2025 Community Dissemination Report

BioCanRx-Cancer Stakeholder Alliance Learning Institute

A Summary of Current Immunotherapy Research discussed at the 2025 BioCanRx Summit for Cancer Immunotherapy

Written by: Participating Learning Institute Patients and Caregivers, in Collaboration with Early Career Researchers

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Welcome

From BioCanRx

We are proud to share this publicly available Community Dissemination Report written by the participants of the 2025 BioCanRx-Cancer Stakeholder Alliance Learning Institute. We are very happy to have hosted the Learning Institute at the 2025 Summit for Cancer Immunotherapy (Summit4CI) from April 6th- 8th, in Toronto, Ontario. We would like to thank the BioCanRx staff and the CSA-LI Working Group for planning and facilitating an amazing event. We would also like to congratulate the Learning Institute participants for bringing such enthusiasm and commitment in completing this program.

The Learning Institute piloted at the 2017 Summit for Cancer Immunotherapy and has since 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 for the invaluable time and focus that participants have committed to developing this important patient engagement initiative.

This Dissemination Report serves to highlight and share the key research take-aways presented at the Summit4CI as well as group reflections of the Learning Institute. The report is targeted toward the boarder oncology patient and researcher community, BioCanRx network, Cancer Community Partnership, and general public.

We look forward to hosting another successful event in the future. You can learn more about the Summit4CI at www.cancersummit.ca.

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

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

Stéphanie Michaud, Ph.D.
President and CEO,
BioCanRx

BioCanRx
Canada's Immunotherapy Network
Le réseau canadien d'immunothérapie

From the BioCanRx Cancer Stakeholder Alliance

In 2017, on the advice of the Cancer Stakeholder Alliance and with inspiration from the Community AIDS Treatment Information Exchange (CATIE) – Canadians Association for HIV Research (CAHR) Learning Institute, BioCanRx created the Learning Institute. The Learning Institute was built with the following objectives in mind:

- Create a model of learning that encourages, supports, and facilitates the integration of patient leaders into the annual BioCanRx Summit for Cancer Immunotherapy (Summit4CI);
- Integrate the patient/caregiver perspective to ensure that cancer research is well informed by the patient voice and lived experience;
- Ensure that scientific research presented at the conference is accessible so that patients can be advocates to their communities.

As part of the Learning Institute, trainees working in cancer immunotherapy research are paired with patient advocates. Together, they attend Summit4CI and learn from each other through a bi-directional exchange of information during the conference.

Trainees guide patient advocates through the conference and help them to better understand the scientific knowledge and general scientific process, as well as to practice their knowledge-translation skills. Patient advocates help trainees understand the real-world implications and importance of their work while passing on their own lived experience both within and outside of the cancer landscape.

I believe we have created something very valuable for patients and researchers alike. It is important to remember that patients have a lot to teach others about the cancer landscape and this initiative helps the patient voice be heard.

I want to thank and commend BioCanRx for being so committed to patient engagement in cancer research through initiatives like the Learning Institute.

Louise Binder,
Chair of the Cancer Stakeholder Alliance Working Group,
Health Policy Consultant, Save Your Skin Foundation

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The Learning Institute

What is the Learning Institute?

The BioCanRx-Cancer Stakeholder Alliance Learning Institute **brings together** leaders from oncology patient communities (**patient scholars**) and BioCanRx Trainees (**academic scholars**) from the immunotherapy research community to engage in **interactive, collaborative, and bidirectional knowledge exchange** activities at the annual Summit for Cancer Immunotherapy. The overall aim of the Learning Institute is to ensure that novel cancer immunotherapy research is **accessible** to the cancer patient community.

Goals

- ☑ Create a model of learning that encourages, supports and creates the integration of patient leaders into the scientific conference
- ☑ Integrate the patient/caregiver perspective to ensure cancer research is well-informed by the patient voice and lived experience
- ☑ Ensure that cancer immunotherapy research is accessible so that patients can be advocates to their community
- ☑ Bridge the knowledge gap between patients and researchers through bi-directional learning
- ☑ Connect patients and caregivers with researchers to facilitate patient involvement in cancer research projects

The Main Components of the Learning Institute

PRE-SUMMIT TRAINING

Familiarization of basic cancer biology and immunotherapy concepts in advance of the Summit for Cancer Immunotherapy.

BUDDY SYSTEM

The buddy system involves pairing a technical expert (academic scholar) with people with lived cancer experience (patient scholars) for sharing of their respective expertise.

KNOWLEDGE EXCHANGE SYSTEM

Buddy groups get together and discuss the research they have heard. After discussion, buddy groups present to the group and explain the key take-aways of the research.

DISSEMINATION REPORT

Co-authorship of a community dissemination report outlining key takeaways from the Summit. The report is available to the public and is written in lay language to make it accessible.

2025 Learning Institute

This year's initiative brought together eight Patient Scholars from the cancer patient/caregiver community, and eight Academic Scholars from the BioCanRx trainee community. Participants came to the Learning Institute from coast to coast across Canada to represent a diverse range of research and life experiences.

Figure 1: 2025 BioCanRx-CCP Learning Institute participants

Together, Learning Institute participants participated in a series of interactive and collaborative "Knowledge Exchange sessions" that enabled them to process and share knowledge based on research being presented at the conference. These high-energy sessions included small group discussions followed by group presentations highlighting the accessibility, science, and key takeaways from the talks.

Figure 2: A collage of photos from the Learning Institute Knowledge Exchange Sessions

Table 2: Full List of the participants in the 2025 Learning Institute

Patient Leaders/Caregivers who participated as "Patient Scholars":	
Michelle Audoin **Sandra Dudych** **Anne Goodbody** **Milan Heck** **Harjeet Kaur**	**Cynthia Mitchell** **Daryna Skybina** **Raymond Vles**
BioCanRx Trainees who participated as "Academic Scholars":	
Grace Bernard **Gillian Carleton** **Jessica López Espinosa** **Paul Jerard Layug** **Heejae Lee**	**Victor Negrea Puskas** **Khushi Rathod** **Dylan Thomas**
CSA Learning Institute Working Group members who participated as "mentors":	
Paul O'Connell, Co-Chair The Leukemia & Lymphoma Society of Canada (LLSC) **Catherine Wilhelmy, Co-Chair** Centre de recherche du CHUS **Lauralie Short** Academic Scholar Advisor	**Victoria Gilchrist** Academic Scholar Advisor **Randy Thompson** Patient Scholar Advisor **Nadine Frisk** Patient Scholar Advisor

Interested in Participating?

For more information, please visit the BioCanRx website at biocanrx.com or email us at info@biocanrx.com

Plenary Session 1: Clinical Testing of Innovative T Cell Therapies for Cancer

Notes contributed by: Sandra Dudych, Paul Jerard Layug, Michelle Audoin, Khushi Rathod

Plain Language Summary:
T cell therapies are changing how we treat cancer today. This plenary session examined innovative methods for training the immune system, particularly T cells, to combat difficult-to-treat cancers. Scientists can now reprogram patients' T cells into “living” drugs that specifically target their cancer. This is achieved by equipping T cells with specialized tools, such as CARs (chimeric antigen receptors) and TCRs (T cell receptors). These therapies have already helped many people with blood cancers, including leukemia and lymphoma.

Currently, researchers are striving to extend these treatments to address additional cancer types, including patients with solid tumours and those with relapsed disease. These cases are more challenging to manage because they often evade detection by the immune system or establish barriers that inhibit immune cells from accessing them. The speakers provided early findings from clinical trials and outlined the necessary improvements for these therapies to reach broader utility.

1. Doug Mahoney - GPNMB-Targeting CAR T Cell Therapy for MiTF Fusion-Driven Cancers

Focus of the Talk:
Dr. Mahoney opened this plenary by highlighting the potential of using CAR T cell therapy to treat solid tumours. Despite its remarkable results for blood cancers, solid tumours present a different set of complexities that limit the application of CAR T cell therapies. They often lack clear targets (tumour-specific antigens are rare) and are more challenging for immune cells to access due to their exclusive environment (immunosuppressive tumour microenvironment).

Key Takeaways:
His team focused on GPNMB, a protein overexpressed in sarcomas but rare in healthy cells. They developed CAR T cell GCAR1 to target GPNMB. In animal studies, GCAR1 showed excellent efficacy. Early patient testing indicated it was safe with good activity. The CAR T cells expanded in the body, with mild side effects like skin rashes.

In one patient, smaller tumours disappeared, but larger ones remained. The team believes CAR T cells struggled to reach the bigger tumours. They are now exploring ways to help these cells reach deep into these tumours, including combination treatments to protect CAR T cells in the hostile tumour environment.

Final Thoughts:
Dr. Mahoney's research demonstrates that CAR T cell therapy could help people with solid tumours, especially highlighting its use in rare sarcomas. Further testing is required, but the results are encouraging. With additional improvements, this therapy could emerge as a viable option for individuals with limited treatment choices. Dr. Mahoney and the team also emphasize the true collective effort from various Canadian institutions to secure approval for these first-in-human tests and ensure their success.

