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# Immuno-oncology Translational Research Initiative Planning Workshop Report

Thursday, November 26, 2015
8:00 a.m. – 5:00 p.m.
Location: OICR | West Tower Boardroom 5-20/21

## Attendees

| Invited | |
|---|---|
| Rebecca Auer | Ottawa Hospital Research Institute |
| Jonathan Bramson | McMaster University |
| Mark Bray | University Health Network |
| David Brooks | Princess Margaret Cancer Centre |
| Marcus Butler | Princess Margaret Cancer Centre |
| Greg Dekaban | Western University |
| Jean Sebastian Delisle | Université de Montréal |
| Jean Gariepy | Sunnybrook Research Institute |
| Naoto Hirano | Princess Margaret Cancer Centre |
| Rob Holt | British Columbia Cancer Agency |
| Bob Korneluk | Children's Hospital of Eastern Ontario Research Institute |
| Greg Korpanty | National Cancer Institute Canada Clinical Trials Group |
| John Kuruvilla | Princess Margaret Cancer Centre |
| Brian Lichty | McMaster University |
| Tracy McGaha | Princess Margaret Cancer Centre |
| Tak Mak | Princess Margaret Cancer Centre |
| Pam Ohashi | Princess Margaret Cancer Centre |
| Amit Oza | Princess Margaret Cancer Centre |
| Christopher Paige | University Health Network |
| Trevor Pugh | University of Toronto |
| Lillian Siu | Princess Margaret Cancer Centre |
| David Spaner | Sunnybrook Research Institute |
| John Stagg | Université de Montréal |
| David Stodjl | Children's Hospital of Eastern Ontario |
| Simon Turcotte | Université de Montréal |
| Yonghong Wan | McMaster University |
| Brad Wouters | University Health Network |

| OICR & FACIT | |
|---|---|
| Philip Awadalla | Senior Investigator |
| John Bartlett | Program Director, Transformative Pathology |
| John Bell | Program Director, Immuno- and Bio-therapies |
| Neil Berinstein | Director, Translational Research |
| Rob Campos | Head, Research Operations |
| Jeff Courtney | Chief Commercial Officer, FACIT |
| Janet Dancey | Scientific Director, Canadian Cancer Clinical Trials Network |
| Craig Earle | Program Director, Health Services Research |
| Tom Hudson | President and Scientific Director |
| Nicole Onetto | Deputy Director and Chief Scientific Officer |
| David O'Neill | Vice President, Business Development, FACIT |
| Lincoln Stein | Program Director, Informatics & Bio-computing |
| Rebecca Tamarchak | Director, Strategic Planning and Outreach |
| Martin Yaffe | Co-Program Director, Smarter Imaging |

| Guests | |
|---|---|
| Melissa Anders | Program Manager, Cancer Stem Cells Program |
| Dawn Richards | Medical Writer |

**Please note that this is a summary of the workshop prepared by the organizers. For more details please contact the TRI workshop leaders:**

- John Bell: jbell@ohri.ca
- Pam Ohashi: pohashi@uhnresearch.ca
- Neil Berinstein: neil.berinstein@oicr.on.ca

***Preamble:*** On November 25th, 2015 " ***A Symposium on Immunotherapy: The Ontario Landscape***" jointly supported by the Princess Margaret Cancer Centre, the Ontario Institute for Cancer Research and the Ontario Institute for Regenerative Medicine was held, providing a venue for scientists and clinician scientists in Ontario to profile their interest and activity in the field of immune-oncology. The following day a working group (42 participants) from across the province met to present ideas about projects that could be considered for incorporation into a TRI application. An expert advisory panel composed of scientist and clinician-scientists from outside of Ontario attended both the symposium and the workshop. The panel participated in the workshop discussion and later met by telephone (early in 2016) to offer their perspectives on the merits of the proposed projects and suggested a framework for a proposed TRI application. (Expert Panel Members: Rob Holt BCCA, Jean-Sebastien Delisle, Simon Turcotte and John Stagg Université de Montréal)

***Introductory Remarks: November 26th Workshop***

***Tom Hudson*** (CEO – OICR) presented a series of slides outlining the concept and objectives of the newly instituted TRI program. He stressed the value of bringing together a collaborative team, conducting cutting edge science and creating a program with a clear clinical path forward.

