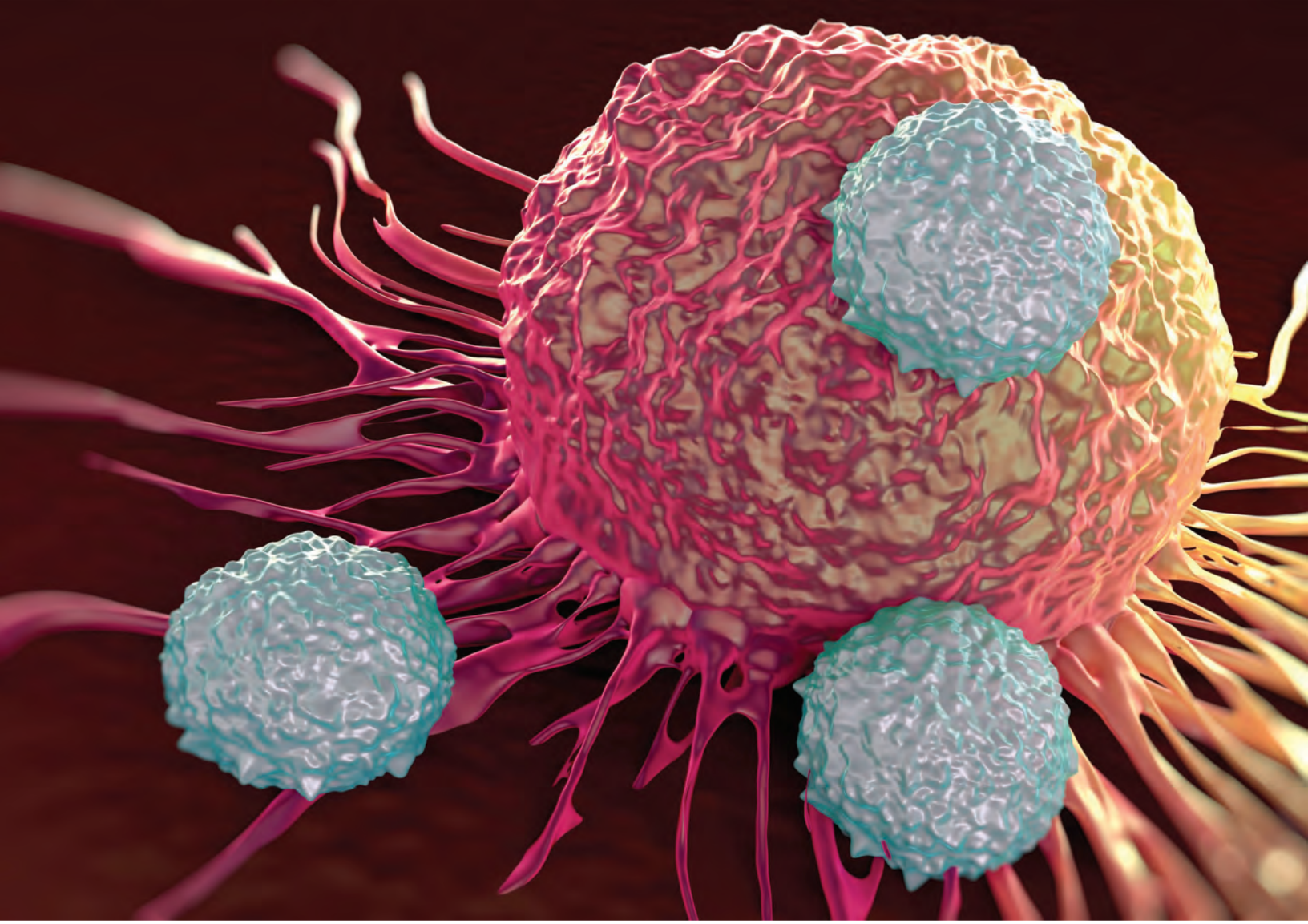

CIHR IRSC

Human Immunology Consensus Workshop

November 25th and 26th 2014
Sheraton Toronto Airport Hotel
& Conference Centre, Toronto, On

Canadian Institutes of Health Research
Institute of Infection and Immunity

Canadian Institutes of Health Research
Instituts de recherche en santé du Canada

Canada

Written by: Isabelle Létourneau, PhD
Creative Design by: Service de graphisme
du CHU de Québec

Canadian Institutes of Health Research
160 Elgin Street, Room 97
Address Locator 4809A
Ottawa, ON K1A 0W9

CIHR Institute of Infection and Immunity
Centre de recherche du CHU de Québec
CHUL – Room TR-62
2705, Laurier Blvd
Québec, QC G1V 4G2
Phone: 418-577-4688
Fax: 418-577-4689
www.cihr.gc.ca

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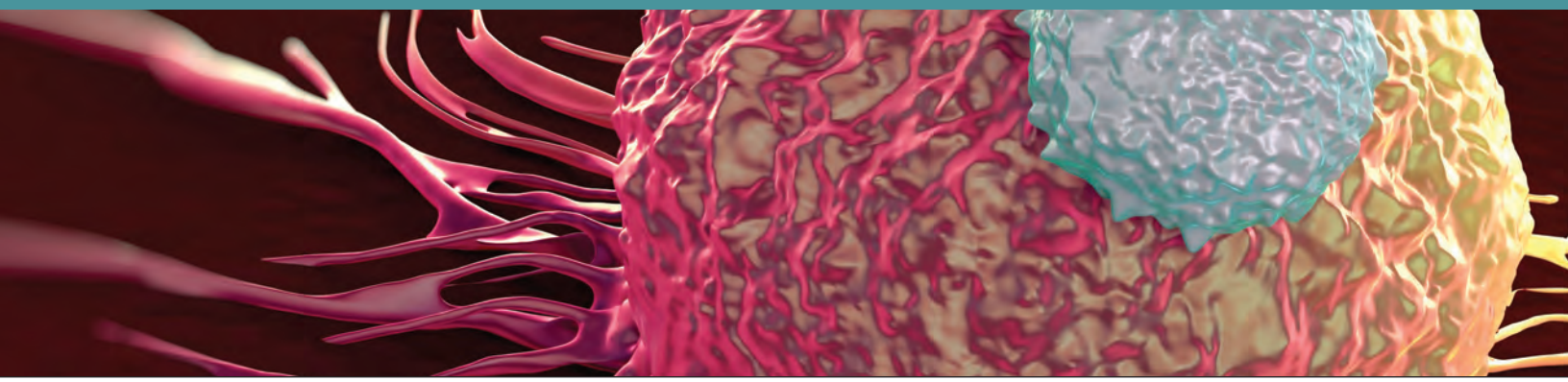

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Executive summary

Background

The Canadian Institute of Health Research (CIHR), Canada's premier health research funding agency, is comprised of 13 virtual Institutes – one of which is the Institute of Infection and Immunity (III). In 2010, the Institute's Advisory Board identified human immunology as a field in which strategic investment could have a significant impact in terms of knowledge and clinical outcomes. The lion's share of our knowledge in immunology comes from research with mice models, but current thinking suggests that the murine and human immune systems are often very different. Major advancements are therefore needed to understand human immune-related disease and immune therapy. These would open the door to more pointed questions and various applications of this research, which would undoubtedly have a positive impact on the health of Canadians.

Consultation workshop

A consultation workshop was held to inform III and partner Institutes how best to strategically invest in human immunology research in Canada. Seventy-five participants represented research, research management and support or the pharmaceutical industry from across Canada, and included 2 International participants. The goals of the workshop were to stimulate discussion among the community; identify their needs; and hear from experts in human immunology on their work and perspectives regarding the state of research in terms of needs for moving forward. The workshop provided a forum to gather recommendations on how best to address current challenges, respond to the needs of the research community and have a positive impact on the health of Canadians.

The consultation workshop took place on November 25th and 26th, 2014 in Toronto at the Sheraton Toronto Airport Hotel & Conference Centre. Many participants noted that the human immunology community rarely had the opportunity to exchange given their tendency to work more with the research community of a particular disease rather than the physiological system that they study.

Outcomes and recommendations

A number of key recurrent ideas emerging from the workshop discussions are summarized as follows:

- The human immunology community would benefit from increased interaction/collaboration/communication between the different areas within the field, offsetting the 'working in silos' effect.
- It is critical that the issue of standardization be addressed in the funding initiative given that currently a lack of standardization regarding procedures is seen as a substantial barrier to advancing the field (e.g. reproducing data between laboratories).
- To be sustainable with acquiring funding, there needs to be significant success and progress over a short time-line (5 years) and therefore the community needs to be strategic such as building on current knowledge, focussing on cohorts, biobanks and linking with existing resources.
- Basic knowledge remains to be acquired – understanding the healthy functioning of the human immune system. Research needs to be translational and applied to improve human health.
- Participants from different areas explored both commonalities and differences among diseases and populations.
- Concerns were expressed regarding the potential for a CIHR initiative to hamper optimal team building should the initiative be too prescriptive as well as from the non-human researchers regarding the possibility of being marginalized.

- The funding should also be oriented toward clinically relevant problems; to understand the mechanisms of diseases, methods of patient stratification (biomarkers or age/sex and ethnicity), and mechanisms of action of the therapeutics, and development of new therapeutics.
- Need to increase the capacity of the community to attract and train future researchers.

Path forward

In collaboration with partners, III will explore which programs and models would be most effective in having the most potential impact within the human immunology field. There are several options available including funding based on a multidisciplinary team approach or the formation of one large or several smaller networks. The path forward definitely requires collaboration among the various funded laboratories to ensure exchange on standardization and the exclusion of funding individual laboratories without an upper governance structure. It is hoped that this workshop will have prepared the human immunology community for this collaboration.