2. Marie Bleakley - TCR-T Cell Therapy Targeting Minor Histocompatibility Antigens

Focus of the Talk:
Dr. Bleakley discussed TCR-T cell therapy, another way to train T cells to fight cancer. Unlike CAR T cells, TCR-T cells can find cancer signals hidden inside the cell, making them useful for cancers without surface markers or "flags."

Key Takeaways:
TCR-T therapy may be more effective for cancers such as solid tumours and relapsed blood cancers, where the usual targets are absent. These cancers can evade CAR T cells, but TCR-T cells can detect cancer differently.

To explain the difference, imagine you're a cancer cell going through airport security. CAR T cells are like TSA agents performing a pat-down, checking only the surface. TCR-T cells are like sniffer dogs, which can detect what is hidden. This illustrates why different tools are necessary for various types of threats or cancers.

Final Thoughts:
TCR-T cell therapy could help people whose cancer does not respond to current treatment modalities. It offers hope for patients who are running out of options, including those who have relapsed blood cancers. Dr. Bleakley's work demonstrates that there is no "one-size-fits-all" immunotherapy for cancers, and that exploring the potential of various T cell therapies can improve care for more cancer patients.

3. Leanne Palichuk - Using Double-Negative T cells to Enhance the Innate like Anti-Leukemic Activity of CD8+ T Cells Against Relapsed Pediatric Acute Myeloid Leukemia

Focus of the Talk:
Leanne's talk focused on enhancing stem cell transplantation (SCT) using a special population of T cells called **double negative T cells** (DNT). Stem cell transplantation for cancer, like acute myeloid leukemia (AML), involves replacing diseased bone marrow with healthy stem cells to help the body make new, cancer-free blood cells. However, sometimes the donor cells can start attacking the patient's healthy tissue and causing graft verse host disease (GvHD).

Key Takeaways :

- AML has a low survival rate and high relapse rate with SCT being the conventional treatment
- SCT often leads to GvHD which can serious complications and limit the effectiveness of the therapy
- Leane is establishing protocols on how DNT cells can be grown alongside stem cells to enhance their effectiveness and help avoid GvHD
- **Stem cells** co-cultured with **DNT and AML cells** showed **enhanced killing of AML**

Final Thoughts:
Overall, this research provides a method to increase the effectiveness of SCT and its safety profile. This is a novel inexpensive method to enhance the anti-cancer ability of stem cell transplants.

Though the research that Leanne presented is in the pre-clinical phase, the work is targeting a rare subtype of the AML population, who have a high rate of relapse, no standard of care, and a low survival rate. The problem is very real.
This approach, of using DNT cells that are not donor specific and can be grown save time, money, and can reach more patients. The need to enhance the effectiveness of stem cell therapy in order to reduce the chances of relapse is always a priority for patients and their families, especially offering hope and better outcomes in a rare cancer population.

4. Christian Hinrichs - Cell Therapy for Viral and Non-Viral Epithelial Cancers

Focus of the Talk:
Dr. Hinrich's group focuses on developing immunotherapies for viral epithelial cancers. Cancers that arise from an HPV infection often present with unique viral markers that can be targeted using engineered T cells.

Key Takeaways:

- **Tumour infiltrating lymphocyte (TIL) therapy** is where doctors will take immune cells within the tumour, grow them up in a lab, and then put them back into the patient. These TILs are better at finding and killing tumour cell. However, this is a very **expensive** treatment.
- **T cells** (part of the immune system) can instead be engineered with a **receptor** that can recognize **viral marker E7** in HPV cancers. These T cells are great at recognizing and killing tumour cells that show E7 on their surface.
- Clinical trials with HPV engineered T cells showed responses in 6/12 patients with increased tumour control and survival.
- This therapy also helps to avoid cytokine release syndrome (CRS), which is a common side effect of CAR-T therapy

Final Thoughts:
T cell receptor therapy (TCR) is a new method of engineering T cells to target very specific and unique markers presented by tumour cells. Multiple patients showed tumour control and tumour regression post treatment with limited toxicity. This treatment also helps to avoid CRS, a common side effect of other T cell-based therapies (ex CAR-T).

Much of the research described by Dr. Hinrichs showed the powerful potential of how engineering T cells from good responders can contribute to breakthroughs. The fact that half of the patients treated with this therapy had a good and visible response on scans but for whom, the response to treatment was inconsistent should be regarded as positive step towards understanding the mechanisms of resistance after treatment. Future studies can plan and adapt to this, hopefully leading to new treatments addressing the unmet need for cell therapy for epithelial cancers, especially HPV related cancers.

Plenary Session 2: Nobody Say T Cells

Notes contributed by: Anne Goodbody, Victor Negrea Puskas, Daryna Skybina, Gillian Carleton

Plain Language Summary:
When people talk about cancer immunotherapy, they almost always focus on T cells, those aggressive little white blood cells that hunt down and destroy cancer. But guess what? T cells aren't the only immune cells in the fight! There's a whole squad of other white blood cells: B cells, natural killer (NK) cells, and macrophages, working just as hard to help the immune system recognize and attack cancer. In fact, T cells can do a better job with the help of these other members of the squad. It's all about the teamwork between every part of the immune system to make sure any abnormal cells are found and destroyed.

B cells are responsible for making antibodies, which act like "wanted" posters, marking cancer cells, so the immune system can find and attack them. NK cells are stealthy assassins that don't need permission (or T cells) to take out cancerous or infected cells, they just go for it. Macrophages, the big eaters of the immune system, act as the cleanup crew by gobbling up dead cells, signaling for reinforcements and can even be prompted to eat cancer cells directly!

This session flipped the script. Here, the spotlight shines on these "forgotten" immune heroes to explore how they contribute to cancer treatment in ways that go beyond what T cells can do alone.

1. Brad Nelson - How B Cells Leverage Self- Reactivity to Promote Long-Term Patient

Focus of the Talk:
In ovarian cancer, the tumour environment can be very immunosuppressive making it a challenge for currently available immunotherapy treatments to be effective. However, patients with longer overall survival have been shown to have a higher number of immune cells in their tumours which are known as "hot tumours." In these hot tumours, when B cells were present with T cells, patients had a better survival outcome than those with T cells alone. Typically, the T cells are located within the tumour, while the B cells are situated in the surrounding connective tissue (called the stroma). However, why the presence of B cells leads to a better outcome remains unclear. In this talk, the research team raised questions like: "What are the mechanisms behind B cells effectiveness in the tumour? How can this be leveraged to improve treatment options for patients?"

As described in this session, Dr. Brad Nelson and his team are investigating how the antibodies made by B cells could be targeting tumour cells and leading to their destruction. B cells could be responsible for boosting the activity of T cells or producing antibodies, Y-shaped protein 'missiles' that target and help to 'flag' unwanted cells for elimination by other immune cells.

Key Takeaways:
A process of B cell evolution exists enabling the development of highly specific antibodies. This is like a family tree where the 'mother' is the simplest B cell population that gradually evolves and multiples into more specialized daughter cells, producing more specific antibodies.

Dr. Nelson's team discovered, through RNA sequencing, family trees of B cells inside the tumour which differ and expand. They found and made 51 suitable antibodies of which 82% target intracellular proteins and 18% target cell surface proteins. To date from his team, two protein targets have been identified: KDM4a & NUMA. Interestingly, both targets are present universally across healthy cells with NUMA already being linked with autoimmunity.

A tumour can avoid being specifically targeted by removing its 'cancer' markers that the T cells can identify. As a result, B cells can come in and start producing less specific antibodies that target more broad self-antigens which are present universally across cells. Then, other immune cells like macrophages and NK cells can then destroy these flagged tumour cells despite the absence of the 'typical cancer' markers they express.

To avoid an immune system attack on healthy cells causing autoimmunity, there needs to be a way to control this. Dr. Brad Nelson and his team believe that the B cells need to evolve to generate a local auto-immune attack on the tumour to prevent the cancer cells from escaping attack by the immune cells.

Dr. Nelson also hypothesizes that whole-body auto-immune reactions are avoided because somehow (still not known) the B cells direct this 'localized' attack or burn in only the tumour and not across the whole organ where the tumour is located.

Why is this important for patients? By continuing to understand what the antibodies produced from B cells inside the tumour are targeting on tumour cells and the mechanisms of how these antibodies avoid healthy cells, the researchers could find antibodies that have ideal tumour targets for immunotherapy. In a therapy, these antibodies could act as 'wanted posters' for immune cells to then direct them to destroy tumour cells.

Final Thoughts:
By harnessing B cell self-reactivity for targeting and killing the tumour cells, and sparing healthy tissue, our body could have a way of performing a 'controlled burn' similar to how controlled fires are started in a section of the forest to maintain a healthier ecosystem. In addition, with new antibody discoveries, tumour-associated proteins could be identified as suitable targets in future immunotherapies.