- ***The TRI Concept:***
    - Large scale, multi-disciplinary collaborations between laboratory and clinical scientists advancing Ontario assets and improving cancer patient outcomes.
    - Must have a clinical focus that builds on innovations and leadership derived from Ontario Hospitals, Research Institutes and Academic Institutions.
    - Ideally TRI projects would leverage existing networks supported by the OICR (e.g., Global Alliance for Genomics & Health, Ontario Tumour Bank, Canadian Cancer Clinical Trials Network) and/or OICR's Technology Programs.

- ***TRI Structure:***
    - Successful projects will include 2-5 major projects and possibly some smaller *catalyst/blue sky* projects
    - There must be a clinical trial initiated within the first 2 years of funding
    - Budget of up to $10 million over four years with a commitment of at least $2 million towards a clinical trial
    - Highly encouraged to establish co-funding partnerships

- ***TRI Proposal Evaluation Criteria:***
    - Applications will be evaluated against defined criteria by an international peer-review panel
    - Preferably, projects should contain an Ontario innovation or asset
    - There should exist a reasonable potential for clinical/healthcare adoption in the next 5-10 years
    - It is expected that at least some projects have a high likelihood of commercialization in Ontario. Members of FACIT, the commercialization arm of the OICR were present at the meeting and will be available to partner on select projects

***John Bell*** (Ottawa Hospital Research Institute) presented the philosophy of ORBiT, the OICR's original Immuno and Biotherapeutics program. The ORBiT program was focused on translating fundamental science discoveries from the labs of Ontario scientists into clinical products for the last decade. Much like the proposed TRI program, ORBiT funded a blend of clinical trials and pipeline projects with potential for clinical translation. Examples included a dendritic cell vaccine clinical trial for prostate cancer patients that was conducted

at the Juravinski Cancer Centre in Hamilton. Seed funding for a lentivirus based vaccine for colon cancer and an NK cell therapy product was provided to investigators in Toronto. An oncolytic vaccinia virus was manufactured in Ottawa and clinically tested at the Juravinski Cancer Centre and Ottawa Regional Cancer Centre. The product was acquired by Transgene (France) and Sillajen (Korea) and is currently in phase III testing. Catalyst projects supported in Hamilton and Ottawa led to the development of the " *Maraba oncolytic vaccine"* strategy that is now in phase I/II trials in Ottawa, Hamilton, Toronto and Vancouver and has led to the spin-out of an Ontario based biotech company called Turnstone Biologics. Bell suggested that an Immuno-oncology TRI project could be built using the approach pioneered in the ORBiT program. He briefly described a federally funded NCE program in anti-cancer biotherapeutics that is an excellent potential funding partner to maximize a TRI investment. Following the introductory remarks by Drs. Hudson and Bell, the rest of the day was dedicated to presentations and discussions of ideas for the development of an Immuno-Oncology TRI (moderated by Drs. Bell, Ohashi and Berinstein).

### ***Session One: Novel Immunotherapeutic Strategies***

This first session (moderated by J. Bell) consisted of a series of presentations followed by questions and discussions revolving around novel therapeutic strategies being developed in Ontario.

### (1) Development of an Oncolytic Virus Adoptive Cell Therapy Combination Trial

***Brian Lichty*** (McMaster) provided background information regarding the development of the Maraba Oncolytic Virus Vaccine strategy including an outline of our current understanding of how this platform produces unprecedented immune responses in murine and NHP models. This newly discovered biology revealed that a Maraba virus encoding a tumour antigen potently boosts central memory T cells and suggests a novel interplay between the virus and immune system that could be therapeutically exploited to enhance adoptive cell therapy.

***Yonghong Wan*** (McMaster) further expanded on this work and described some early studies with Dr. Cassian Yee (MD Anderson) that demonstrated it is possible to prepare central memory T cell products using a sophisticated, GMP grade flow cytometer. Dr. Wan has now adapted the early phases of T cell culture from Dr. Yee's process but furthered enhanced the procedure to eliminate the T cell sorting component while maintaining enrichment of TCM. Wan has also established a collaboration with Jonathan Shneck (Johns Hopkins) using nano-□APCs that can simultaneously enrich for multiple antigen specific T cells. This process could be compared and contrasted with the artificial antigen presenting cell technology currently in development in the labs of Drs. Hirano and Butler (Toronto) with the goal of optimizing a process that could be ultimately be transitioned into the Princess Margaret Immune Cell Therapy GMP suite.