Background

A lot of our knowledge in the field of immunity comes from experiments conducted with cells and mice. The genetically modified mice created a perfect model to try to understand the role of all molecules and cells involved in immune system activity. However, the mice model does not always reflect what happens in the human body. More studies are required to understand how the human immune system functions in health and disease. The better we understand this, the better we can hope to modulate its function to treat or cure immune-related diseases, and also to modulate it to treat non-immune related diseases such as cancer.

Immune related disease can touch every single organ in the body. It can be relatively common, such as rheumatoid arthritis, or rare such as pemphigus. Severity can also vary according to the organ or function affected. The level of knowledge and understanding as well as the availability of treatment also varies considerably between diseases.

For a long time we used the vaccine to teach the immune system to recognize pathogens and protect us from diseases. More recently, immune therapy has made several major advancements – including in the treatment of cancer. Another fast developing area, is the discovery and use of biologics in the treatment of various immune conditions. In 2014, of the top 25 best selling drugs, 10 were biologics[1]. The conditions targeted with biologics are diverse and not limited to immune mediated diseases as some of them are used for cancer treatment.

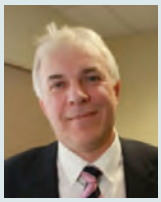
The Institute of Infection and Immunity and his partners would like to put in place an initiative to promote research in the field of human immunology in Canada.

1 See The Top 25 Best-Selling Drug of 2014, Genetic Engineering & Biotechnology News, Feb 23, 2015

Workshop Steering Committee

A steering committee, comprised of researchers reflecting the different health research themes of the Institute and fields of human immunology research, worked with III staff to organize the workshop.


Megan Levings
Chair


Anthony Jevnikar
Vice Chair


Jonathan Bramson


Kent HayGlass


Robert Holt


Joaquin Madrenas


Rae Yeung

Workshop objectives

The consultation workshop in human immunology had the following objectives :

- Provide an overview of the Canadian human immunology field, identifying current challenges and opportunities;
- Identify key research areas that are not being adequately addressed through existing funding sources and mechanisms;
- Propose recommendations to III staff and the expert steering committee on the scope and range of potential strategic research initiatives that would enhance research in human immunology;
- Improve dialogue, networking and communication across diverse research groups and pillars involved in human immunology research;
- Identify opportunities to leverage existing programs and resources;
- Generate a workshop report describing the conclusions and recommended directions to support research in human immunology in Canada.

Roundtable Discussions

The participants were assigned to a table to ensure geographical and area of interest diversity at each table. For each table a note taker was assigned to compile the different comments. At the end of each roundtable sessions, a period was allowed to report to the whole group. Notes of those reporting-back sessions were also compiled and used to produce this report.

Dr. Ellis Reinherz

Dr. Ellis Reinherz is the chair of the Human Immunology Project Consortium (HIPC)[2] that was established in 2010 by the National Institute of Allergy and Infectious Disease (NIAID) Division of Allergy, Immunology and Transplantation of the National Institute of Health (NIH) of the United States. The goal of HIPC is to foster collaboration in standardizing data and establishing quality criteria for inclusion/exclusion of data in their comprehensive, centralized database. The scientific goals of the program also include defining profiles or fingerprints of both steady-state and activated human immune system. The centralized knowledge base and resource database for the scientific community will facilitate investigation of human immunity and develop novel applications for human disease. This will allow the study of the perturbation of the steady state by infection, vaccination or adjuvant administration. To achieve their goals, the human transcriptome and proteome will be studied. The program included $100 M plus a $20M for infrastructure and pilot projects. HIPC is divided in three subcommittees: Samples & Assays, Biostatistics & Bioinformatics and Clinical research. The research projects evaluate the response to vaccines (influenza, Hepatitis B, pneumococcal polysaccharide, varicella zoster and malaria) and infections (varicella zoster, malaria and west Nile virus). The cohort in these studies have no restrictions and include infant, adult elderly twins, healthy and sick individuals (affected with immune disorders). The project uses several technologies, and also develops new tools and analytic approaches. The HIPC website shares new tools with application to clinical activities. Since 2010, HIPC research teams have published 74 publications and the HIPC infrastructure operating fund is supporting a clinical trial on the system biology of influenza A vaccine.

Dr. Reinherz also presented other organisations working in human immunology: the Center for Human Immunology Inflammation (CHII) which is a cooperative enterprise which includes several NIH institutions which focus on human immunology in normal and pathologic conditions (autoimmunity, inflammation in cancer, athero-sclerosis and neurologic degeneration); the Singapore Immunology Network (SIgN) whose scientific mission is to investigate the complexity of the human immune system with the aim to study immune regulation in physiological conditions and during infection and inflammation (including cancer); the Center for Human Immunology from France, whose goal is to deliver new validated clinical concepts focusing on developing technology platforms to support translational research, develop an interdisciplinary human immunology program and to partner with industry to translate discoveries into clinical practice; and the Advanced Immunization Technologies (ADITEC) which regroup 13 European countries aiming to accelerate the development of novel and powerful immunisation technologies for the next generation of vaccines.

Dr. Ola Winqvist

Dr. Ola Winqvist is an immunologist performing clinical research and the vice-chair of the European Network for Translational Immunology Research and Education (ENTIRE)[3]. There are two trends in human immunology, the personalized medicine and the multiplex analysis. The ENTIRE network is interested in moving research and knowledge from immunomonitoring to personalised immunotherapy. ENTIRE focuses on immune mediated disease (IMID), which covers more than 80 distinct diseases including allergies, rheumatoid arthritis, Crohn's disease and multiple sclerosis.

The ENTIRE group is working with a €100K-150K envelope for travel and meeting costs, allowing the research group to meet. ENTIRE funding does not cover direct research costs but promotes the development of networks to the end of becoming competitive in funding competitions. ENTIRE

2 See http://www.immuneprofiling.org/hipc/page/show

3 See http://entire-net.eu/

is open to all countries and thus far 11 centers throughout Europe are participating and 7 others have applied to join.

The primary objective of this Network is to define the immunotype of healthy individuals and IMID patients before, during and after immunomodulation treatment. Secondary objectives include:

- Identify and define the different aspects of immune function that are relevant to IMIDs and establish a minimal set of functional tests to evaluate each immunotype.
- Develop, standardise, and/or validate the panel of tests.
- Define the alterations of the immunotype in different IMIDs in comparison with a large cohort of healthy individuals by using such panels.
- Assess the impact of targeted immuno-modulation on the immunotype across different IMIDs and apply the immunotyping in joint proof-of-concept clinical trials with new targeted therapies in different IMID populations.
- Build a strong and large network of leading European centres in the field of translational immunology which develops guidelines for immunomonitoring and provides advice to regulatory authorities and pharmaceutical companies.
- Train a new generation of young physicians and researchers in translational and interventional immunology in the context of personalized medicine for IMIDs.

Dr. Winqvist presented some of the challenges facing the field of human immunology. He spoke of the difference between academic and clinical analysis. For example, in academia, samples are often frozen before being analysed while this is not the case in the clinical setting. To address this issue, a working group is targeting standardization of panels for clinical human whole blood immunophenotyping, method(s) of immunophenotyping, data collection and analysis; and allowing aggregation of data from many centers for biomarkers of disease, aging, monitoring of immunomodulatory therapies etc. The Standard Operating Procedures (SOPs) and panels are continually updated and can be found on the ENTIRE website.

A subgroup is trying to establish the boundaries of a healthy immune system by immunotyping a large cohort of healthy individuals including sex and age aspects. IMID patient cohorts are also immunotyped and compared (sex and age are also included). These studies will allow to further answer questions relating to immunomodulation: How does immunomodulation affect the immunotype? Can immunotype predict response to therapy? Can the immunotype define biological remission?

Other working groups are responsible for the web-based platform, the education and outreach activities, the publication of SOPs and for the management of high throughput experiments and clinical data; and for training and education by involving senior researchers in reviews and teaching of master level classes, promoting short-term visits by junior fellows for learning techniques, and web-based educational activities and; for networking and outreach activities including the coordination of interactions with other research programs and EU consortia, organizations in clinical immunology, the pharmaceutical industry and regulatory authorities.

Dr. Winqvist also described the strengths and challenges of the ENTIRE network. Strengths include the development of the Federation of Clinical Immunology Societies (FOCIS)[4] for the active exchange of ideas through meetings and a training school. Moreover, ENTIRE is not publication driven. Challenges include addition of centers with various foci into the process, limited funding and activities taking longer than expected.

4 see http://www.focisnet.org/

THEME 1

Transformational Therapeutics and Diagnostics

Dr. Pam Ohashi presented the *Prime Time for Cancer Immune Therapy: The Canadian Landscape*. In 2013, Science magazine declared cancer immunotherapy the breakthrough of the year. At this point, immunotherapy is targeting inhibitory molecules. For example, 2 monoclonal antibody to bloc PD-1 are approved by the Food and Drug Administration in the US and have been shown to work for a variety of cancers. The key strategies in immune therapy include the checkpoint blockage and the chimeric antigen receptors. There is also the adoptive T cell therapy based on tumour infiltrating lymphocyte that is gaining interest across the world. Other strategies under development include the transduction of tumor specific T cell receptor and the vaccine approach. These techniques are designed for patients that do not respond to checkpoint blockage, or relapse after such treatment and patients that have many tumor sites. Finally the last strategy presented is to target the tumor itself to prevent it from escaping from the immune system. She concluded by mentioning that across Canada, several research centers are conducting immunotherapy studies for cancer using several strategies and there is a growing network and collaborations between these groups.