2. Jeanette Boudreau - Sharpening natural killer cells' activity as cell therapies for pancreatic cancer

Focus of Talk:
Pancreatic cancer is difficult to treat with the 5-year overall survival being 10-13%. Typically, progression is quick with these tumours being immunologically cold, and genetically diverse as they contain "burst" mutations which enable the tumours to evade immune recognition. One important type of immune cell in the fight against cancer is the NK cell. NK cells are white blood cells that release enzymes to kill virally infected cells and cancerous cells. NK cells bring together an array of receptors that contribute to the activation or inhibition of enzyme release. This allows the NK cell to determine if a particular cell should be destroyed based on the signals it receives from these co-expressed receptors. We can begin to think of NK cells as 'immune specialists' that don't need a specific target to destroy tumour cells. Rather they become 'educated' based on the messages from the activation/inhibition receptors. This contrasts with T cells that require a certain target protein to be presented by the tumour cell, which enables tumours to avoid T-cell attack through the lack of protein expression. Thus, the education of an NK cell becomes very important as it allows for the NK cell to kill a tumour cell that tries to hide. In contrast, non-educated NK cells, which don't have all these receptors, cannot kill tumour cells that have evaded the immune system. Importantly, NK cells also communicate their actions with T-cells to help regulate immune development and response.

As described in this talk, Dr. Jeanette Boudreau and her team are investigating the tumour-killing role of NK cells and how their education could be exploited to kill pancreatic cancer cells that evade the immune system.

Key takeaways:
Using the genetic analysis of NK cells in pancreatic tumours and mouse models, the team found that a series of NK receptors called NKG2D and NKG2A were vital to NK education.

In addition, they found that inflammation plays a key role in NK cell functionality where increased inflammation in the tumour lead to increased protein expression of HLA (a marker of self for our body's cells) on the pancreatic tumour cells which was found to strongly inhibit educated NKs.

Using mouse models with different levels of HLA expression, they found that educated donor NK cells given to a recipient remained educated, regardless of HLA expression of the individual mouse.

Why is this important for patients? The sustainability of NK education demonstrates the possibility of giving educated NK cells as a treatment and ensuring these NK cells are able to remain functional and destroy hard-to-kill tumour cells in a patient. In a dose-response experiment in mice, the researchers investigated the potential harmful side effects of using NK cells as a therapy. They saw that there were no harmful effects with increasing NK cell dosages. This is quite remarkable considering T cell therapies have been shown to have harmful side effects that can affect the quality of life for the patient and sometimes stop treatment all together.

Final Thoughts:
NK cells can be seen as playing the role of a 'murderous' musical conductor in managing the killing of tumour cells, and the intricacies of their education are still being understood. Yet there have already been some remarkable discoveries. Treatments in mice involving NK cells have shown little to no harmful side effects and NK cells have demonstrated the ability to destroy tumour cells that evade other mechanisms of the immune system. Thus, there is a strong push in the medical field to learn more about NK cells and utilize them as an immunotherapy.

3. Emilie Ollame-Omvane - The Major Roles of TRAIL-R2 Death-Receptor in Acute Lymphoblastic Leukemia Lysis by ThINKK-primed NK Cells

Focus of Talk:
The talk by Emilie Ollame-Omvane focused on a cell type called Natural Killer (NK) cells, and how they can be used to treat acute lymphoblastic leukemia (ALL). Previously, work from their lab showed that NK cells can be activated using a strategy called ThINKK (Therapeutic Inducers of Natural Killer cell Killing), and this approach leads to increased death of ALL cells. Emilie Ollame-Omvane's research explored the mechanism behind this enhanced killing, and they discovered that NK cells recognize a specific receptor called TRAIL-R2 that is present on ALL cells. When NK cells bind ALL cells through this receptor, tumour killing is turned on. This can be compared to a lock and key mechanism, but instead of opening the door, the key leads to everything in the room behind the door to be destroyed.

Final Thoughts:
From a patient perspective, the typical treatment for ALL involves a stem cell transplant, which leads to the production of new immune cells including NK cells. These new NK cells could be activated to kill ALL cells using Emilie Ollame-Omvane's strategy, which would potentially improve the success of this treatment.

4. Michael Klichinsky - Engineering Macrophages for Cancer, Liver Fibrosis, and Autoimmunity

Focus of Talk:
Michael Klichinsky's talk presented a new take on CAR-T cell therapy by applying the technology to a different type of immune cell – the macrophage – to create a therapy called CAR-M therapy. This therapy was tested in breast, esophageal, and liver cancers. Unfortunately, the efficacy of this therapy was limited, with most cases showing stable or progressive disease. The likely explanation for this lack of efficacy is that macrophages have low persistence, which means that they die quickly once in the body. To overcome this, Dr. Klichinsky proposed using monocytes instead of macrophages to generate the CAR-M therapy. As monocytes are the precursors to macrophages, they would likely survive longer while retaining the same positive characteristics for tumour cell killing. Dr. Klichinsky will be exploring this new approach in future research.

Final Thoughts:
From a patient perspective, the main benefit of using monocytes or macrophages instead of T cells for CAR therapy means that the patient would not be required to go through lymphodepletion before receiving treatment.

Plenary Session 3: Fueling the Fight - Modulating Immune Metabolism in Cancer

Notes contributed by: Cynthia Mitchell, Dylan Thomas, Milan Heck, Grace Bernard, Raymond Vles, Heejae Lee, Jessica López Espinosa, Harjeet Kaur

Plain Language Summary:
Our immune system plays a key role in fighting cancer, but sometimes cancer finds ways to weaken or exhaust immune cells, making them less effective. This plenary session will explore how understanding and changing the way immune cells use energy—also known as immune metabolism—could improve cancer treatment.

Experts in the field will share the latest research on how immune cells function in cancer. Dr. Greg Delgoffe (University of Pittsburgh) will explain how immune cells become exhausted in tumours and how their metabolism can be reprogrammed to restore their function. Dr. John Stagg (Université de Montréal) will present new insights into targeting immune metabolism to

improve therapy. Meghan Kates, a PhD student at the University of Toronto, will discuss how a drug called halofuginone may help reinvigorate immune cells used in cancer treatment. Finally, Dr. Sue Tsai (University of Alberta) will explore the role of insulin signaling in shaping anti-cancer immune responses.

By better understanding how immune cells get their energy and how we can improve their performance, this research could lead to more effective and longer-lasting cancer treatments. This session will provide scientists and patient partners with a deeper understanding of cutting-edge immunotherapy strategies and how they might shape the future of cancer care.

1. Greg M Delgoffe - Immunometabolic Underpinnings of T Cell Exhaustion

Focus of the Talk:
Dr. Greg Delgoffe's presentation focused on improving the effectiveness of **adoptive cell therapies (ACTs)**, such as **CAR-T cells** and **tumour-infiltrating lymphocytes (TILs)**. These are personalized immunotherapies that involve taking a patient's T cells, expanding them in the lab, and then reinfusing them to help fight cancer. However, these cells often struggle to survive and function once reintroduced into the harsh tumour environment.

Key Takeaways:

- T cells expanded in the lab are typically grown in a **glucose-rich** environment. This causes them to rely heavily on **aerobic glycolysis**.
- Tumours also consume large amounts of glucose, making it scarce in the **tumour microenvironment**. This leaves TILs metabolically disadvantaged when they enter the tumour.
- Dr. Delgoffe's lab is investigating how to **reprogram T cells metabolically** so they are better suited to survive and function inside tumours.
- His team discovered that using a drug called **DCA (dichloroacetate)** during T cell expansion pushes the cells to use different energy sources and shifts metabolism away from glycolysis.
- T cells expanded with DCA show improved **mitochondrial function**, **memory-like features**, and **greater anti-tumour activity** in mouse models.

Final Thoughts:
This research underscores the importance of mimicking the **tumour's metabolic environment** during lab-based T cell expansion. By metabolically conditioning these cells ahead of time, we may be able to significantly improve the success of ACTs in cancer patients. Future immunotherapies could benefit from combining such metabolic reprogramming strategies with existing ACT platforms.

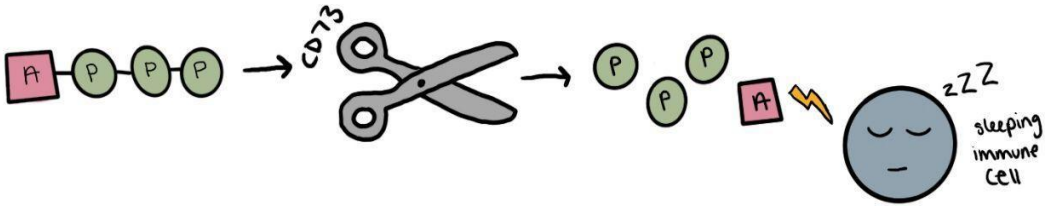
Aa a patient, advancements in mimicking tumour metabolic environments for T cell expansion represent an impactful step forward in the field of cancer immunotherapy. This work offers the potential to revolutionize treatment protocols and improve patient outcomes. These

advancements are promising in that they may offer more effective and personalized care; bringing renewed hope to patients.