***Marcus Butler*** (Princess Margaret Cancer Centre) presented the concept for a clinical study based on the hypothesis that adoptively transferred tumour-specific, central memory T cells can engraft and be expanded by a Maraba oncolytic vaccination. The primary endpoint was safety and dose-limiting toxicities of adoptive cellular therapy (ACT) with central memory T cells followed by treatment with MG1MA3 (MAGE-A3 virus). The trial schema included potential vaccination pre-ACT infusion, just after ACT infusion, or making two cell products and performing the vaccination after the second infusion (in this case the patient is their own internal control). A discussion about this work highlighted the

importance of this trial in terms of groundbreaking regulatory requirements- that is, administration of two investigational immunotherapies at the same time. Providing two such treatments in close proximity could change the mindset of Health Canada to build on that with other innovative trials. The challenges in personalizing the approach were discussed, from starting with candidate antigens, loading antigen presenting cells (APC), and making more personalized viruses. There were ideas around performing a proof of concept study with an artificial TCR expressing cell product in combination with oncolytic virus, which might require a collaboration between Turnstone, Adaptimmune and/or Takara. There was further dialogue about antigen spreading and the potential regulatory agency hurdles. Finally, the two main questions this trial could address were highlighted namely: can a virus be used to help ameliorate T cell shutdown after ACT, a phenomenon common to all T cell clinical trials and; can virus be used to increase T cell infiltration into tumours and increase the repertoire of tumour reactive T cells?

**(2) Testing Immuno-modulators to enhance Adoptive Cell Therapy**

***Naoto Hirano*** (Princess Margaret Cancer Centre) presented his recent work at developing and optimizing T cell receptors (TCRs) and using these to program peripheral blood mononuclear cells (PBMC) to recognize and attack melanoma cells expressing the MART1 tumour cell antigen. He then showed that epigenetic manipulation of T cell grafts via manipulation of T cell differentiation could effectively generate T cells with the central memory phenotype. Using mouse models and epigenetic modifiers he was able to demonstrate it was possible to improve the quality of T cell grafts that could be used for example in combination with the Maraba virus oncolytic vaccine.

**(3) Engineering Suppression-resistant Dendritic Cell (DC) Immunotherapy: Overcoming Immunosuppression by Preventing It**

***David Brooks*** (Princess Margaret Cancer Centre) described work in his lab aimed at engineering antigen presenting cells (APCs) that would not be affected by an immunosuppressive microenvironment and thus be able to function within the tumour milieu. Since Dendritic Cells potently activate T cell responses and simultaneously express multiple immune stimulatory factors, suppression resistant cells could enhance many other immunotherapy approaches being studied. They will drive/guide adoptive T cell immunotherapies, will enhance previously exhausted T cells restored by checkpoint inhibitors, could work in combination with OV therapy to enhance antigen presentation to T cells and are conducive to engineered expressions of chemokines/cytokines to recruit and guide response. There were questions about these immunosuppression-resistant cells needing to be "*killed later*" and concepts discussed about controlling DCs remotely with antibodies, small molecules, or peptides (if antigens are known) to ensure these cells are turned off when required.

***(4) Development of Maraba-IL-12 Infected Cell Vaccines for the Treatment of Periotoneal Carcinomatosis***

***Rebecca Auer*** (Ottawa Hospital Research Institute) described her work wherein she uses a Maraba virus expressing a cytokine to infect autologous tumor cells creating a therapeutic vaccine. This so-called infected cell vaccine (ICV) is introduced into the peritoneal cavity of tumour bearing mice recruiting highly activated T cells, natural killer (NK) cells and dendritic cells to the tumour bed. They have shown that Maraba/cytokine-

ICV vaccination can eradicate bulky peritoneal disease in mice and result in durable cures. For translation to the clinic particular hurdles remain including: how to manufacture personalized vaccines and; safety concerns about using a cytokine expressing replication competent virus. In this latter regard, Dr. Auer suggested that it may be possible to utilize an anti-cytokine antibody product to safeguard against cytokine mediated toxicity, and she proposes to prove the concept in monkeys. A number of synergies in Ontario exist that could bring the ICV from concept to a clinical study.