Dr. Scott Tebbut presented *Biomarkers: the road from discovery to implementation*. He is the chief scientific officer of the Prevention of Organ Failure (PROOF) Centre of Excellence which assists in the development of several biomarkers in transplant, lung disease (chronic obstructive pulmonary disease), heart failure, and kidney disease. He described the process from the identification of the clinical question and the clinical need to the identification of biomarker candidates, their validation and their use in the clinic. He emphasized that in the discovery of biomarkers, patients have to be considered as partners, but several other partners are also essential: data analytics, clinical expertise, intellectual property and regulation, and health economics. The clinical question that biomarkers try to answer should also assess the need of a biomarker in that particular situation. Using omics data along with biomarker algorithms and combinatorial algorithms, and targeting a specific tissue can add to the robustness and performance of the biomarker. However, most of the projects fail in the transition from the validation in a small patient population to testing in a larger patient population as researchers tend to underestimate the expertise, time and equipment necessary to successfully complete these last steps which fall beyond traditional research but which are critical to evolve/improve patient care.

Through his presentation, **Dr. Jan Dutz** addresses innovation in the use of biologics to treat autoimmunity. In the case of chronic plaque psoriasis, TNF-α inhibition achieved a higher response than acting on T-cell depletion or T-cell migration. Deregulation of IL-17 inhibitor showed a downregulation of IL-17. The other approach is to block IL-17, however trials demonstrated off-target effects. Following administration of TNF inhibitors, there has been report of cutaneous side effect as well as hypotension, hypertension and palpitation. Inhibition of TNF increases the expression of interferon α, explaining why eczema is a common side effect of skin therapy. The production of defensin, a natural antibiotic produced by the polymorphonuclear and epithelial cell, is also decreased by treatment with TNF inhibitors. Patients also develop long term tolerance to the TNF inhibitors. At this point, the problems with biologics are the off-target side effects, the need for continuous therapy and the gradual loss of efficacy. Some of the solutions proposed include, Treg generation and low dose IL-2 therapy.

The participants were then asked to address the 4 following questions regarding the therapeutics and diagnostics.

- *What therapeutic approaches are close to clinical testing? Of these which ones would have the biggest impact?*
- *Are there opportunities to test current/emerging immune therapies in new indications and/or patient populations?*
- *What diagnostic/patient stratification methods have the greatest potential to advance diagnosis/ treatment of immunological diseases?*
- *Are there immunological diseases for which Canada is uniquely poised to have a significant research impact?*

The following paragraphs summarize the round-table discussion. The group felt that is was too premature at this point to identify the most promising and impactful therapeutic approaches and that the topic of human immunology is so diverse that different answers would emerge depending on the interest of each participant. The following therapeutic approaches were listed, with reserve: immunotherapy, immunotolerogenic therapy, vaccination and Treg cell expansion. It was also suggested to look at the following different aspects related to drug treatment: repurposing drugs; tolerance; side effects and drug responses; immune response upon vaccination; and also, building on our strengths by combining new biologics with already commercialized drugs in order to enhance their effectiveness. Other suggestions regarding areas of interest were: diagnostics, prognostics, predisposition and family related risks.

Little is known on the normal immune system and on the maintenance of health. Understanding the variation in immune activity/response and disease susceptibility through different age groups (pediatric and elderly) and between sexes was also of interest. This should be expanded in order to better understand diseases and performing the patient phenotyping. It was also suggested that a better understanding of the disease is required in order to find treatment. Advantages of monogenic deficiency should be taken into consideration in understanding the role of each key element of the human immune system, as well as identifying the genetic cause of the autoimmune disease. The role of the environment in the modulation of the immune system and in triggering immune related disease was also mentioned as an area of interest. The immune response also needs to be better monitored through the various treatments (e.g. joint replacement) and this could provide information about its modulation. The researchers present suggested defining a standardized immune score that could be used to report observations between the different research teams.

The regulation of the immune system depends on the individual to be treated; therefore immune therapies are likely to become personalized. Blood analysis is a good way to acquire information on the individual's immune system activity. However, there may be discrepancies between what is seen in the blood and what is seen in the affected organs, therefore access to solid organ samples is also important and can be a challenge, a point which will be addressed in greater detail later.

There might be some commonalities and knowledge that could be shared between disciplines. It has often been mentioned that the approaches used in cancer immunotherapy are the opposite of what is required to treat inflammatory diseases. Researchers could also learn from each other about tolerance and side effects from specific agents. The creation of a matrix of the different molecular and cellular targets across the different diseases could be a way of introducing collaboration between research groups and could include the expertise already present in HIV and cancer therapies. This could enable repositioning some drugs and therapies.

The immune-related conditions are too diverse to identify diagnostics/patient stratification. However, it was mentioned that the actual biomarkers are not effective in patients over 65 and that biomarkers should not be the only tool used to decide who would benefit from treatment, but could help to better design clinical trial and select patients for them. At the same time, research in patient stratification can apply to different

diseases and could be an area of collaboration. Several approaches got enumerated such as the genome analysis, single cell analysis, microbiome interaction, phenotype definition, establishment of a panel of biomarkers.

A unique aspect of Canada is its remote population and their unmet needs as well as the presence of various immigrant populations. On the other hand, Canada also has some unique homogeneous populations that can be studied as well.

THEME 2

Barriers and Opportunities

This section began with a presentation from **Dr. Quim Madrenas**, director of the CIHR Human Immunology Network (CHIN), funded by CIHR since July 2011 under the Network Catalyst Program. While not a funding network, its main role is knowledge dissemination and translation and the promotion of human immunology research. The initial nodes were based on the FOCIS centres of excellent and national centre of excellence (NCE) and since, others have joined. CHIN has been successful at developing national and international activities of knowledge dissemination in human immunology through the creation of Centres of human immunology in institutions, the organisation of seminars, workshops, symposia (local, national and collaboration with internal), Café Scientifique and the promotion of Canadian investigators. It has also been successful at engaging national and international human immunology stakeholder in promoting research in human immunology, including leveraging funds at the institutional level. CHIN was also aiming to be a source of standardized protocols for human immunology research. However, the lack of funding did not allow it to complete this task. Also no agreement has been achieved on the value of standardized regulatory protocols. CHIN also aims to facilitate access to research material and technologies. The later has been difficult to achieve beyond each individual centre. The challenges that CHIN has faced include: lack of funding to become a research network, lack of consensus, difficulties in establishing transdisciplinary collaboration, attracting and sustaining trainees in human immunology, difficulties with peer review of human immunology output, and sustainability beyond the 3 years of funding. CHIN has shown to be more successful in knowledge dissemination rather than knowledge generation.

Dr. Kent HayGlass presented *Dating Tips: Practical Strategies to Build Multidisciplinary Collaborations that Work*. The main research community includes the lab-based researcher, the clinical-based researcher and clinician scientists and epidemiologists. According to Dr. HayGlass, some of the reasons why several interdisciplinary collaborations fail include: goal incompatibility among the different players, differing assumptions in the level of commitment on both sides, lack of definition of the different roles and expectations of each partner and interpersonal skills. Therefore, to ensure successful collaboration, there should be respect, time investment, good communication and making sure it is a win-win collaboration. For longer term collaboration, the long term goal should be identified and shared, carefully select the best suitable collaborator for the project, clearly define the role, expectation, responsibilities and limit of each partner, be honest about the expected outcome for each collaborator, define the plan of action, maintain ongoing communication, be financially transparent, provide credit to collaborator, and always show respect and gratitude.

The section concluded by a presentation on ethics, *Biobanking and cohort studies: the critical role of public engagement*, by **Dr. Michael Burgess**. He explained that ethicists are engaged in controversy. Engaging the public in the discussion and decision making demonstrates that we care about them. The process should include a diversity of the population because demographic origin and

personal experience will affect the perception of the public toward the discussion. Consulting with the public also allows the possibility of changing their perception of health care and research and demonstrates accountability for public funds. There are different ways to consult and engage the public: surveys collect superficial opinions; town hall events collect vested interests; focus groups do not produce group decisions and consultation often does not allow enough time to cover all the issues. The public that we consult should know enough about the question topics to have an opinion. Deliberation allows to focus on the decision once they understand deeply an issue. As part of the process include information and Q&A session before the actual deliberation. Dr. Burgess presented several biobanks that included public consultation which lead to revised guidelines, policies and practices, and the generation of community advisory boards. He concluded by mentioning that biobanks had a higher success rate when they took into account the input from the public, they can incorporate technical and societal information and contribute to decision making.

Presentations where then followed by roundtable discussions inspired by the following questions:

- *What barriers prevent/hinder human immunology research in Canada?*
- *What non-traditional collaborations need to be fostered to enable the discovery and development of cutting edge therapies and diagnostics?*
- *What training and mentoring is lacking in different fields to support growth in human immunology?*
- *What is the role of the public/patients in promoting and participating in human immunology research?*

Workshop participants mentioned that the term human immunology should be better defined. Does working with human samples equate to doing human immunology? Human immunology should be defined by the study of the immune mechanism in human health and disease.

Participants mentioned the difficulty in accessing human samples as well as the fact that human samples are rarely drug naïve as patients are often receiving drugs for diverse conditions. There is also need for longitudinal samples, a standardization of sample collection and the sustainability of cohorts and biobanks. Canadian Blood Service and Héma-Québec should be contacted to determine if they could provide blood samples and collaborate. To increase the access to samples, better integration and collaboration with clinicians is required. Clinicians should be encouraged and trained to participate in studies, provide samples when possible, as well as educate and involve patients as well as patient societies.

Working with human samples also leads to all the ethical questions regarding the collection and use of patient samples and clinical information. This challenge is increased when the work is carried out at multiple institutions as there are no guidelines for uniformity. It was suggested that ethics approval should also be standardized between the different institutions in order to facilitate the transfer of samples and data between the different research centers. Regarding the ethics questions related to the use of patient samples and data, the input of patients and citizens should be taken in consideration.