2. John Stagg - Metabolic Regulation through Adenosine Uptake Suppresses Anti-Tumour T Cells

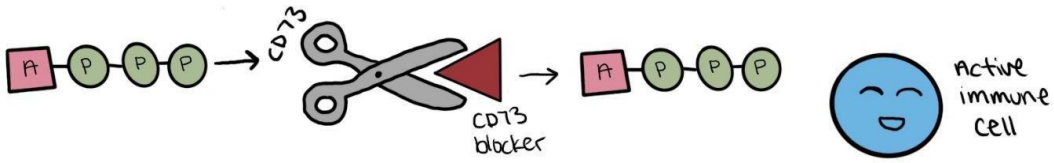
Focus of Talk:

All cells need energy, which is present in the form of adenosine triphosphate (ATP). We can think of this as a key building block for cells. This block can be broken down into smaller pieces, one of which is adenosine on its own. When there is too much adenosine in a cell the immune system gets shut off, and tumours are able to take advantage of this. Tumours will upregulate the machinery that breaks ATP down into adenosine, which is CD73, an enzyme on the cell's surface.



Key Takeaways:

Blocking CD73 with an antibody caused less immune suppression, and this was tested for pancreatic, lung, and skin cancer. Additionally, when they blocked a transporter of adenosine (ENT1), they saw the same effect.



Final Thoughts:

Blocking the conversion of ATP to adenosine, or the transport of adenosine into cells was able to mitigate suppression of the immune system caused by tumours. These methods could be used in combination with existing cancer therapies like immune checkpoint inhibitors (ex: PD1) to improve treatment outcomes.

3. Meghan Kates - Halofuginone Treatment Reinvigorates Melanoma TIL Mitochondrial Metabolism during Ex Vivo Culture

Focus of Talk:
The use of TIL – tumour infiltrating lymphocytes – is a promising approach to cancer treatment. This therapy takes a type of lymphocytes (a white blood cell that is part of the body's immune system) called T cells from a patient's tumour, treats them in the laboratory to increase their cancer fighting effectiveness, and then reinfused into the patient, where they go to work killing cancer cells.

At first, the tumour begins to shrink. As time goes on, it has been observed that T cells begin to lose their cancer fighting effectiveness.

Competition with cancer cells for energy seems to be the cause of the problem. Once inside the tumour, T cells require energy to function, which they draw from the surrounding environment. Unfortunately, cancer cells draw their energy from the very same source. T cells are often outcompeted by cancer cells for this energy, which seriously weakens their cancer fighting ability.

This study found that treating T cells with a drug called Halofuginone can revitalize exhausted T cells in melanoma (skin cancer tumours) in mice. T cells that were treated with Halofuginone were more effective in killing cancer cells than untreated T cells.

Further examination of the treated T cells once in the mice showed that Halofuginone enabled them to find a whole new source of energy, where they would not be in competition with cancer cells.

Since the study is still ongoing, it is too early to assess the effectiveness of the treated T cells in shrinking and eventually eliminating the tumours.
Nonetheless, it showed a potential solution to the problem of energy- deprived T cell exhaustion that limits the effectiveness of TIL therapy.

Key Takeaways:
Technology available today allows researchers to understand precisely why promising therapies are not working as expected. This opens the door to
solutions which can overcome these obstacles.

4. Sue Tsai - Insulin Signalling and Anti-Tumour Immunity

Focus of Talk:
Dr. Tsai delivered a talk on the relationship between insulin, obesity, and anti-tumour immunity. Her work addresses the "obesity-cancer paradox": although obesity increases cancer risk, these patients respond better to immune checkpoint blockade (ICB) therapy, like PD-L1 inhibitors.

Using mouse models fed a high-fat diet, Dr. Tsai's team investigated this at the cellular level. When the obese mice were immunized (vaccinated), their immune cells showed weaker responses compared to lean mice, indicating impaired T cell function. After injecting them with cancer cells, tumours grew larger in obese mice. Interestingly, these mice had more T cells in the tumour (cells that kill cancer), but they expressed fewer killing molecules and more PD-L1. PD-L1 is a protein that acts as a brake on the immune system, preventing T cells from attacking cancer cells, and it is the target for ICB. This suggests T cells were present but dysfunctional, like soldiers without their weapons.

To test if PD-L1 caused the differences in tumour size, they genetically removed PD-L1 and found that this erased the difference in tumour size between obese and lean mice. It was as if the cancer had installed more "blinds" on its windows to evade immune attack—but when PD-L1 was removed, those windows were exposed again. This supports the idea that tumours in obese patients express more PD-L1, making them more immune-resistant but more responsive to anti-PD-L1 therapy.

Dr. Tsai explored how obesity and tumours induce insulin resistance in T cells. Just like muscle or liver cells, T cells need insulin to function. When this is impaired, immune responses weaken. The result is a vicious cycle: insulin resistance leads to higher insulin levels, which in turn may increase tumour PD-L1 expression and immune dysfunction.

By connecting the dots between metabolism and immunity, Dr. Tsai proposes that insulin is more than a metabolic regulator—it's a potential immune checkpoint. Targeting this hormone could unlock new strategies to restore T cell function and improve cancer therapy, especially in patients with obesity or metabolic disorders.

The "Big House, Small House" analogy. In obese mice, the "big house" represents a tumour-rich environment with increased PD-L1 — a house with many large windows that only stores more (tumour size) but makes intruders (immune checkpoints) easier to detect. This enables a better response to ICB. Lean mice are a "small house" with fewer contents and windows—smaller tumour and less PD-L1—making targets harder to detect and resulting in weaker ICB treatment.

Key Takeaways:

- Obesity increases cancer risk but can make some treatments, like immune checkpoint blockers (ICB), work better.
- In obese mice, immune cells were weaker and tumours grew faster, but those tumours had more PD-L1, a protein that helps tumours hide.

- Extra PD-L1 makes tumours more vulnerable to ICB drugs, which explains why some patients respond better to these treatments.
- High insulin levels drive this PD-L1 increase and weaken immune cells.
- When PD-L1 is removed, the difference between lean and obese mice disappears.
- Targeting insulin might boost immune responses and improve cancer treatments.

Final Thoughts:
One of the key takeaways was how insulin signalling can affect how well the immune system works in people with cancer. This is especially important for people living with obesity, diabetes, or insulin resistance. We want people to remember how, although tumours are more common amongst obese populations, these can be a "big house with many windows"—easy for the immune system to find and attack if the right treatment is used. From a patient perspective, it's comforting to know that scientists are looking for personalized solutions, considering body types, conditions, and how we each respond to treatment. This research gives new hope that future cancer care will be more tailored, inclusive, and effective, especially for people living with comorbidities. I hope patients take away this message: research is evolving, and scientists are getting closer to creating treatments that are as unique as we are. And as someone who lives with cancer, that gives me a lot of encouragement.

Plenary Session 4: Implementation of High Parameter Technologies to Map Tumours and Immunity at High Resolution

Notes contributed by: Milan Heck, Grace Bernard, Raymond Vles, Heejae Lee

Plain Language Summary:
Spatial biology is a relatively new type of science in which investigators study tumours without breaking them apart. We use antibodies to tag different types of proteins within tumours, and that allows us to tell what types of cells there are. We have learned that tumours are busy ecosystems, and often contain many immune cells. Immune cells can perform different functions depending on the signals that they receive from each other and from their environments. Spatial biology can give us important clues about how cells interact (or fail to) and highlight opportunities to improve biotherapeutics for cancer. These spatial biology approaches have quickly become popular in cancer research, and they generate large datasets. Our symposium will explore how data obtained in spatial biology experiments is being used to understand the biology of tumours.