**(5) Using patient derived B cells to create human monoclonal therapeutics**

***Tak Mak*** (Princess Margaret Cancer Centre) provided an overview of facilities available in his group that make it possible to rapidly generate new anti-cancer therapeutics including therapeutic antibodies. His project pipeline included a new target which synergizes strongly with anti-PDL1 in treatment of the CT26 syngeneic model, a new anti-PD1 antibody with a higher affinity than the molecules currently available in the clinic and a bi-specific antibody that would recognize PD1 and a tumour antigen. He aggressively protects his work with intellectual property filings and feels there are still many more targets available that need to be developed. He expressed an avid and sincere interest in collaborating with the participants at the workshop.

**(6) SMAC Mimetics: A Broad Based Pharmacologic Platform to Increase the Efficacy of Cancer Immunotherapy**

***Bob Korneluk*** (Children's Hospital of Eastern Ontario) has been studying the biology of SMAC inhibitors for over a decade. He presented data that suggests that SMAC inhibitors are safe and well tolerated (>1000 patients treated). To date SMAC inhibitors have been combined with traditional chemotherapies, but Dr. Korneluk feels there is an opportunity to combine these with immunotherapeutics. They function via a mechanism of action that switches TNF signaling from survival to death pathways for cancer or endothelial cells via turning on an alternative NF-□B signaling (e.g., to promote T cell co-stimulation). Cytokine induction leads to bystander cancer cell death in the presence of a SMAC mimetic. There has been work around SMAC mimetics with immunostimulants to cure mice of CT-2A brain tumours. There were four immediate potential clinical paths suggested for SMAC-based combination cancer immunotherapy: 1. SMAC and anti-PD1; 2. SMAC and Maraba MG1-OV; 3. SMACs to enhance activity of approved immunotherapies (e.g., ECG and interferon □); and, 4. SMACs to enhance adoptive cell therapy-mediated killing of cancer cells. Currently there is no clinical SMAC mimetic product available to the group to test these ideas.

***(7) Manipulation of Myeloid Stress and Cell Death Responses to Promote Anti-cancer Immunity***

***Tracy McGaha*** (Princess Margaret Cancer Centre) presented his concepts around control points in the tumour such as the mTOR pathway (Mammalian target of rapamycin) and the integrated stress response (ISR) (cellular stress sensing pathways that can be examined via looking at amino acid starvation). For instance GCN2 drives amino acid starvation stress and there appears to be a great deal of cross talk between GCN2 and the unfolded protein response (UPR). UPR stress itself is driven by 3 pathways (IRE1□, PERK, and ATF6). Dr. McGaha is interested in utilizing his background in systemic autoimmune diseases (lupus) to see how those principles and pathways can be applied or affect cancers as well, and why therapies that drive tumour cell death do not drive a potent immune

response. Through tweaking seemingly minor steps in a pathway, he proposes to convert an immunosuppressive response into one that is inflammatory. There was a discussion about specific potential targets for this line of work such as IDO (several inhibitors in the pipeline), PERK (GSK has some in their pipeline), and screens being set up in the McGaha lab for GCN2 relative to cancer versus autoimmunity.

### *(8) Creating a CEA based vaccine to block metastasis*

***Jean Gariepy*** (Sunnybrook) discussed his interest in using CEA (carcinoembryonic antigen) as a therapeutic target as it is associated with numerous types of solid tumours and high CEA expression levels correlate with metastatic growth. He is studying the IgV-like N-terminal domain of 132 amino acids that allows CEA to bind to fibrinogen. His novel CEA-based vaccine (MetVax) has an N-terminal domain lacking glycosylation and displays a non-natural C-terminus. MetVax is delivered by IP injection, produces IgG Ab and generates a Th9 immune response that activates mast cells and results in sterilizing immunity. Their work in a colon cancer mouse model (MC38.CEA) has helped determine the pathway through which the vaccine works to eradicate most tumours without causing pathologies in normal tissues. His data suggests that his vaccine primarily works through the inhibition of metastatic cell growth and speculated it could be combined with immune checkpoint therapeutics.

