differ much from platform trial
    - Adaptive trial - can make changes on the go, adding or changing cohort. Lack of transparency in design and ethical concerns

**Group Reflections**

- Clinical trials require considerable pre-planning to achieve the optimal results

***"Accelerating bench to bedside translation of therapies", Manoj Lalu and Dean Fergusson, Ottawa Hospital Research Institute***

Key Take-Away Messages

- 80% of clinical trials fail to accrue patients in anticipated time
- OHRI excelerator program was established to increase the efficiency of clinical trials
- This program provides the conceptual framework to address obstacles and improve translation of potential therapies
- A rigorous and informed trial design enhances successful start-up and execution
- They discussed patient partner involvement, the role and the various aspects that would benefit as a result of this involvement
- These included the patient perspective, interpretation of interview study results, crafting accessible summaries of work, writing letters in support of Research Ethics Board (REB) applications, and review of informed consent documents

Group Reflections

- Room for improvement in the implementation
    - Early engagement of HTA
    - Broader engagement of patients/stakeholders
- They introduced the talk by saying that $210 billion is wasted annually in biomedical research
    - What does wasted mean?
    - Are they just referring to how much pre-clinical research never becomes clinical?
        - Wasted is probably the wrong word to use for that!

## Plenary Session 6: Antigen Discovery and Neo-epitopes

### *"Prioritizing Tumor Neoantigens", Robert Holt, BC Cancer Agency*

Key Take-Away Messages

- A neoantigen is an antigen that arises from mutation
- Neoantigens are only expressed by tumor cells, but not normal cells, which make them good targets
- Neoantigens can elicit effective anti-cancer T-cell responses
- Neoantigen-reactive T-cells are the main active ingredient in TIL therapy
- Many methods can be used to identify neoantigens
    - I.e. computational models, mass spectrometry, etc.
- This research is focusing on nudging the immune system to recognize tumour mutations as foreign

Group Reflections

- The presenter admitted in the beginning of the talk that his way of approaching this scientific question is not the only way, there are other methods of interpretation that can be used to approach this type of problem
- The presentation itself was too technical and made it very hard for the audience to understand
    - He did include some nice definitions and a great slide explaining peptide presentation (cartoon with chicken legs!)

### *"The Human Immuno-Peptidome Project", Etienne Caron, ETH Zurich*

Key Take-Away Messages

- Etienne spoke about the various methods that are used to detect antigens
- He focused on mass spectrometry and discussed its benefits and challenges
    - **Benefits**: reproducible, accurate, sensitive, and capable of predicting peptides
    - **Challenges**: Does not detect all peptides
- The bank is for ALL scientists → new biomarkers and immunotherapy targets

Group Reflections

- Reminder of the long and complicated process of cancer therapy from start to administration

***"Adoptive T cell therapy targeting HLA-DP-restricted WT1 peptide", Chung-Hsi (Brett) Wang, Princess Margaret Cancer Centre***

Key Take-Away Messages

- Brett provided an overview of adoptive T-cell therapy
- He explained that there are many antigen targets and many clinical trials underway
- Gene-engineered TCRs are usually MHC I-targeted (this is because CD8+ killer T cells recognize peptides presented by MHC I on the surface of target cells)
- TCRs directed to HLA Class II may be safer than Class I because CD4+ helper cells recognize MHC/HLA II and do not typically kill the presenting cell; this means that healthy cells expressing antigen will not be attacked, thereby avoiding off-target, tumour toxicity."
- His findings focused on HLA-DP4-restrcied WT1 peptide
- DP4 is the most frequent HLA II allele, so using a DP4 restricted peptide target will allow this strategy to be applied to many patients
- WT1 is a promising and well-established tumor antigen
- Clone 9 TCR T cells can mediate anti-tumor responses against DP4/WT1 cells *in vitro* and *in vivo*

Group Reflections

- This speaker used storytelling as a means of communicating concepts during his presentation

***"Functional Identification and Therapeutic Targeting of Tumor Neoantigens", Stephen Schoenberger, LaJolla institute***

Key Take-Away Messages

- Stephen presented his research to try to identify verifiable neoantigens predicted by their algorithms
- Used patients' own blood to verify ability of predicted neoantigens to stimulate immune cells (assumption: blood of patients is a proxy for immune cells in tumours)
- The proof-of-concept of the prediction was tested in mice (personalized vaccine), which showed promise (partially in combination with checkpoint inhibition)
- This work could lead to personalized medicine
- Phase 1B clinical trial underway → personalized medicine → cured tumors

Group Reflections

- Bonus → not restricted to HLAs
    - So what?
        - Necessary step for personalized cancer treatment

## Plenary Session 7: Combination Immunotherapy Strategies

### *"Oncolytic adenovirus-based strategies to 'warm-up' tumors for immunotherapy", Florian Kühnel, Hannover Medical School*