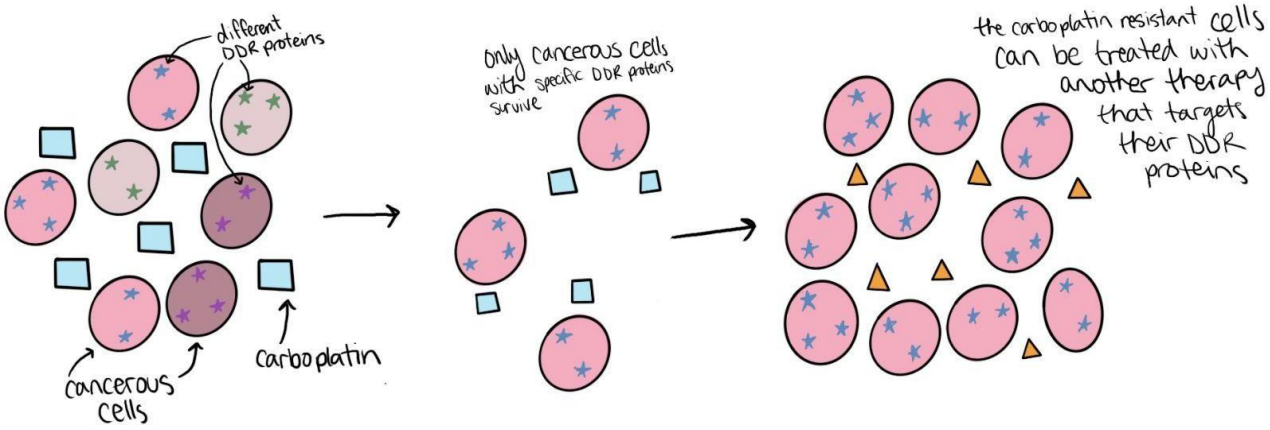
1. Wendy Fantl - Coordinated Protein Modules Define DNA Damage Responses to Carboplatin at Single Cell Resolution in Human Ovarian Tumour Cells

Focus of Talk:

Ovarian cancers are often treated with chemotherapies that contain platinum because of its ability to cause DNA damage. One of the most commonly used chemotherapies is called carboplatin. Many patients become resistant to this therapy and thus, there is a need to distinguish which patients become resistant, and why. Single cell proteomics is a methodology that allows researchers to define protein networks that distinguish resistant cells from sensitive cells.

Key Takeaways:

DNA damage repair (DDR) proteins were identified as important causes of cell sensitivity to carboplatin. Differences in the activities of DDR proteins over time indicate the extent to which a cell is sensitive. Using a cellular model of ovarian cancer, Dr. Fantl's team found that cells will uptake comparable levels of carboplatin, but it is the activity of DDR proteins within each individual cell that determine the outcome.



Final Thoughts:

There is a need for personalized strategies to integrate drugs that target DDR receptors with standard chemotherapy treatments. Specific drugs can be chosen based on the protein molecules an individual patient has.

2. Hartland Jackson - Parsing Human Pancreatic Cancer Tumour Immune Microenvironments using Spatial Proteomics

Focus of Talk:
Pancreatic cancer is known to be very complex and aggressive, with poor outcomes and no minimal unique markers that are targetable by therapies. Pancreatic tumours actually have multiple environments within them that can be thought of as different neighbourhoods and can be studied; the immune, stromal, and localized tumour. Better understanding these different components of a tumour can help create more effective therapies for the overall "city" that is the tumour.

Key Takeaways: Spatial proteomics is a technique that allows us to see where different proteins are and what they are doing in each separate component of the tumour. It also allows for the visualization of interactions between the different environments and how cells within the tumour can move through the different areas.

Final Thoughts:
Spatial proteomic analysis helped to uncover the features of each component that have historically responded well to different types of treatment. This helps to inform researchers and doctors of specific cells and/or proteins present in specific areas that can be treated and that different environments could potentially have a unique treatment option that will be most effective.

3. Sarah Nersesian - Epitype-Immune Interactions in High-Grade Serous Ovarian Cancer

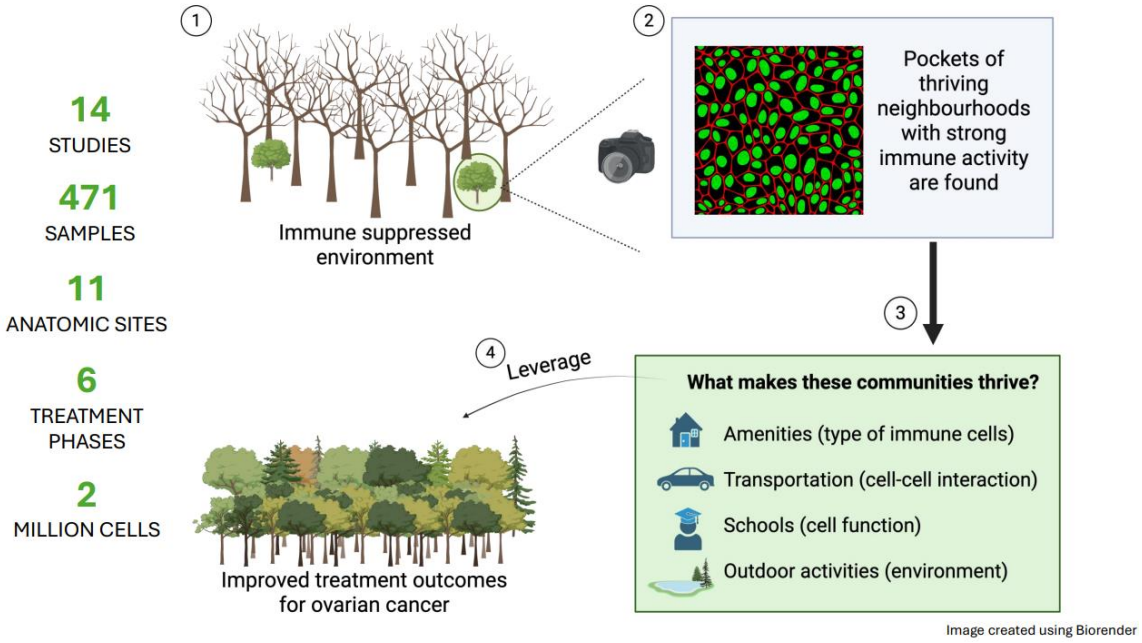
Focus of Talk:
Ovarian cancer is difficult to treat because of its ability to suppress the cancer fighting cells of the body's immune system. Yet, close examination of ovarian cancer tumours reveals pockets of thriving immune cells scattered throughout the tumour.

For this study, cellular imaging of 471 ovarian cancer samples was undertaken, adding up to 2 million cells. Groups of thriving immune cells - neighbourhoods the researchers called them - were identified.

The next step in the study is to determine the characteristics that enables these neighbourhoods of immune cells to survive in the hostile environment of a tumour. Four possibilities will be evaluated:

- Types of ovarian cancer cells (they are not all the same)
- The type of immune cell represented
- The interactions between different ovarian cancer cells and immune cells
- The environment of the neighbourhood

Knowing what enables these “neighbourhoods” of immune cells to survive and thrive could lead to the development of more effective therapies for ovarian cancer.



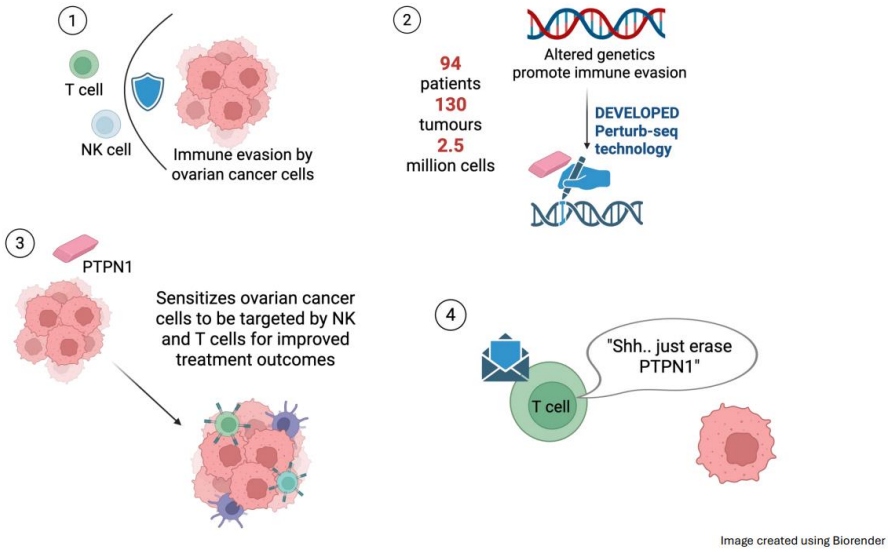
Key Takeaways:
In the same way as a biologist studying the health of individual trees needs to consider the surrounding forest, researchers who study cancer must consider how the immediate environment of immune cells affects their ability to fight the cancer.

4. Livnat Jerby - Developing Mechanisms to Unleash Targeted Immune Responses

Focus of Talk:
This presentation covered two different studies which explored how immune cells could be modified to enhance treatment outcomes.

In the first study, a technology called Perturb-seq was used to analyze 130 ovarian cancer tumour samples from 94 patients. The analysis revealed that a gene called PTPN1 was helping ovarian cancer cells hide from the immune system.