## *Session Two: Immunogenomics and Biomarkers*

This session (moderated by P. Ohashi and N. Berinstein) was framed for workshop participants as being a discussion around key questions in the field. While immunotherapy is impacting patients, it is important to discuss how clinicians will ultimately decide the combinations that are best for each patient and which treatment will be received by a patient based on their defined immune profile, T cell response, antibody response, etc., as potentially determined by their genetics. There are a number of unknowns about this treatment paradigm so this discussion's goals were to: 1. Define biomarkers to stratify for therapy; 2. Explore immunity to tumours, barriers, changes during therapy; and, 3. How best to perform in-depth analysis of patient samples from clinical trials.

### *(1) Biomarker Analyses of Cancer Immunotherapies*

***Neil Berinstein*** (Sunnybrook) stated that while there have been many successes in terms of checkpoint inhibitors and oncolytic viruses, it is recognized that a plateau has been reached in clinical activity of approximately 20-30% across tumours. It will be important to understand how novel therapeutics are working and who is most likely to respond, for example in the case of ipilimumab, using CD8 lymphocytes to determine responders. There are also other considerations such as mutational load and its variation within tumour types, and caveats associated with PDL1 expression such as being measured various ways giving rise to different ways of labeling people as PDL1 positive. In the checkpoint inhibitor field, there are some biomarkers to differentiate who will benefit from this type of therapy, however not all questions have been answered and for combination therapies there is a lack of predictors in terms of response.

***John Bartlett*** (OICR) followed this presentation with a discussion of the Transformative Pathology Program at the OICR, which is becoming a diagnostic development model given its abilities and expertise. Some Program projects include: TILs as predictors of adjuvant anthracycline therapy aimed at discovering and validating multiple

biomarker approaches to predict patients who could benefit from immunotherapy; and, PRONTO, a prostate cancer project which undertook assay development of 7 biomarkers in parallel, followed by parallel validation.
Questions from the workshop participants included clarification on intellectual property generated from collaborations (all collaborators retain their background intellectual property, while shared intellectual property is generated by the collaboration, a model used successfully with PRONTO, and facilitated by FACIT) as well as access to multispectral immunohistochemistry (available via work with OICR's Smarter Imaging Platform centered at Sunnybrook Research Institute and a collaboration with GE's Global Research Centre).

***Philip Awadalla*** (OICR) demonstrated some of the genomic and data capabilities available to workshop participants through sharing two projects: 1. Capturing rare/*de novo* mutations impact and load; and, 2. HLA Haplotype Inference. The first project included tumour and normal tissue, uneven data sources, *de novo* mutations, and various recombination patterns. They were specifically interested in capturing somatic mutations. In terms of mutation load and the impact of those mutations, they were interested in developing tools to predict severity of mutations as well as integrating functional –omic data with genomic information to predict mutation impact. In the second project, they examined dynamic HLA haplotype variation in association with exposure to antigen to see if they could use HLA haplotypes study expression variation amongst individuals and across tumours, and co-expression between these. P. Awadalla concluded by stating that these approaches could be used to elucidate biomarkers from immunotherapy.

### *(2) Emerging Genomic Technologies to Characterize Cancer and Immune Systems in Primary Tissue Tumours*

***Trevor Pugh*** (University of Toronto) is interested in the association between high mutation rate and outcome, and determining if mutation load can be measured by sequencing 555 cancer genes or less. They have determined that the minimum number of cancer genes needing to be sequenced to predict mutation load is between 200-555 genes, which is very exciting from a clinical trials point of view. The Hi5 panel is being validated clinically by Suzanne Kamal-Reid at UHN. However, in some cases it is likely that mutation burden will not predict patients that will benefit from PD-1 blockade. Therefore the Pugh and colleagues have decided to begin to profile the microenvironment (e.g., tumour, immune and other cell types). Dr. Pugh discussed the 'immune score' and looking at specific immune cell signatures that define certain tumour types. Additionally, the T cell receptor repertoire could be profiled orthogonally to augment the overall immune score. Dr. Pugh argued that it makes sense to combine the genomics and biology together and they are using low quality materials to see if they could do this noninvasively and even on poor quality materials. A discussion ensued about the Fluidigm C1 which enables RNA sequencing of 96 or 800 cells from single cells suspensions, DropSeq may enable scaling to >50,000 cells to track clonal shifts in cancer, immune and other populations, applications of single cell immunogenomics, and the single cell atlas. Since there could potentially be some caveats in terms of using the Hi5 panel for lung cancer patients for mutation counting, there is a need to get into the single cell transcriptome space to see what is really going on in cells. The workshop participants agreed that since the best biomarkers are not understood here, the microenvironment may be more predictive than mutation load. Dr. Pugh indicated they are doing work in ovarian cancer long-term survivors examining mutation load, immune response and microenvironment.