Health Canada (HC), as the regulator for the approval of new therapeutics and clinical trials, should be involved in providing guidance to research teams. The Public Health Agency of Canada (PHAC) could also be involved for their role in evaluative medicine. These collaborative relationships with Health Canada and PHAC would also have a positive impact on the sustainability of the field of human immunology.

Some participants believed that CIHR should limit its collaboration with the pharmaceutical industry in order to limit the cost of the new treatment once on the market. The new therapies presently on the market are not affordable and there exists a real need to find alternatives in the manufacturing process. Others, however,

believed that researchers can have a good exchange of information and support with the pharmaceutical industry resulting in advances in the field of human immunology as well as the promotion of commercialization of the discovery. Prevention should also be incorporated into the studies; however, this is not attractive to pharmaceutical companies and does not lead to commercialization of discovery.

Provinces should also be involved, through their funding agencies, but also because of the public health system. Researchers would like to take advantage of the Canadian public health system to follow up on the health status of patients. Furthermore, the healthcare system should be more involved in the research, through the various Networks of Centres of Excellence that are based in research centres affiliated with hospitals.

As mentioned earlier, the training of clinicians to participate in research projects could be improved. One way could be to increase funding for fellows to complete a training in research, and include the possibility of doing research rotations in their curriculum. The training of doctorate students regarding clinical/human immunology studies is also lacking according to the researchers present. The students are required to collect and publish results in order to complete their thesis, while human immunology studies last longer than a regular doctoral degree. Students and fellows should be more involved in clinical trials. To achieve a proper training, students and fellows should receive cross-disciplinary exposure during their training as well as an integration of clinical trial training.

Working with human samples and data will also generate an important database from which it could potentially be difficult to extract information. This will require well trained biostatisticians and bioinformaticians.

The public can also have a huge impact. The "Je suis Michèle" publicity, that had an impact on the budget decision for research funding in Québec, was referred to as an example of the power of the combination of researchers and public effort. This demonstrates that public awareness is important and can have a real impact. The public should be educated on hypothesis-based research, clinical trials and regulatory steps. They could become very good advocates and the research community would look more transparent. On the other hand, the public should also be informed on the outcomes of research such as via *Cafés Scientifiques*, lay abstracts from publications and other knowledge transfer activities.

THEME 3

Technology and Partnership

Dr. Felix Breden presented *Immune Repertoire Profiling*. He began by talking about antibody diversity. Because of different genes encoding different parts of the antibody, there is a possibility of 10^{13} different antibody sequences. The next generation sequencing is now allowing the mining of this information. Recently a high throughput sequencing of the zebrafish antibody repertoire and profiling T-cell receptor β chain was done. New technologies will also be beneficial for patients. For example, deep sequencing of T-lineage acute lymphoblastic leukemia/lymphoma showed a better sensitivity at detecting mixed residual disease than flow cytometry. New technologies can have multiple applications and can be used to screen natural repertoire and engineered libraries of antibodies, to identify a therapeutic antibody lead, to sequence T-cell receptor repertoire of T-cells associated with tumors in order to discover shared T-cell receptors between patients with the same type of cancer or to identify the T-cell repertoire in the synovium of patients with newly diagnosed rheumatoid arthritis. However, to use these data optimally, the immune response must be well understood to be able to predict and control its

behaviour. For example, to better understand the B-cell and T-cell response based upon a cellular subset requires animal modelling, markers to define the subset, sequencing technologies and an understanding of the germline variability and its effect on the naïve immune repertoire. The new technologies produce a lot of new data that need to be stored and analysed appropriately. The value of the data is also increased when patient data are included. To this end, several algorithms, analysis tools and databases have been developed. There is need now to train students in bioinformatics specifically to treat those immune repertoire data and to integrate the databases with biobanked samples.

Dr. Denis-Claude Roy then presented CellCAN and the cellular therapy which could be used for the treatment of a wide variety of disorders (i.e. cancer, infections, immune disorders, transplantation and regeneration of damaged tissues). It is expected to be the curative medicine of the 21st century as it will improve the patient survival and quality of life, reduce the economic burden of chronic diseases and provide new treatment for incurable diseases. The market for cell therapy is estimated to be $ 67.6 billion USD by 2020. CellCAN is a network that started in 2009 as the Stem Cell Network and became a Knowledge Mobilization Initiative Network funded by the Network Centres of Excellence in 2014. The goal of CellCAN is to disseminate appropriate, accurate and timely knowledge to enhance the development of regenerative cell therapy with the specific aims of making efficient use of capacity; manage and centralize regulatory issues; develop human resources; facilitate business development; enhance Canada's international position in clinical and translational research and to leverage investments and resources through partnerships. It also unifies different groups, including care providers, the scientific community, treatment centers, cell manufacturers and the population. CellCAN will make sure that the knowledge is shared between the knowledge producers, the knowledge users and the end users using the different media and technologies.

Dr. Jim Richards concluded this section with a presentation on Expertise, Facilities and Opportunities for Collaboration at the National Research Council (NRC) of Canada. He started by presenting the NRC which is a program-based research and technology organization with a mandate to stimulate sustainable domestic prosperity by providing innovation support, strategic research, scientific and technical services to develop and deploy solutions to meet Canada's current and future industrial and societal needs. NRC has a division on Human Health Therapeutics (HHT) which includes the Biologics and Vaccine Program. The program provides innovation support in developing biologics, vaccine and manufacturing processes, conducts strategic research and transfers assets and tools that offer solutions to the industry. This also helps projects in academia to reach Good manufacturing processes (GMP) facilities and eventually reach the market. The targeted area of HHT include (re)emerging infections, cancer and chronic diseases and provides different platforms such as glycoconjugates, animal models, adjuvants/biomarkers, bioprocessing/ manufacturing, immune monitoring, recombinant vectors and delivery, analytics and Virus-like particles (VLPs). NRC interacts with a wide variety of biopharmaceuticals industries, research centres and laboratories and can sometimes make the link between academic laboratories and industry. To the industry, NRC can provide advisory services, financial assistance and networking linkages. Dr. Richards concluded his presentation by mentioning that immunological assays need to be validated and kept as simple as possible to facilitate approval by the FDA and HC. Finally, he presented Biomarkers for Vaccine Immosafety (BioVacSafe), an initiative in Belgium, funded by the European Union.

The workshop participants had the opportunity to discuss topics related to partnership and technologies.

- *List major technological innovations that are, or are poised to, impact human immunology. Comment on how soon each is likely to be used in clinical applications*

- *What facilities are available in Canada that could be leveraged to advance human immunology?*
- *What unique areas of expertise in Canada could be leveraged to advance human immunology?*
- *Which key national and international partners (academic, government, NGO, private sector) need to be involved and how can they be engaged?*

Several imaging systems, such as new immunochemistry techniques and a mix of confocal microscopy and flow cytometry are more and more common in laboratories and allow visualizing multiple parameters within the same sample. The technological knowledge and infrastructures that were listed by the participants are the cyclotron, 30 colors flow cytometry, new immunohistology staining, cyTOF, and the presence in Canada of the world's largest germ-free animal facility. The recent technologies related to the next generation sequencing and the deep sequencing could also be useful to move the field of human immunology forward, but we should take into consideration what it could imply for the patient on the ethics and insurance fronts. It was also suggested that the technology used should remain as simple as possible in order to reduce the education and training that would be required, and also that there is a need for better and more rapid and sensitive functional analysis. The need to have standardized techniques was also discussed several times throughout the meeting. Several Canadian and International groups have started to write standard operating practices (SOP) that could be used. That was the case for the ENTIRE group in Europe. Collaboration with these groups would certainly facilitate the elaboration of standardization practices in human immunology in Canada.

We have good strength in virology (HIV, Hepatitis C, and influenza), autoimmune disorders, mucosal immunity, chronic inflammatory disorders and in metagenomics and epigenetics. Canadian researchers also have good expertise in clinical trials and we have several cohorts and clinical data. The presence of several Networks of Centres of Excellence (NCE) in the field of immunology is an indication of the Canadian strength in immunology: AllenGen, CanVac, and Canadian Arthritis Network. The Canadian Human Immunology Network (CHIN) is providing the human immunology community with some expertise in networking, communication and training.

Several groups brought up the availability of unique cohorts in Canada for which a lot of money and efforts have been invested: the Child birth cohort and the Longitudinal aging study. It was suggested to optimize the use of these cohorts. Investing in cohorts, biobanks and data sharing platforms could be a strategic investment for the research community. In order to foster communication between disease research areas there is a need for a common approach to collecting and analysing data. The collection of samples and data, processing and storage would however need to be standardized to allow proper collaboration between the different laboratories and disciplines. It is these large data banks that would likely attract industry collaboration.

There are several partners that could be involved in human immunology research, such as the NRC, CQDM, Centre for Drug Research and Development (CDRD) and the Genome centres. The Canadian Society of Allergy and Clinical Immunology should also be surveyed for their interest in participating in research activities. The patient organization should be real partners for this initiative as they give access to specific populations and can make the connection to the patient groups as well as having input on ethical questions brought up by working with human samples and data and setting privacy guidelines. Patients can be very good advocates if we educate them on scientific literacy and the regulatory environment.

Collaboration between academic researchers / government researchers / industry could be beneficial in studying the effect of the drugs, their mechanisms of action and their side effects.