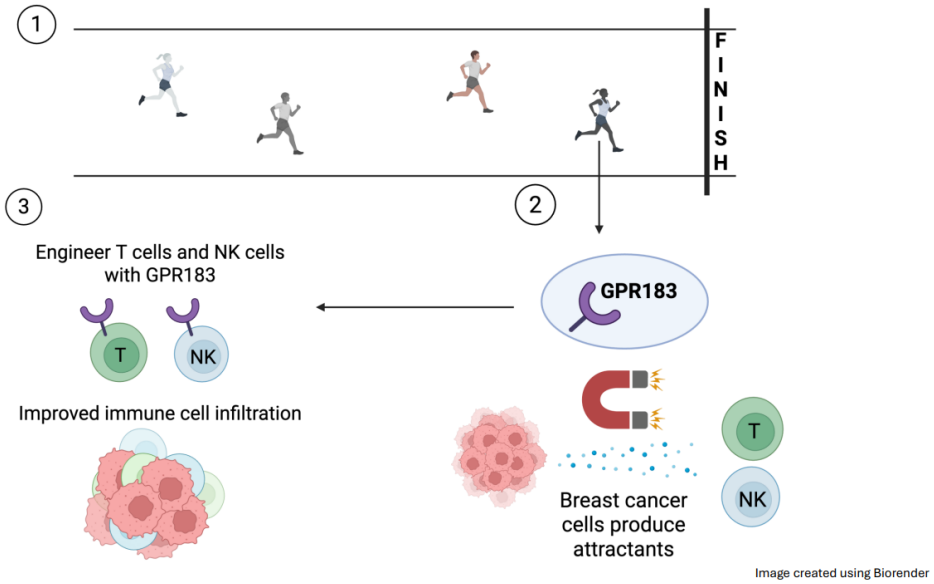
The next step will be to engineer T cells which could deliver a message to ovarian cancer cells telling it erase the PTPN1 gene. This will make ovarian cancer cells vulnerable to being recognized and destroyed by potent immune cells like T cells and natural killer (NK) cells.



The objective of the second study was to determine ways to improve immune cell penetration into breast cancer tumours. NK cells were modified in different ways and injected into breast cancer tumour-bearing mice. They were then tracked to see which ones best penetrated the tumour.

NK cells that best penetrated the tumour site had a gene called GPR183 which is attracted like iron filings to a magnet by the lipids (fats) that breast cancer cells produce. This gene made it easier for the NK cells to infiltrate the tumour.

The next step was to add the GPR183 gene to cancer killing T and NK cells. When these genetically modified cells were injected in mice with breast cancer tumours, a greater number of them infiltrated the tumour than control cells that were injected at the same time.



Key Takeaway:
Research into cancer treatment is moving from drug design to cell design.

Plenary Session 5: mRNA-Based Innovations in Cancer Immunotherapy

Notes contributed by: Michelle Audoin, Khushi Rathod, Cynthia Mitchell, Dylan Thomas

Plain Language Summary:
mRNA-based cancer immunotherapy is an innovative approach that uses messenger RNA (mRNA) to help the immune system recognize and attack cancer cells. mRNA serves as a set of instructions, teaching cells to produce proteins that stimulate a strong and targeted immune response against tumours. This technology allows for rapid development of personalized treatments tailored to a patient's specific cancer. By leveraging the body's natural immune mechanisms, mRNA-based therapies hold great promise for improving outcomes in cancer treatment. This session will explore how mRNA is revolutionizing immunotherapy and its potential to transform cancer care.

1. Bowen Li - TITUR: A Tumour-Specific mRNA Nanomedicine for Enhanced Cancer Immunotherapy

Focus of the talk:
Dr. Li's research focuses on developing new **lipid nanoparticles (LNPs)** that are **safer** and better at delivering a **therapeutic payload**.

Key Takeaways:
- Different LNP designs affect how efficiently a payload can be delivered and whether it will accumulate in the liver causing off-target effects
- After screening an LNP library, a new LNP design coined **4T1** was developed. Mouse studies showed that 4T1 preferentially accumulated in the tumour whilst **avoiding liver toxicity**. In comparison, the current commercially available LNP shows high off target toxicity via liver accumulation.
- By encoding the **4HB protein into a 4T1 LNP**, researchers were able to sensitive triple negative breast tumours to anti-PD-1 therapy.

Final Thoughts:
This research allows for the development of **safe LNPs** that are **highly targeted** compared to the current commercially available LNPs. Moreover, by encoding therapeutic targets within the LNP (ex 4HB), this therapeutic can be used in synergy with other immunotherapies.

Precision medicine and personalized cancer treatments are not only buzz words in the oncology landscape, they are important innovations that can improve outcomes by providing safe and effective treatments. The challenge faced by Dr Li's team is develop a customizable LNP product that doesn't create liver toxicities or off-target expression. Patients who undergo systemic therapy for cancer are screened regularly for liver toxicity, and if identified, can not

only cause delays in treatment, but have serious long term effects that may require them to go off treatment. Enhancing cancer immunotherapy through LNP and tumour-specific mRNAs are hopefully the future of cancer care that improves the response and treatment outcomes for cancer patients.

2. Mathias Vormehr - Therapeutic Induction of Tumour specific T Cell responses using mRNA Nanoparticles

Focus of the Talk:
Dr. Mathias Vormehr discussed BioNTech's use of **mRNA vaccine technology** to develop personalized cancer vaccines. While BioNTech became widely known for creating one of the first approved COVID-19 vaccines, their original mission was focused on treating cancer.

Key Takeaways:

- BioNTech's cancer vaccines begin by sequencing a patient's tumour to identify **neoantigens**—unique markers found only on cancer cells.
- These neoantigens are encoded into **mRNA molecules**, which are then packaged into **lipid nanoparticles (LNPs)** and injected into the patient.
- Once inside the body, the mRNA instructs immune cells to recognize and attack the cancer cells displaying the neoantigens.
- This approach allows for **highly personalized therapy**, with benefits such as rapid development, scalability, and adaptability to different cancers.
- Dr. Vormehr presented a new platform called **ribocytokine**, which co-delivers **IL-2** (an immune-boosting molecule) alongside tumour antigens. IL-2 helps T cells grow and function.
- In early studies, patients with **pancreatic ductal adenocarcinoma (PDAC)** who received this vaccine after surgery showed significant improvements in **progression-free survival**—an exciting development for a cancer with traditionally poor outcomes.

Final Thoughts:
This work represents a promising leap forward in the fight against cancer using **mRNA vaccine technology**. By combining immune-stimulating molecules with tumour-specific antigens, BioNTech's approach could enhance the body's ability to fight cancer from within. Future directions include testing other cytokines and expanding to additional cancer types.
As a patient, personalized cancer vaccines, especially those using mRNA technology offer great promise and hope. The potential for rapid development of these vaccines means that new treatments could be made available to patients more quickly than with existing methods. The scalability of mRNA vaccines is also encouraging as it is possible that these treatments might be produced in larger quantities; making them accessible to more patients with various cancers. The potential for adaptability of this approach is equally promising given that more personalized approaches in cancer care could significantly improve treatment efficacy, quality of life, and overall outcomes.

3. Abishek Wadhwa - Comprehensive mRNA-LNP Characterization using Single- Cell Techniques reveal Tumour Microenvironment Reprogramming for Cancer Immunotherapy

Focus of the Talk:
Abishek Wadhwa, a PhD student, presented a novel use of **lipid nanoparticles (LNPs)** not just as delivery vehicles for mRNA, but as **therapeutic agents themselves**.

Key Takeaways:
- LNPs are typically used to deliver mRNA or other molecules into cells, protecting their cargo from degradation.
- Wadhwa's LNPs were specially designed to **target and destroy tumour-associated macrophages (TAMs)**—a type of immune cell that often helps tumours evade detection and suppresses T cell activity.
- Using advanced **single-cell sequencing**, it was shown that these LNPs could nearly eliminate TAMs in tumour-bearing mice, while control LNPs did not.
- Removing these **pro-tumour immune cells** could make the tumour environment more hospitable to other therapies, including T cell-based treatments.

Final Thoughts:
This research opens the door to a **new generation of LNP-based therapies** that do more than just deliver drugs—they could also **selectively target harmful cells** within the tumour. Before clinical use, further studies are needed to ensure safety, especially by confirming that only the right types of macrophages are being eliminated and that liver function remains unaffected. Still, this approach has strong potential to enhance existing cancer immunotherapies.

As a patient, the possibility of using LNPs as therapeutic agents is very promising. It's encouraging to learn that LNPs may be capable of more than just delivering medication. The potential for them to selectively target harmful cells while avoiding healthy ones, ultimately minimising side effects and improving outcomes offers great hope to patients. However, it is understood that more research is required before this treatment could be safely used in a clinical setting.

4. Denis Migliorini - RNA based Immune Cell Engineering for Malignant Glioma

Focus of the talk:
Dr. Migliorini is developing **mRNA-based CAR T cell therapies** to overcome challenges in treating **glioblastoma**. Traditional CAR T cell therapy—which involves extracting a patient's T cells, engineering them in a lab to target cancer, and reinfusing them—is less effective for brain tumours due to the blood-brain barrier. To address this, Dr. Migliorini is exploring direct delivery of mRNA to T cells, enabling them to produce CARs inside the body. This approach avoids complex lab processing and may enhance CAR T cell access to brain tumours.