Key Take-Away Messages

- Florian presented on oncolytic adenovirotherapy
- Virotherapy is a treatment using selective viral replication in the tumour tissue
- Antibody retargeting (antiviral antibodies that will induce antibody-dependent cellular cytotoxicity after virotherapy) can immuno-activate a tumor for PD-1 immunotherapy
- 'Virotherapy leads to strong oncolysis and tumor inflammation
- Oncolytic virus inflammation modulates the tumor micro-environment
- Patients who received virotherapy as first time saw a greater benefit

Group Reflections

- Excellent introduction to the topic with good background information

### *"Molecular potentiators of oncolytic immunotherapy", Jean-Simon Diallo, Ottawa Hospital Research Institute*

Key Take-Away Messages

- Talked about small molecules that his lab found based on vanadium, which help oncolytic viruses replicate and infect cancer cells
- Vanadium based PT pan-inhibitors enhance oncolytic virus activity
- Act "synergistically" with the virus to provide a better treatment
- Some of these molecules target the interferon (gamma) response to help the viruses replicate (i.e. help viruses to use cancer's hiding abilities to their advantage)

Group Reflections

- Jean-Simon did a good job at explaining oncolytic viruses in general
    - Better than the others and some who pretty much omitted this explanation
- It may have been a tough topic to get across to the whole audience, but he did an excellent job of it
- Sometimes a little technical (a bunch of abbreviations/drug names that can get confusing)

***"NKT cell activation in combination with oncolytic VSV expressing IL-15 induces pancreatic tumor regression", Adam Nelson, Dalhousie University***

Key Take-Away Messages

- Adam explained that when you have viral lysis, there is the release of tumour antigens which aid in NKT cell activation, leading to higher survival
- He also explained that Natural Killer T cell (NKT) activation reduces MDSC immunosuppression
- Study utilized an experimental mouse model where a combination of NKT and Vesicular Stomatitis Virus (VSV) expressing IL-15 (Interleukin 15 cytokine) promoted pancreatic tumour regression and increased mouse survival times
- A combination of NKT activation and IL15 producing VSV increases cytotoxicity and cytokine production of NK, NKT, and CD8 T-cells
- In humans, reducing tumour burden may enable more effective surgical procedures

Group Reflections

- What are next steps?
    - Clinical trial on the horizon or further experimentation required
- Might have difficulty translating to humans as humans and mice have opposing ratios for the two populations of NK cells
- Highlights the importance of evaluating combination therapies vs. singular therapeutic approaches
- Very accessible and very interesting talk
- He had a good flow of his presentation, spoke clearly, and his diagrams were simple yet helpful

***"Virally driven extracellular vesicles: A viable way to reprogram the tumour microenvironment", Carolina Ilkow, Ottawa Hospital Research Institute***

Key Take-Away Messages

- Infecting tumour cells can be challenging depending on stromal density
    - Tumour cells in the periphery may be infected, but not the entire tumour mass, posing a challenge to oncolytic virus therapy
    - Targeting tumour-associated fibroblasts in conjunction to tumour cells may be of therapeutic value
- Oncolytic viruses can work in two ways:
    - **(1)** It can infect and kill tumour cells directly or;
    - **(2)** By inducing immunogenicity, triggering an anti-tumour immune response.
- Carolina explained that her research work found a set of artificial micro RNAs to enhance therapies using viruses

    - One of them was amiR6 which seemed to target epigenetic regulators and cytoskeleton stability
- Dr. Ilkow showed that combining amiR6 in combination with a compound (GSK126, an inhibitor of the enzyme Ezh2, which is involved in epigenetic changes in the DNA) leads to tumour cell death and controls tumour growth
- The combination proved to be more effective than either treatment alone

Group Reflections

- Carolina took the time to walk the audience through her presentation slides
    - This kept the audience very engaged!

## Helpful Websites

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

Canadian Cancer Society http://www.cancer.ca/en/research-horizons/e/c/9/immunotherapy-promising-new-field-treatment/

Clinical Trials http://www.canadiancancertrials.ca/ and https://www.cancer.gov/about-cancer/treatment/clinical-trials/advanced-search

Leukemia and Lymphoma Society of Canada http://www.llscanada.org/treatment/types-of-treatment/immunotherapy

NCRI Consumer Forum https://www.ncri.org.uk/

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

US American Cancer Society https://www.cancer.org/treatment/treatments-and-side-effects/treatment-types/immunotherapy/what-is-immunotherapy.html

US Cancer Research Institute https://www.cancerresearch.org/immunotherapy/what-is-immunotherapy

US Cancer Support Community https://www.cancersupportcommunity.org/immunotherapy-cancer-it-right-you