THEME 4

Funding Mechanisms and Impact

Dr. Deborah Marshall presented *Measuring the value in personalized medicine*. The value of personalized medicine can be measured in terms of its efficacy, its cost and its preferences. Factors increasing the cost effectiveness of a personalized treatment are the relatively high frequency of the variant allele, the severity of the disease, a current poor monitoring of drug response, a strong association between the allele variant and the clinical outcomes, and the low cost of the personalized treatment and associated tests. The evaluation of the economics of personalized medicine include several issues such as: the exact question to answer; the characterisation of the population; identification of the comparators; evaluation of effectiveness; and outcomes to be measured. At this point there are lot of emerging tests that have not been evaluated for their value. Their performance strongly influences cost effectiveness. In real life the patient outcome is likely influenced by multiple genes, and each gene can influence multiple outcomes, which increases the complexity of the performance measurements. Another factor to consider in performance measurement are patient preferences, which will effect predicting utilization and value. In conclusion, building an evidence base that captures relevant data (health burden utilisation, clinical utility, health service impact, cost effectiveness, and preferences) is critical.

Dr. Lori West, Director of the Canadian National Transplant Research Program (CNTRP) explained to the audience how their network formed. Previous to CNTRP, there was very little integration between the solid organ transplant (SOT) and hematopoietic cell transplant (HCT) communities. The research community, together with CIHR and partners, suggested the creation of a clinically transformative national transplantation research network. CIHR launched in 2012 a funding opportunity to support a network meeting several criteria: combination of SOT, HCT and donation research, inclusion of at least 3 of the 4 CIHR pillars (Biomedical; Clinical; Health systems services; Social, cultural, environmental and population health), researchers from at least 5 provinces, 4 independent projects and a training plan, with an investment of $ 10 million for 5 years by CIHR and partners. CNTRP was launched in 2013, with sites across 9 provinces, 6 interrelated projects interacting with 3 cores (see below), 4 pillars, and reaching out to partners to achieve an investment of 23 million over 5 years. The program incorporated partnership with every organ donation organisation across Canada. CNTRP's goals are to increase availability of transplants, extend the longevity of grafts and, improve long term survival and quality of life of transplant patients. CNTRP provides nationwide structure to move from pre-clinical, to clinical research, to knowledge translation and commercialization. CNTRP also interact with patients, professional organisations and policy makers. The three cores include: an ethics, economics, legal and social platform; a research infrastructure and registries support platform; and an academic career development platform. CNTRP also gathers long-term outcomes data on CNTRP patients by linking with national and provincial registries. It also has a virtual repository that is responsible for the standardization of the collection and storage of the research samples and linking sample collections across CNTRP.

Helen Loughrey, from the partnership branch at CIHR presented *Collaboration with industry, what do they expect?* She started by mentioning that in order to have a successful collaboration with industry, the dialog between the partner needs to start early in the process. CIHR as developed a Partnership branch that can facilitate the process of discussion between these two parties, and link industry with academic laboratories. The risks and outcomes for academia and industry are different, with the innovative idea often coming from academia. An important point to consider is that the collaboration can bring success to both parties so that it becomes a win-win situation.

Finally, **Isabelle Létourneau**, Associate Strategic Initiatives at the Institute of Infection and Immunity and **Marilyn Desrosiers**, Deputy Director, Strategic

Initiative Branch, at CIHR briefly explained the *Design of a funding opportunity*. The first point to consider in the design of a new initiative is the goal and specific objective of the program that we want to create, whether it is to create more capacity in an area, create linkages between different fields of research, with industry or with international researchers, increase knowledge or to have research develop high risk-high economic return ideas. Once this is determined, we can start building an initiative that will include or exclude criteria to make sure that it corresponds the best to the desired funding opportunity that will serve the community. In addition to what we want to achieve now, the future also needs to be considered by determining where we want to be in 5-10 years and what success would look like in the field of interest. Training and knowledge translation also have to be considered when designing the initiative. In the case of this initiative in human immunology, defining success will also involve stakeholder and partners (CIHR Institutes, governmental and non-governmental organizations, pharmas and industries and other international funding agencies).

In the last roundtable, participants began exchanging on the following topics.

- *What funding mechanisms would best catalyze human immunology research? List the pros and cons of various options.*
- *What key partners are needed to enable different funding mechanisms?*
- *What outcomes would you expect in the short (3 years), medium (5 years) and long term (beyond 5) and how can they be measured?*
- *What are the "low hanging fruit" in human immunology*

The objectives of the initiative should be clearly stated - do we want to attain sustainability or do we want to solve a precise issue? If the initiative is disease-specific, it is easier to bring partners on board, especially NGOs and industry (pharmaceuticals). We also need to find overlapping interest with pharmaceutical companies to get them on board.

Sustainability is often a problem in funding research, the funding of strategic initiatives is intermittent. After the first 5 years of funding, the community should have progressed and obtained results to interest the public and the government enough to get additional funding. To do so, the results will need to be shared with the public, and therefore good knowledge transfer will be required.

The lengths of funding and progress assessment were also discussed. The same project should not be funded for a long period and there should be a constant evaluation of the impact in order to redirect the funding opportunities as needed to adjust to success and failure. For example, this is done by the German Competence Network and the NIH HIV initiative, in that funding is distributed in blocks every few years with assessments in between.

The capacity of the Canadian researchers to work in teams was highlighted as well as their capacity to be innovative with little money. In the short term, the workshop group believes that researchers have demonstrated that they can work together, through joint publications, joint training, networking between teams, and identification of common links between fields. They also hoped that an initiative in human immunology could promote interest in translational immunology.

A matrix system was suggested where the different teams share their skills and knowledge on phenotype and functional analysis with the other teams. To achieve this, the team(s) would need to meet more often than only once a year and have a lean overhead structure. Also, it was suggested that the team(s) should be built to be functional rather than prescriptive against the number of participants and orientation (pillar). Building teams around technologies (for example, infrastructure for studying immune cells in solid tissues) or themes (mucosal immunity, respirology) was proposed. A mix of common and rare diseases within a single team was also suggested so that the rare disease field can tap into the expertise of the more common disease area. However, the field of human immunology is really diverse and the formation of a unique network/team is not likely to be functional.

The need for standardization and the need for biobanks and cohorts has been a recurrent subject of discussion throughout the whole workshop. The investment required to standardize the laboratories and build patient cohorts would be considerable, more than 1 million a year for 5 years. Also, it was mentioned that funding for 4-5 years is a really short time frame to really achieve a translational goal, and that interventional projects can be very long. And in the case of building cohorts, there will be a need for a longer funding period to ensure longevity. Could the Canada Foundation for Innovation and CIHR collaborate to fund and support biobanks and core facilities?

The participants questioned whether having a catalyst grant would be beneficial to building stronger projects and teams. Some participants asked to be sure that the promotion of translational immunology through this initiative is not made to the disadvantage of the basic, animal and *in vitro* experimental system.

There is a possibility to team up with a consortium or networks that already exist in Canada (e.g. CANARIE), but also within Europe and the US. Europe is the preference, as they are working with budgets similar to ours.

In the long term, an initiative in human immunology should lead to commercialization (3-5 years), patient benefits (5-10 years) and finally reduction in healthcare costs (10-15 years).

Regarding training, the longer term goal is to increase interest in translational immunology and increase the number of fellows with proper training that will take part in the different projects.

Recommendations

What will be transformative is difficult to predict. If we want to be successful, we would need to work on something that we have already gained knowledge on rather than start something new. We are not at the stage of doing clinical trials yet, but we could build cohorts and biobanks, and this can be a short term low hanging fruit described by some. To be successful, we should also use what we have already available, such as tissue banks, and link it to this initiative.

The community of human immunology seems interested and ready to have a funding opportunity that will support them and offer them the opportunity to work together and exchange between different areas of the field. It was mentioned a few times that the normal healthy activity of the human immune system was not fully understood and should be further investigated, but the funding should also be oriented toward clinically relevant problems; to understand the mechanisms of diseases, methods of patient stratification (biomarkers or age/sex and ethnicity), and mechanisms of action of the therapeutics, and development of new therapeutics.

There is a need for a better standardization among the laboratories, which is at this time lacking and hindering collaboration between research groups.

Regrding the training of students, fellows and new researcher,there needs to be an increase in the capacity to attract, train and maintain research activity in this field in Canada.

Participants expressed their concerns for requirements that CIHR may impose on research team formation. Strict requirement (CIHR pillar representations, number of researchers, number of provinces represented) might force collaboration between researchers, without necessarily creating strong research teams. However, from the presentations, it was clear that all 4 CIHR pillars have an important role to play in human immunology research. Also, it is generally agreed that including patient perspectives would be an asset to research projects.

Participants list

Name and organization	Research interests
 **Gregorio Aversa** Senior Vice President Drug Development Centre for Drug Research and Development (CRDR) gaversa@cdrd.ca	CDRD is Canada's national, not-for-profit drug development and commercialization centre. Their mandate is to de-risk discoveries stemming from publicly funded research to create viable investment opportunities for the private sector—thereby bridging the commercialization gap between early-stage academic research and industry.
 **Amit Bar-Or** Associate Professor Montreal Neurological Institute McGill University amit.bar-or@mcgill.ca	Interest in B cell, antigen presenting cell, and T cell responses and their involvement in central nervous system inflammation. Studies of the immature immune system in the context of early onset (pediatric) MS, reconstitution following immune ablation and immuneneural interactions. He established a program in 'Experimental Therapeutics', which aims to develop and incorporate novel immune assays into well-designed clinical trials of MS.
 **John Bell** Senior Scientist Cancer Therapeutics Program Ottawa Hospital Research Institute jbell@ohri.ca	We are optimizing and selecting for virus strains with improved efficacy as anti-cancer therapeutics. We are carrying out a detailed analysis of the behavior of tumour microenvironment cells during oncolytic virus therapy. In particular we have shown in both mouse models and samples taken from patients undergoing OV therapy that our viruses can infect and disrupt tumour vasculature.
 **Jonathan Bramson** Professor Pathology and Molecular Medicine McMaster University bramsonj@mcmaster.ca	My lab has taken a multi-modal approach to treating cancer by employing a combination of cancer vaccines, adoptive T cell therapies and oncolytic viruses. We believe that such multi-pronged strategies are the best way to attack the tumor.
 **Felix Breden** Professor Population Genetics & Genomics Simon Fraser University breden@sfu.ca	How complex biological interactions control the divergence of genes, individuals and populations. In order to understand the interaction of genetic forces at multiple levels of biological organization, I have chosen to study tractable systems for which there is extensive background knowledge, such as the guppy, and systems with important applied outcomes, such as human immunoglobulin loci.