### *(3)* Imaging strategies for immunotherapy trials

***Greg Dekaban*** (University of Western Ontario) presented collaborative work done with Paula Foster using a positive contrast agent that quantitatively measures fluorine by comparing it to $^{19}F$ levels. Fluorine is an advantageous label since it is not found endogenously in humans; fluorine-carbon bonds are not enzymatically broken naturally; and, fluorine is detected with MRI non-radioactively. Work using a commercial GMP-grade $^{19}F$ perfluororcarbon agent called Cell Sense was described. A full clinical trial application (CTA) and research ethics board (REB) submission is being prepared (the pre-CTA meeting with Health Canada was positive) for this work, with a goal to optimize PBMC Cell Sense labeling for use in prostate cancer patients without compromising feasibility and safety. Lastly there was a brief note on P. Foster's imaging work related to breast cancer and creation of a cell fate map (brain, liver and lymph node) for a longitudinal study.

**Martin Yaffe** (Sunnybrook) introduced OICR's Smarter Imaging Program with the premise that workshop participants may wish to incorporate imaging into their studies. The group: is undertaking studies to make imaging of biomarkers more quantitative; has developed whole mount histopathology, large slide digitization, imagine display and processing; and, is working with the GE Global Research Centre (multi-channel immunohistochemistry, up to over 200 markers, have done about 30 at once). The latter technology is quantitative and the team is currently calibrating this system to understand how they can identify and measure cellular components. Workshop participants were invited to bring forward collaboration ideas.

### *(4)* Biomarker validation

***Janet Dancey*** (NCIC-CTG) reviewed considerations for biomarker work in clinical trial design, determining treatment options for patients, to measure if biomarkers are working, etc. Currently there are many biomarkers and their validation is expensive. Key questions to ask around biomarker development include: what is the purpose/need? Is the specific need/intervention potentially generalizable? Is this likely to be used in clinical practice? Will markers for virus, vaccines, cell therapies, checkpoint inhibitors be the same? If testing is done across centres, what are requirements to ensure consistent quality and handling of samples? Training and quality control are important in single centres as well as especially for multi-centre studies. She reminded the workshop participants that biomarkers in early development are usually not useful since there are only a small number of patients. Requirements for biomarker development include: good assays, standard operating procedures, and good samples. In early development, there is not a need for: clinical grade assays and labs, large sample sizes, clinical trials. In early development, you will identify biological correlates, but probably not clinical correlates. Currently there are no predictive biomarkers for PD1 and PDL1 inhibitors, and new immunotherapy drugs are so expensive that managing health economics has become a key priority and predictive biomarkers could help in patient selection. At the NCIC CTG, there will be immunotherapy trials starting in the next year, and samples and datasets will become available after that.

### *(5) Gene Expression Analysis of Exhausted and Functionally Restored Virus-specific and Tumour-specific CD8 T cells*

***David Brooks*** (Princess Margaret Cancer Centre) presented an approach to single cell RNA-seq transcriptomic analysis to understand what is happening to T cells that are functionally restored. The approach includes sorting single cells for RNAseq from virus- and tumour-specific CD8 T cells isolated from persistent LCMV infection (spleen) and tumour

(melanoma), before and after anti-PDL1 therapy. They will utilize the increase in IFN□ and TNF□ activity (functions which are restored by anti-PDL1) to identify which cells have been functionally restored by therapy. Lastly they will take CD8 T cells from tumours once they have a baseline understanding of pathways involved, and use this to correlate with cancer therapy outcome.