Key Takeaways:

- A bi-specific CAR T therapy targeting two glioblastoma antigens was delivered to patients. The mRNA encoding the CAR was chosen based on it's safety profile and ability to specifically target glioblastoma cells.
- An intraventricular delivery of mRNA-CAR T was used to deliver directly to the brain tumour.
- Scans showed immediate reductions in tumour size post treatment, but patients experienced relapses.
- Future studies are looking at developing a triple mRNA CAR that can target the heterogeneity of glioblastomas.

Final Thoughts:

This research lays the groundwork for developing CAR T cell therapies for hard-to-treat cancers like glioblastoma. By eliminating the need to extract and engineer a patient's T cells in a lab, this approach is not only less invasive but also more cost-effective. Future efforts will aim to reduce relapse rates and address the challenge of glioblastoma's genetic and cellular heterogeneity.

Glioblastoma is a hard-to-treat brain cancer. The challenge of applying CAR T cell therapies in this population is the inability of the treatments to pass the blood-brain barrier. After initial treatments, patients and their families are left with a poor prognosis due to high rates or relapse and lack of treatment options. The novel approach of delivering the therapy directly to the tumour shows innovative approaches that displayed immediate reductions of the cancer. This offers hope for the future, including the potential studies that are addressing the complex challenges of treating glioblastoma by developing a triple mRNA CAR T cell therapy.

Acronyms List

AAV: Adeno-associated virus
Ab: Antibody
ACT: Adoptive cell therapy
Ag: Antigen
ALL: Acute lymphoblastic leukemia
AML: Acute myeloid leukemia
APC: Antigen presenting cells
CAR-T: Chimeric antigen receptor T-cell
CD8+: Cluster of differentiation 8 positive T-cell
CD19: Cluster of Differentiation 19
CD22: Cluster of Differentiation 22
CI: Confidence interval
CPI: Checkpoint inhibitor
DC: Dendritic cell
DLBCL: Diffuse large B-cell lymphoma
DNA: Deoxyribonucleic acid
ELISA: Enzyme-linked immunosorbent assay
GBM: Glioblastoma multiforme
GPNMB: Glycoprotein non-metastatic melanoma protein B
HLA: Human leukocyte antigen
HPSC: CAR-hemopoietic stem cells
ICB: Immune checkpoint blockade
IFN: Interferons
IHC: Immunohistochemistry
IL: Interleukins
IO: Immune-oncology
IRAE: Immune-related adverse events
iPSC: Induced pluripotent stem cells
LNP: Lipid nanoparticle
MCL: Mantle cell lymphoma
MHC: Major histocompatibility complex
MiTF: Microphthalmia-associated transcription factor
mRNA: Messenger ribonucleic acid
mRNA-LNP: Messenger ribonucleic acid- lipid nanoparticle
NGS: Next-generation sequencing
NHL: Non-Hodgkin lymphoma
NK Cell: Natural killer cells
NSCLC: Non-small cell lung cancer
OV: Oncolytic viruses
PD-1: Programmed cell death 1
qPCR: Quantitative polymerase chain reaction
RNA-seq: RNA sequencing
scRNA-seq: Single-cell RNA sequencing
TCR: T-cell receptor
TCR-T: T-cell receptor-engineered T-cell therapy
TIL: Tumour infiltrating lymphocyte
TITUR: Tumour immune tolerance and resistance
TME: Tumour microenvironment
TNF: Tumour necrosis factor
TRAIL-R2: TNF-related apoptosis-inducing ligand receptor 2

Glossary

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***Adoptive Cell Therapy** – A treatment used to help the immune system fight diseases, such as cancer and infections with certain viruses. T cells are collected from a patient and grown in the laboratory. This increases the number of T cells that are able to kill cancer cells or fight infections. These T cells are given back to the patient to help the immune system fight disease. Also called cellular adoptive immunotherapy.

Antibody – A protein created by B-cells in direct response to specific antigens. An antibody attaches itself to its respective antigen, marking it for other immune cells to "see" and destroy.

Antigen – A protein produced by a cell, virus or bacteria. In the case of cancer antigens, the protein or part of a protein is on the surface of the cancer cell. It alerts the immune system and causes the production of antibodies or the creation of T-cells that can recognize and potentially destroy the cancer cells expressing that antigen. Neo-antigens are a variation of antigen, which arise from new mutations.

Antigen-presenting cells (APCs) – Special cells that digest invading cells or soluble (can be dissolved in water) protein antigens and present them to the T-cells and B-cells so they know what to attack.

B-cells – Immune cells that produce antibodies for specific antigens that will bind to the antigens and mark them for destruction by other immune cells.

Biologic product – Medications made from living organisms, such as vaccines, human cells and tissues, and gene therapies.

***Biomarkers** – A biological molecule found in blood, other body fluids, or tissues that is a sign of a normal or abnormal process, or of a condition or disease. A biomarker may be used to see how well the body responds to a treatment for a disease or condition. Also called molecular marker and signature molecule.

Biosimilar – A product approved as an alternative to an FDA-approved biologic product based on its similarities and meeting standards for interchangeability, with no clinically meaningful differences between the two. The first FDA-approved biosimilar is filgrastim sndz (Zarxio), approved in 2015.

Bispecific antibodies – Bispecific antibodies are an innovative type of immunotherapy used to treat cancers. They are engineered to bind to two different antigens simultaneously, which

enhances the immune system's ability to target and destroy cancer cells. One part of the antibody binds to an antigen on the cancer cell, while the other part binds to an antigen on an immune cell, such as a T cell. This brings the cancer cell and the immune cell into close proximity, facilitating the immune cell's ability to attack and kill the cancer cell.

Cancer cells – Cells with damaged DNA that causes mutations in normal cell growth and division. New cancer cells grow uncontrollably, and old cancer cells don't die when they should, resulting in a malignant tumour or cancer.

***CAR T cells** – A type of treatment in which a patient's T cells (a type of immune system cell) are engineered in the laboratory so they will attack cancer cells. T cells are taken from a patient's blood. Then the gene for a special receptor that binds to a certain protein on the patient's cancer cells is added in the laboratory. The special receptor is called a chimeric antigen receptor (CAR). Large numbers of the CAR T cells are grown in the laboratory and given to the patient by infusion. CAR T-cell therapy is being studied in the treatment of some types of cancer. Also called chimeric antigen receptor T-cell therapy.

Cluster of differentiation - The cluster of differentiation (CD) designation refers to cell surface proteins. Each unique molecule is assigned a different number designation, which allows identification of cell phenotypes.

***Combination Immunotherapy** – Therapy that combines more than one method of immunotherapy-based treatment. Also called multimodality therapy and multimodality treatment.

Co-stimulatory signal – The second stimulation required for T-cells to become fully activated (also called Signal 2).

CTLA-4 (cytotoxic T lymphocyte associated antigen 4) – A protein receptor found on the surface of T-cells. This protein is part of the CTLA-4 checkpoint pathway, which can shut down an immune system response in its early stages. Certain cancer cells have the ability to turn on this checkpoint, which stops the immune response against the cancer cells.

Cytokines – Proteins released by immune cells to communicate with other immune cells. Certain cytokines, such as interferon and interleukin, help regulate specific immune system functions.

Dendritic cell (DC) – A type of antigen-presenting cell responsible for processing antigen material and presenting it to the T-cells and B-cells for activation. DCs also are able to help regulate other immune cells.

Double-negative T cells – These are a type of immune cell that lack two of the usual surface markers (CD4 and CD8) found on most T cells.

Downregulation – Reducing either the overall immune system response or the specific responses of certain immune cells.

Epithelial - Refers to the cells that line the internal and external surfaces of the body.

***Epitope/Neo-**epitope – An epitope is one small part of a molecule that an antibody will recognize and bind to. A neo-epitope is an epitope that arises from a changed or mutated host antigen.

***Exosome** – A tiny sac-like structure that is formed inside a cell and contains some of the cell's proteins, DNA, and RNA. Exosomes get released into the blood by many types of cells, including cancer cells, and travel through the blood to other parts of the body. They are able to transfer the proteins, DNA, and RNA they contain into other cells. Exosomes may play a role in the spread of cancer and may also keep immune cells from killing cancer cells. They are being studied in the laboratory to help develop new ways of diagnosing and treating cancer, including preventing the spread of cancer cells in the body.

Granulocyte-macrophage colony stimulating factor (GM-CSF) – A protein responsible for stimulating bone marrow and promoting the growth of immune cells, especially dendritic cells. GM-CSF is currently used to restore white blood cells that have been depleted in people receiving chemotherapy and is being used and studied as a treatment boost when combined with other immunotherapies.

Immune cells – The cells of the immune system involved in defending the body against infectious disease, foreign invaders, and cancer cells.
Immune checkpoint inhibitors – Drugs that block the activation of specific immune checkpoint pathways. These drugs allow the immune system to 'take the brakes off,' which allows the immune system to recognize and attack cancer cells.

Immune checkpoint pathways – The system of checks and balances in place to prevent overactivation of the immune system. Different pathways function at different stages of the immune response to help regulate the length and intensity of T-cell activity; turning on an immune checkpoint typically results in shutting down the immune system response.