Ryan Brinkman
Associate Professor

Medical Genetics,
University of British Columbia

rbrinkman@bccrc.ca

Applying bioinformatics techniques to flow cytometry data. We are leading an international effort to develop a systemic approach to modeling, capturing, analyzing and disseminating flow cytometry data. Work is focused on developing a community-based standard for recording and reporting flow cytometry data, testing our high throughput analysis methods to analyze flow cytometry data on datasets for the high throughput analysis of lymphoma, Graft versus Host Disease and innate immunity.

Michael Burgess
Professor

Chair in Biomedical Ethics
School of Population
and Public Health
University of British Columbia

mburgess@exchange.ubc.ca

Focus on science and technology policy and public engagement based on theories of deliberative democracy. "Building a GE3LS Architecture" genome science projects in microbial genomics of forest soils and military explosives. Deliberative engagements on biobanks in BC, the Mayo Clinic and in Western Australia. Deliberative design has also been used on salmon genomics, bioremediation of military explosive RDX, epidemiological research using health records and biofuels

Debby Burshtyn
Associate Professor

Dept. of Medical Microbiology
and Immunology
University of Alberta

burshtyn@ualberta.ca

We study the cell and molecular biology of several receptors that regulate Natural Killer (NK) cells and viral regulation of the ligands of these receptors. Our current focus is on the Leukocyte Ig-Like Receptor-B1 Regulation and Function and HCMV infection Modulation of NK-ligands by poxviruses

David Burt
Director R&D,

GlaxoSmithKline

david.burt@gsk.com

Dr. Burt is currently managing the Laval R&D team in the areas of prophylactic vaccines and representing the North American vaccine R&D activities on the global Vaccine Discovery and Development Leadership Team (VDD-LT).

Marcus Butler
Medical Oncologist

Immune Therapy Program
Princess Margaret Cancer
Centre
Assistant Professor,
University of Toronto

marcus.butler@uhn.ca

Interest in the translational development of immune-based therapies for cancer patients. He cares for patients with melanoma and gynecologic malignancies. His work focuses on the development of immunotherapy trials, which include studies, alone and in combination, of immune checkpoint blocking antibodies, immunomodulators, and adoptive cell transfer.

Christopher Carlsten

Associate Professor &
Chair in Occupational and
Environmental Lung Disease
School of Population and
Public Health
University of British Columbia

carlsten@mail.ubc.ca

Research Interests:

- Air pollution health effects (diesel exhaust, respiratory and immunologic effects, oxidative stress)
- Controlled inhalation models (humans; '*in vivo*')
- Effects of complex inhaled exposures ('synergy'; complementing experimental with epidemiologic models)
- Translational research
- Understanding effects of genetics on pollutant effect (gene-by-environment analysis, recognizing its limitations)

Nicolas Chomont

Chercheur et Professeur
Associé

Département de
Microbiologie,
Infectiologie et Immunologie
Université de Montréal

nicolas.chomont@umontreal.ca

Understanding of how HIV infections persist, despite effective anti-HIV medications wiping out detectable levels of the virus – an important step in eradicating the disease.Dr. Chomont also helped identify the role of a protein called FOXO3a in the persistence of the HIV virus in infected T cells. Current research focused on defining mechanisms and potential drug targets that could lead to the eradication of persistent HIV and an eventual cure for HIV infection.

Ken Croitoru

Professor of Medicine

Division of gastroenterology
University of Toronto

KCroitoru@mtsinai.on.ca

He is investigating the fundamental mechanisms of intestinal inflammation, in particular the role of T cell effector and regulatory function in the intestinal mucosal in Inflammatory Bowel Disease. The goal of his work is to understand how T cells function serves to maintain intestinal homeostasis in health and what defects in regulatory T cells allow for the breakdown of these mechanisms.

Jayne Danska

Professor

Medical Biophysics,
Faculty of Immunology
University of Toronto

jayne.danska@sickkids.ca

Research Interests:

- Immunogenetics of Type 1 diabetes
- Autoimmune disease
- Lymphoblastic leukaemia/ lymphoma
- Mouse models
- Genomic instability

No picture available

Sarah De La Rue

Assistant Director

CIHR Institute of Human
Development,
Child and youth Health
University of Toronto

SdelaRue@mtsinai.on.ca

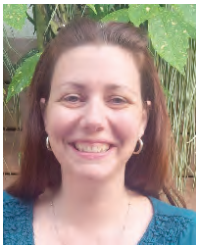
The Institute of Human Development, Child and Youth Health (IHDCYH) supports research that ensures the best start in life for all Canadians and the achievement of their potential for optimal growth and development.

Jean-Sébastien Delisle
Research Professor
of medicine

Université de Montréal

js.delisle@umontreal.ca

Defining the mechanisms that modulate the anti-tumor response, especially by studying the cancer microenvironment and the potently immunosuppressive cytokine TGF-β. A second research axis focusses on other determinants of T cell physiology in the context of hematopoietic cell transplantation. Also working on the differentiation and expansion of human T cells *in vitro* in order to support early phase clinical trials at HMR.



Marilyn Desrosiers
Deputy Director

Strategic Initiative Branch
CIHR, Ottawa

marilyn.desrosiers@cihr-irsc.gc.ca

Jan Dutz
Professor

Department of Dermatology
and Skin Science,
University of British Columbia

Jan.Dutz@vch.ca

Our laboratory is engaged in studies to optimize the use of the skin as an organ to alter systemic immune responses. In separate projects, we are studying the priming or activation of T cells involved in models of systemic lupus erythematosus and juvenile onset diabetes mellitus.

Goetz Ehrhardt

Department of Immunology
University of Toronto

goetz.ehrhardt@utoronto.ca

The first project centers on the regulation of human memory B cells by FCRL proteins. A separate project aims at harnessing the adaptive immune system of the evolutionary distant sea lamprey for biomarker discovery.

Bertus Eksteen
Associate Professor

Department of Medicine,
Division of Gastroenterology
University of Calgary

b.eksteen@ucalgary.ca

His research and clinical interests are focused on chronic inflammatory liver diseases such as Primary Sclerosing Cholangitis (PSC) and the immune processes that underpin them.
Discovering a role for mucosal T cells in PSC and Inflammatory Bowel Disease (IBD).
Defining that intestinal dendritic cells control gut trafficking of T and B cells by retinoic acid secretion.

Hani El-Gabalawy
Scientific Director

CIHR institute of Musculoskeletal Health and Arthritis
University of Manitoba

Hani.Elgabalawy@med.umanitoba.ca

His current research interests centre round the pathogenesis of RA and the mechanisms involved in the initiation of synovial inflammation. Dr El-Gabalawy has established a unique cohort of high risk First Nations family members of RA patients who are being followed longitudinally for the earliest evidence of RA onset.

May Faraj
Associate Professor

Department of Nutrition,
Université de Montréal

may.faraj@umontreal.ca

Exploring novel mechanisms for the development of cardiometabolic diseases in humans, such as type 2 diabetes and atherosclerosis, with special focus on the role of atherogenic lipoproteins and dysfunctional adipose tissue in this process. Moreover, we examine the effect of various nutritional interventions as therapeutic tools to reverse early cardiometabolic abnormalities.

Nicolas Flamand
Professor

Department of Medicine
Université Laval

nicolas.flamand.1@ulaval.ca

- Understanding the roles of chemokines and bioactive lipids in the regulation of human eosinophil traficking into the airways in mild and severe asthma.
- Understanding the regulation of human neutrophil functions by bioactive lipids and chemoattractants.
- Understanding the regulation of inflammation and host defense by endocannabinoids, eicosanoids, and related bioactive lipids in humans.

Paul Fortin
Professor

Dept. of Medicine
Univertité Laval

Paul.Fortin@crchudequebec.ulaval.ca

Understanding the bio-psycho-social impact on the chronic rheumatoid disease such as systemic lupus erythematosus (SLE), antiphospholipid syndrome (APS) rheumatoid arthiritis, arthritis, systemic autoiummune rheumatic disease (SARD). He is mostly interested in the development of intervention in the treatment of those diseases

Tamàs Fülöp
Professor

Department of medecine /
Research center of aging
Université de Sherbrooke

Tamas.Fulop@USherbrooke.ca

- Immunological changes with aging; signal transduction of lymphocyte subpopulations (naïve, memory,...).
- Immunosenescence in the development and progression of Alzheimer disease (AD).
- Immunosenescence in the tolerability of chemotherapy in elderly subjects.
- Role of the innate and adaptive immune response in altered vaccine response of elderly subjects.

Bob Goldstein
Chief Scientific Officer

JDRF Canada

gold@jdrf.ca

JDRF is the leading global organization focused on type 1 diabetes (T1D) research. Driven by passionate, grassroots volunteers connected to children, adolescents, and adults with this disease, JDRF is now the largest charitable supporter of T1D research. The goal of JDRF research is to improve the lives of all people affected by T1D by accelerating progress on the most promising opportunities for curing, better treating, and preventing T1D.