### *(6) Novel Strategies to Predicting PD-1 Responders*

***Pam Ohashi*** (Princess Margaret Cancer Centre) The current hypothesis in the literature is that patients with a high mutation burden respond to PD-1 blockade, however to date this has not been thoroughly validated. For example, peptides from overexpressed antigens can be used as effectively in a dendritic cell vaccine as neo-epitope peptides in protecting against tumour growth. Dr. Ohashi stressed that there still is a need to understand the biology of the disease, and thinks that perhaps genomic instability, rather than mutated antigens is driving stress and strong anti-tumour response. Her group would like to further explore whether or not tumours with mutated antigens are more activated versus tumour models with few mutations. She speculates that over-expressed antigens rather than neo-epitopes may be the most relevant therapeutic targets. Dr. Ohashi would like to look at markers of stress response such as hypoxia in activated dendritic cells to see if there is some type of clinical correlation. Workshop participants agreed this would be important, and there was also a suggestion to compare renal cancer (only 40-50 somatic mutations per tumour) to melanoma when picking low mutation and antigen presenting cells as comparators. Other ideas included looking at activated dendritic cells to see if they are not expressing or releasing suppressive agents.

### *(7)Immune-oncology and Lymphoma*

***John Kuruvilla*** (Princess Margaret Cancer Centre) discussed clinical trials they have undertaken:
1. NCIC LY17. A randomized phase 2 study of a relapsed lymphoma population and it is designed as curative therapy. There will be 64 participants in multiple arms to evaluate biomarkers and promising regimens will be taken in to a phase 3 clinical trial. They are collecting primary tissue, circulating tumour DNA at multiple time points, and blood.
2. NCIC HD9. This is an adaptive design phase 2-3 clinical trial in Hodgkin's lymphoma, randomized 1:1:1, relapsed versus refractory, with 82 participants, and many biospecimens will be collected.
Their groups would be pleased to collaborate on biomarker and sample analysis.
Discussion ensued that there are currently plenty of biomarkers in lymphoma, including genetic classifiers (Nanostring from the BC Cancer Agency), immune signatures, key events (MYC and BCL2 by FISH/IHC), and other markers (immune – PDL1, etc.). They are interested in whether or not mutational load predict response to immunotherapy in lymphoma, working in Hodgkin's and non-Hodgkin's populations.

***Workshop Wrap up***: The TRI workshop moderators (Ohashi, Berinstein and Bell) agreed that a lot of provocative and exciting science was presented over the day and clearly further deliberations would be required to begin to create a focused proposal. Participants would be contacted by email to describe next steps. Bell encouraged participants to put together

ideas based on what they heard at the workshop and begin to self select some collaborative teams that could be part of a TRI proposal while keeping in mind the goals and purpose of the TRI program.

# Immuno-oncology Translational Research Initiative Planning Workshop

Thursday, November 26, 2015
8:00 a.m. – 5:00 p.m.
Light breakfast will be served at 8:00 a.m.
Location: OICR | West Tower Boardroom 5-20/21

| TIME | AGENDA ITEM | PRESENTER |
|---|---|---|
| **8:00 a.m.** | **Arrivals and light breakfast** | |
| **8:30 a.m.** | **Opening remarks**<br>• Workshop goals and deliverables/outcomes<br>• Funding opportunities and timeline | *John Bell*<br>*Neil Berinstein*<br>*Pam Ohashi* |
| **8:40 a.m.** | **Background**<br>• OICR Strategic Plan 2016-2021: overview<br>• Translational Research Initiatives | *Tom Hudson* |
| **8:50 a.m.** | **Introduction**<br>• OICR's Immuno- and Bio-therapies (ORBiT) Program | *John Bell* |
| **9:00 a.m. – 12:00 noon** | **Discussion**<br>• **Combination strategies**<br>  ○ Oncolytic viruses<br>  ○ Adoptive cell therapy<br>  ○ Immune modulators<br>  ○ New targets/vaccines | *John Bell to lead discussion* |
| **10:30 a.m.** | **Break** | |
| **12:30 p.m.** | **Lunch** | |
| **1:00 p.m. – 3:30 p.m.** | **Discussion**<br>• **Immuno-genomics**<br>  ○ Biomarker development<br>  ○ Biomarker validation<br>  ○ Clinical and translational research | *Pam Ohashi to lead discussion* |
| **2:00 p.m.** | **Break** | |
| **3:30 p.m.** | **Potential TRI projects, potential collaborations and next steps** | |
| **5:00 p.m.** | **Adjourn** | |