Immunosuppression – A condition in which the immune system is prevented from launching successful attacks to protect the body against infection and disease.
Immunotherapy – A type of cancer treatment that focuses on using the body's own immune system to fight cancer.

Immune-related adverse events (IRAEs) – Auto- immune reactions that occur as a result of boosting the immune system. Severe reactions may include colitis, dermatitis, and hepatitis.
Interferon – A protein released by immune cells that helps regulate different immune cell activity; types of interferon include alpha, beta, gamma, and lambda. Different types help regulate different functions, including prompting increased T-cell activity, stimulating natural

killer cells, or affecting certain cell functions that influence tumour cell growth. Laboratory-made versions of the IFN-alpha protein are currently FDA-approved to treat certain types of cancer.

Interleukin – A protein produced by cells of the immune system that helps regulate the production of certain immune cells, how they function during an immune response and their production of cytokines. The laboratory-made version of this protein, aldesleukin (Proleukin), is currently FDA-approved to treat metastatic melanoma and metastatic renal cell carcinoma (kidney cancer).

In-vivo – (Meaning: Within the living) An experiment that is done in-vivo is done in the body of a living organism.

In-vitro – (Meaning: In Glass): Outside the body or in laboratory. An experiment that is done in-vitro is done outside of the normal biological context.
Ligands – Protein molecules on the surface of a cell that bind to the receptor on the surface of another cell. Most ligands are signal-triggering molecules, which means they send out immune cell signals when engaged by a receptor. These signals help to regulate specific immune system functions.

***Lymphatic system** – The tissues and organs that produce, store, and carry white blood cells that fight infections and other diseases. This system includes the bone marrow, spleen, thymus, lymph nodes, and lymphatic vessels (a network of thin tubes that carry lymph and white blood cells). Lymphatic vessels branch, like blood vessels, into all the tissues of the body. Also called lymph system.

***Lymphocyte** – A type of immune cell that is made in the bone marrow and is found in the blood and in lymph tissue. The two main types of lymphocytes are B lymphocytes and T lymphocytes. B lymphocytes make antibodies, and T lymphocytes can help kill tumour cells and help control immune responses. A lymphocyte is a type of white blood cell.

***Lymph node** – A small bean-shaped structure that is part of the body's immune system. Lymph nodes filter substances that travel through the lymphatic fluid, and they contain lymphocytes (white blood cells) that help the body fight infection and disease. There are hundreds of lymph nodes found throughout the body. They are connected to one another by lymph vessels. Clusters of lymph nodes are found in the neck, axilla (underarm), chest, abdomen, and groin. For example, there are about 20-40 lymph nodes in the axilla. Also called lymph gland.

***Lysis** - In biology, lysis refers to the breakdown of a cell caused by damage to its plasma (outer) membrane. It can be caused by chemical or physical means, or by infection with a strain virus that can lyse cells.

Major histocompatibility complex (MHC) – A set of proteins on the surface of certain immune cells that influence the interaction of normal cells with immune cells. Antigen-presenting cells present digested antigens to T-cells through the MHC on their surface, which allows the T-cells to "see" the antigen and recognize it as foreign. The connection between the MHC and the receptor on the T-cell is the first signal (Signal 1) necessary to activate the T-cell to respond to a tumour and destroy it.

***Macrophage** - A type of white blood cell that surrounds and kills microorganisms, removes dead cells, and stimulates the action of other immune system cells.

Memory cells – T-cells and B-cells from a specific immune reaction that continue to circulate in the body even after the infection is resolved. They "remember" specific antigens and can multiple rapidly upon subsequent exposure, creating an immediate immune response already trained to eliminate the threat.

Microbiome - The microbiome is the community of microorganisms (such as fungi, bacteria and viruses) that exists in a particular environment. In humans, the term is often used to describe the microorganisms that live in or on a particular part of the body, such as the skin or gastrointestinal tract.

Minor histocompatibility antigens – These are small molecules on the surface of cells that can trigger an immune response. They are important in organ transplants and some cancer treatments because the immune system might recognize them as foreign and attack them.

Monoclonal antibodies (mAbs) – Antibodies made in a laboratory that are designed to target specific parts of cancer cells, which may include certain proteins or molecules on the surface of the cancer cells; they are meant to stimulate an immune response in the same way as naturally produced antibodies do.

***Nanoparticle** - A particle of that is smaller than 100 nanometers (one-billionth of a meter). In medicine, nanoparticles can be used to carry antibodies, drugs, imaging agents, or other substances to certain parts of the body. Nanoparticles are being studied in the detection, diagnosis, and treatment of cancer, often in the form of lipid nanoparticles.

Natural killer cells (NK Cells) – White blood cells that contain enzymes that kill virally infected cells and tumour cells. They also communicate with T-cells to help regulate their development and response.

Oncolytic virus – A virus that can infect and multiply within cancer cells, leading them to die. These viruses may be manufactured or naturally occurring and can be used to target and destroy specific tumour cells. They may also induce an immune response.

PD-1 (programmed cell death-1) – The receptor in the PD-1 checkpoint pathway that sends negative signals to the T-cell when it connects to a PD-1 or PD-2 ligand (PD-L1 or PD-L2). These

negative signals normally slow down or stop the immune response when it's no longer necessary. Certain cancer cells have the ability to influence the engagement of this checkpoint, which puts the brakes on the immune response.

***Phase I Clinical Trial** - The first step in testing a new treatment in humans. A phase I study tests the safety, side effects, best dose, and timing of a new treatment. It may also test the best way to give a new treatment (for example, by mouth, infusion into a vein, or injection) and how the treatment affects the body. The dose is usually increased a little at a time in order to find the highest dose that does not cause harmful side effects. Phase I clinical trials usually include only a small number of patients who have not been helped by other treatments. Sometimes they include healthy volunteers.

***Phase 2 Clinical Trial** - A study that tests whether a new treatment works for a certain type of cancer or other disease (for example, whether it shrinks a tumour or improves blood test results). Phase II clinical trials may also provide more information about the safety of the new treatment and how the treatment affects the body.

***Phase 3 Clinical Trial** - A study that tests the safety and how well a new treatment works compared with a standard treatment. For example, phase III clinical trials may compare which group of patients has better survival rates or fewer side effects. In most cases, treatments move into phase III trials only after they meet the goals of phase I and II trials. Phase III clinical trials may include hundreds of people.
Proliferation – Cell division and development (growth).

Receptors (immune receptors) – Proteins on the surface of immune cells that bind to ligands on the surface of other immune cells. This connection typically results in immune cell signaling that regulates specific immune system functions.

Regulatory T-cells – T-cells that help maintain the necessity, strength and duration of an immune response by regulating T-cell activity. They shut down the other T-cells at the end of an immune reaction. Certain tumour cells have the ability to increase regulatory T-cell activity, which decreases the overall immune response.

Signal 1, Signal 2 – The primary and secondary cell signals necessary for the immune system to activate. Signal 1 is the interaction between the antigen-presenting cell and the T-cell through a connection between the major histocompatibility complex (MHC) and a T-cell receptor. Signal 2 can be any number of connections formed by the molecules and receptors on the surfaces of both the antigen-presenting cell and the T-cell.

Standard of care – A treatment regimen that is accepted by medical experts and is widely used as a treatment for a specific type of cancer. This can also be called best practice, standard medical care, and standard therapy.

T cells – Immune cells that recognize specific antigens during antigen presentation. T-cells are the major players in the immune system's fight against cancer. Their activation and activity are two of the main focuses in immunotherapy research.

T cell receptors (TCRs) – Molecules found only on the surface of T-cells. TCRs must bind to special molecules on the surface of antigen-presenting cells before they can receive information about a threat. This connection is the first signal (Signal 1) necessary to activate the T-cell to respond to the tumour.

Targeted Therapy – Targeted therapy for involves using drugs designed to specifically target and interfere with molecules that are involved in the growth, progression, and spread of cancer cells. Targeted therapies work by identifying and attacking specific proteins or genes that are unique to cancer cells. This helps to minimize damage to normal, healthy cells.

***Tumour Infiltrating Lymphocyte** – A type of immune cell that has moved from the blood into a tumour cell. Tumour infiltrating lymphocytes are thought to be a sign that the immune system is trying to attack the cancer. In cancer therapy, tumour infiltrating lymphocytes are removed from a patient's tumour, then treated in the laboratory with substances that make them grow and turn into cells that can kill the patient's cancer cells. Large numbers of these activated lymphocytes are then reinfused into the patient to help the immune system fight cancer. Also called TIL.

Tumour microenvironment – The area surrounding a tumour, inside which normal cells, molecules and blood vessels help sustain the tumour. The microenvironment contributes to the behavior, proliferation and spread of the tumour; the tumour itself is capable of affecting its own microenvironment.

Upregulate – Increase either the overall immune system response or the specific responses of certain immune cells.