John Gordon
Professor

Department of Medicine
University of Saskatchewan

john.gordon@usask.ca

Dendritic cell immunotherapy. Tolerogenic dendritic cells (DCreg) can reverse asthma or peanut anaphylaxis sensitivity in mouse models & ex vivo in asthmatic subjects. We are working towards taking DCreg immunotherapy into the clinic.
Inflammation. We have developed a series of ELR-CXC chemokine (eg, IL-8/CXCL8) antagonists, aka, G31P) that block the activities of these chemokines, and here too are in the process of translating this research into the clinic.

Jennifer Gunning
Associate Director

HIV/AIDS Research Initative
CIHR, Ottawa

jennifer.gunning@cihr-irsc.gc.ca

The CIHR HIV/AIDS Research Initiative is responsible for the management and oversight of the research components of the two major Government of Canada initiatives in HIV/AIDS, namely the Federal Initiative to Address HIV/AIDS in Canada and the Canadian HIV Vaccine Initiative.

Ellie Haddad
Professor of Pediatrics

Université de Montréal

elie.haddad@umontreal.ca

My primary field of expertise is Primary immune deficiencies in which I perform both clinical and fundamental research. I also work with humanized mouse models to study various human diseases such as immune deficiencies, nephrotic syndrome or Rasmussen encephalitis. I study also immunotherapy of childhood cancer and the mechanism of action of mesenchymal stromal cells in Graft versus Host Disease in preclinical models.

Scott Halperin
Professor

Departments of Pediatrics and Microbiology & Immunology.

Director,

Canadian Center
for Vaccinology
Dalhousie University

Scott.Halperin@dal.ca

Dr. Halperin's research focuses on the diagnosis, treatment, and prevention of pertussis and other vaccine-preventable diseases.
Dr. Halperin is head of the Division of Pediatric Infectious Diseases at the IWK and a Professor of Pediatrics and Microbiology & Immunology at Dalhousie University. He is also the Director of the Canadian Center for Vaccinology.

Kent HayGlass
Professor

Departments of Immunology; Medical Microbiology; Pediatrics and Child Health
University of Manitoba

Kent.HayGlass@med.umanitoba.ca

Understand immune regulation and how it determines whether health or chronic disease dominates. We focus on how the human immune response is turned on, how it commits to particular types of immunity (good or bad) and how it is turned off. Our goal is to translate this knowledge to improve human health. Most of our research is on the role of cytokine and chemokine responses that result from innate or antigen-specific T cell activation.

Tony Jevnikar
Professor

Department of Medicine
University of Western Ontario

jevnikar@uwo.ca

Dr. Jevnikar is recognized for basic research in epithelial cell injury and the regulation of cellular death by endogenous inhibitors of apoptosis as a means to promote allograft survival. This work has led to novel discoveries such as the role and inhibition of epithelial cell death receptors that induce «self injury» and organ dysfunction during inflammation.

Tobias Kollmann
Associate Professor

Division of Infectious and Immunological Diseases, Department of Pediatrics, University of British Columbia

tkollmann@cw.bc.ca

The work in our lab focuses on part of the science to help solve this problem: we are developing a vaccine system that with only one immunization given at birth will protect from infectious diseases, as well as from asthma and allergies. We are dissecting the molecular mechanisms important in the human neonatal and infant response to infection or vaccination.

Lakshmi Krishnan
Team Leader

Vaccine Program
National Research Council Canada

Lakshmi.Krishnan@nrc-cnrc.gc.ca

NRC's Human Health Therapeutics (HHT) portfolio works hand in hand with industry to help biotech firms achieve success and save costs. As an R&D partner of choice, NRC-HHT de-risks critical steps in the development of biologics, vaccines, and delivery of large molecules to the brain, to help improve the health of Canadians.

Pascal Lavoie
Associate Professor

Partner Institute, Division of Neonatology, Department of Pediatrics,
University of British Columbia

plavoie@cw.bc.ca

We use a combination research approaches (population-based clinical studies/epidemiology and traditional molecular biology) to understand how the delicate immune system is protecting some healthy preterm infants compared to those who become sick from infections or other diseases.
Innate immune defences in premature babies
Neonatal adaptive T cell immunity
Heritability of bronchopulmonary dysplasia

Lynne LeSauteur
Director

R&D, Human Health Therapeutics at National Research Council Canada

Lynne.LeSauteur@nrc-cnrc.gc.ca

NRC's Human Health Therapeutics (HHT) portfolio works hand in hand with industry to help biotech firms achieve success and save costs. As an R&D partner of choice, NRC-HHT de-risks critical steps in the development of biologics, vaccines, and delivery of large molecules to the brain, to help improve the health of Canadians.

Isabelle Létourneau
Associate

Strategic Initiatives
CIHR Institute of Infection and Immunity
Université Laval

isabelle.letourneau@crchudequebec.ulaval.ca

The Institute of Infection and Immunity (III) supports research and helps to build research capacity in the areas of infectious disease and the body's immune system. Through the Institute's programs, researchers address a wide range of health concerns related to infection and immunity including disease mechanisms, disease prevention and treatment, and health promotion through public policy.

Megan Levings
Professor

Department of Surgery, University of British Columbia

megan.levings@ubc.ca

Research interests:

- Studying the unique cell-signalling pathways in human and mouse Tregs
- Developing biomarkers to track the function of Tregs
- Studying the interaction between Tregs and IL-17-producing cells
- Studying tissue-derived Tregs from patients with graft versus host disease or inflammatory bowel disease (IBD)
- Developing methods to use Tregs as a cellular therapy in transplantation
- Developing biomarkers to predict responses to therapy in (IBD)

Helen Loughrey
Executive-in-Residence / Business Development

Life Sciences Industry
CIHR

helen.loughrey@cihr-irsc.gc.ca

Focus is on developing partnerships with the life sciences industry and the development of a new Commercialization Strategy.

Experience in biopharmaceutical R&D, regulatory (FDA, Health Canada and EMA), pharma-academic partnerships & broad knowledge of life science industry needs

Joaquin (Quim) Madrenas

Canada Research Chair in Human Immunology
Professor and Chairman
Department of Microbiology & Immunology

Director, Microbiome and Disease Tolerance Centre
McGill University
Executive Director, CIHR Human Immunology Network

joaquin.madrenas@mcgill.ca

Research Interests:

- Human Immunology and Microbiome studies
- Immune-mediated mechanisms that promote microbial commensalism and disease tolerance
- Innate and adaptive immune responses to *Staphylococcus aureus* and its toxins
- Regulation of T cell adaptive immune responses

Jean-Christian Maillet

Project Officer

HIV/AIDS Research Initiative
CIHR, Ottawa

jeanchristian.maillet@cihr-irsc.gc.ca

The CIHR HIV/AIDS Research Initiative is responsible for the management and oversight of the research components of the two major Government of Canada initiatives in HIV/AIDS, namely the Federal Initiative to Address HIV/AIDS in Canada and the Canadian HIV Vaccine Initiative.

Mary-Jo Makarchuk,

Assistant Director

CIHR Institute of Nutrition, Metabolism and Diabetes
University of Toronto

mary-jo.makarchuk@sickkids.ca

The Institute of Nutrition, Metabolism and Diabetes's (INMD) mandate supports research to enhance health in relation to diet, digestion, excretion, and metabolism; and to address causes, prevention, screening, diagnosis, treatment, support systems, and palliation for a wide range of conditions and problems associated with hormone, digestive system, kidney, and liver function.

Deborah Marshall

Associate Professor

Department of Community Health Sciences
University of Calgary

damarsha@ucalgary.ca

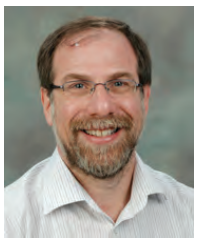
1) Economic evaluation of health programs using decision analysis methodologies, particularly cost effectiveness of testing and treatment interventions in personalized medicine.
2) Planning health system and health services delivery using dynamic simulation modeling
3) Patient preferences methods using conjoint analysis.
4) Health technology assessment and evidence based methods of appraisal

Sylvie Masse
Administrative Assistant

CIHR Institute of Infection and Immunity
Université Laval

Sylvie.masse@crchudequebec.ulaval.ca

The Institute of Infection and Immunity (III) supports research and helps to build research capacity in the areas of infectious disease and the body's immune system. Through the Institute's programs, researchers address a wide range of health concerns related to infection and immunity including disease mechanisms, disease prevention and treatment, and health promotion through public policy.



Bruce Mazer
Professor

Department of Pediatrics
McGill University

bruce.mazer@mcgill.ca

Research Interest:

- Allergic inflammation in asthma and food allergy
- Immune deficiency, B-cell development and antibody deficiency
- Immune Tolerance mechanisms in allergic inflammation
- B cells and immunoglobulins in immune tolerance
- Intravenous immune globulin (IVIG), Ig receptors and regulatory pathways
- Clinical trials in food allergy therapeutics

Janet McElhaney
Professor

Northern Ontario School of Medicine
Senior Scientist,
Advanced Medical Research Institute of Canada
HSN Volunteer Association Chair in Healthy Aging

jmcelhaney@amric.ca

Developing T cell correlates of protection against influenza illness and inflammatory biomarkers that predict risk for catastrophic disability. The goal is to develop new vaccines to prevent disability from influenza and understand the role of inflammation in the multi-morbidity experience of older adults in the discovery of new approaches to promote healthy aging.

Brad Nelson
Professor

Medical Genetics
University of British Columbia

bnelson@bccrc.ca

Use of genomic technologies to map the immune response to ovarian, breast, prostate, and lymphoid cancers before, during and after standard therapy

Development of novel target antigens and immuno-modulatory strategies for vaccine- and cell-based cancer therapies

Kieran O'Doherty
Assistant Professor

Department of Psychology
University of Guelph

odohertk@uoguelph.ca

Community engagement & public deliberation; social & ethical implications of genetics/ genomics; qualitative methods; discourse analysis; risk & uncertainty; human agency.

Topic areas include the social aspects of health and illness, public participation in biotechnology and science, genetic risk, the language of uncertainty, and participatory governance. I am also interested in questions of ethics, human agency, and epistemology and ontology in science and psychology.

Pamela Ohashi
Professor

Departments of Medical Biophysics and Immunology
University of Toronto

pohashi@uhnres.utoronto.ca

Promotion of T cell responses with a goal to understand and control autoimmune and anti-tumor immune responses.

Studying novel ways that dendritic cells are programmed to influence T cell function *in vivo* and how the tissue or tumor microenvironment can impact T cell responses.

Growing tumor infiltrating T cells and characterize their properties. We coordinate clinical trials and are building towards a comprehensive program in immune therapy.

Marc Ouellette
Scientific Director

CIHR Institute of infection and Immunity
Université Laval

marc.ouellette@crchudequebec.ulaval.ca

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Christopher Paige
Professor

Department of Medical Biophysics
University of Toronto

paige@uhnres.utoronto.ca

Cancer vaccines: we have developed a syngeneic cell-based anti-leukemia murine model focused on the expression of IL-12 derived from lentiviral transductions. In that work we showed that syngeneic leukemia cells expressing IL-12 can induce protective, long-lasting and specific immunity. Once initiated, the immune response is effective against all of the leukemia cells, including those that do not express IL-12. This work is being extended to solid tumours as well. In addition, these techniques are now being modified using primary human leukemia cell blasts from AML, ALL, CML, and CLL in experiments which form the basis for subsequent human clinical trials.

Ciriaco Piccirillo
Associate Professor

Department of Microbiology & Immunology
McGill University

ciro.piccirillo@mcgill.ca

My laboratory makes use of cutting-edge experimental strategies to characterize the relative contribution of nTreg cells as a determining factor in establishing resistance or susceptibility to autoimmune and infectious diseases. We try to characterize the functional dynamics of nTreg cell activity in human autoimmune diseases (type 1 diabetes) as well as in animal models of autoimmunity (type 1 diabetes), tumors (spontaneous breast cancer), infections (malaria), and mucosal immunity (inflammatory bowel disease).

Jennifer Raven
Assistant Director

CIHR Institute of Infection and Immunity
CIHR, Ottawa

jennifer.raven@cihr-irsc.gc.ca

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Ellis Reinherz
Professor

Department of Medicine, Harvard Medical School
Chair of the Human Immunology Project Consortium from the NAID, NIH

ellis_reinherz@dfci.harvard.edu

The Human Immunology Project Consortium (HIPC) program was established in 2010 by the NIAID Division of Allergy, Immunology, and Transplantation as part of the overall NIAID focus on human immunology. The purpose of HIPC is to capitalize on recent advances in immune profiling methods in order to create a novel public resource that characterizes diverse states of the human immune system following infection; prior to and following vaccination; or prior to and following treatment with an immune adjuvant.

Jim Richards
Director

R&D; Lead, NRC Vaccine Program at National Reseach Council of Canada
James.Richards@nrc-cnrc.gc.ca

NRC's Human Health Therapeutics (HHT) portfolio works hand in hand with industry to help biotech firms achieve success and save costs. As an R&D partner of choice, NRC-HHT de-risks critical steps in the development of biologics, vaccines, and delivery of large molecules to the brain, to help improve the health of Canadians.

Étienne Richer
Assistant Director

CIHR Institute of Genetics
McGill University

etienne.richer@mcgill.ca

The Institute of Genetics (IG) supports research on the human and model genomes and on all aspects of genetics, basic biochemistry and cell biology related to health and disease, including the translation of knowledge into health policy and practice, and the societal implications of genetic discoveries.

John Rioux
Associate Professor

Department of Medicine
Université de Montréal

John.david.rioux@umontreal.ca

The goal of his research is to discover the genetic risk factors of rare (monogenic) diseases and common (polygenic) diseases and to uncover the biological mechanisms that determine how these genetic variants influence the risk of developing these chronic diseases.

Serge Rivest
Professor

Department of molecular medicine
Université Laval

serge.rivest@crchudequebec.ulaval.ca

Understanding the molecular mechanism involved in the regulation of the innate immune system in the central nervous system and its role in brain diseases and injuries. In particular, we are working with microglial cells and monocytes to eliminate senile plaque and cerebrovascular amyloid in Alzheimer's disease.

Jean-Pierre Routy
Professor

Department of Medicine, Divisions of Experimental Medicine
McGill University

jean-pierre.routy@mcgill.ca

Bring basic laboratory research into clinical trials. Understanding HIV pathogenesis and restoring the immune system of individuals infected with HIV, including the use of interleukin-7 (a cytokine), or a dendritic cell-based therapeutic vaccine, or chloroquine (a commonly used anti-malarial drug) in addition to antiretrovirals to optimaly manage HIV infection. Principle investigator of a national cohort of patients recently infected with HIV.

Denis-Claude Roy
Professor, Director

Cellular Therapy Laboratory
Université de Montréal

denis-claude.roy@umontreal.ca

Research Interests:

- Immunology of leukemia and lymphoma: translational research;
- Autologous and allogenous hematopoietic stem cell transplantation;
- Manipulation of hematopoietic cell grafts: elimination of alloreactive T lymphocytes;
- Targeting of malignant cells, using photodynamic and immunological therapy;
- Study of action mechanisms and optimization of monoclonal antibody and immunoconjugates;
- Growth and expansion factors of hematopoietic stem cells and blood progenitors.

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Marika Sarfati
Professor

Département de microbiologie, infectiologie et immunologie
Faculté de médecine
Université de Montréal

m.sarfati@umontreal.ca

Research Interests:

- Role of dendritic cells in immune response induction;
- Regulation of cytokine production and molecular mechanism;
- Cellular and molecular immunobiology in chronic lymphatic leukemia.

Jamie Scott
Professor

Department of Molecular Biology Biochemistry
Simon Fraser University

scott@sfu.ca

Understanding the molecular basis for antigen recognition by antibodies using peptide as probes of these interactions. Interest in understanding how the peptide recognition profile of an antibody response may be applied to the development of vaccines and autoimmune diagnostics. Search for peptides will bind to human monoclonal antibodies that kill HIV-1 in order to create a vaccine that will elicit these same antibodies in uninfected people, and thus protect them from AIDS.

Philip Sherman
Scientific Director

CIHR Institute of Nutrition, Metabolism and Diabetes
University of Toronto

philip.sherman@sickkids.ca

Research interests:

- Epithelial cell signal transduction responses to pathogenic, commensal and probiotic bacteria
- Microbiome
- Inflammatory bowel disease
- Pediatric gastroenterology

Bhagirath Singh
Department of Microbiology & Immunology
Faculty of Medicine & Dentistry
University of Western Ontario
bsingh@uwo.ca

Research interests:

- Cellular basis for the activation of regulatory CD4+CD25+ and effector Th17 T cells in autoimmune diabetes by microbial agents
- Dendritic cell and Regulatory T cell mediated modulation of autoimmunity in Type I diabetes
- Modulation of islet beta cell expansion in pancreatic tissue

Liz Stirling
Assistant Director
Institute of Musculoskeletal Health and Arthritis
CIHR, Ottawa
Liz.Stirling@cihr-irsc.gc.ca

The Institute of Musculoskeletal Health and Arthritis (IMHA) supports research to enhance active living, mobility and movement, and oral health; and addresses causes, prevention, screening, diagnosis, treatment, support systems, and palliation for a wide range of conditions related to bones, joints, muscles, connective tissue, skin and teeth.

Rachel Syme
Assistant director
CIHR Institute of Cancer Research,
University of Calgary
rmsyme@ucalgary.ca

The Institute of Cancer Research (ICR) funds cancer research in Canada based on internationally accepted standards of excellence, which bear on preventing and treating cancer, and improving the health and quality of life of cancer patients. CIHR is one of the leading cancer research funders in Canada.

Scott Tebbutt
Associate Professor
Department of Medicine
University of British Columbia
Principal Investigator
Centre for Heart Lung Innovation,
St. Paul's Hospital
Vancouver, Canada
scott.tebbutt@hli.ubc.ca

His research program is focused on molecular signatures of complex respiratory disease, including the early and late reactions in atopic asthma and allergic rhinitis. He is also Chief Scientific Officer of the Prevention of Organ Failure (PROOF) Centre of Excellence - a not-for-profit organization dedicated to moving research findings into health care, and focused on non-invasive biomarkers that can diagnose and/or predict organ failure (heart, lung and kidney). His responsibilities include the evaluation of new, high-performance technologies to improve biomarker discovery and translation, as well as computational biology approaches to better deal with cell type heterogeneity.

Elizabeth Theriault
Assistant Scientific Director
CIHR Institute of Neurosciences,
Mental Health and Addiction
University of British Columbia
elizabeth.theriault@ubc.ca

The Institute of Neurosciences, Mental Health and Addiction (INMHA) supports research to enhance mental health, neurological health, vision, hearing, and cognitive functioning and to reduce the burden of related disorders through prevention strategies, screening, diagnosis, treatment, support systems, and palliation.

Emily Torr
Project Officer

CIHR Institute of Human Development, Child &Youth Health
University of Toronto

etorr@mtsinai.on.ca

The Institute of Human Development, Child and Youth Health (IHDCYH) supports research that ensures the best start in life for all Canadians and the achievement of their potential for optimal growth and development.

Stuart Turvey
Associate Professor

Division of Infectious and Immunological Diseases,
Department of Pediatrics,
University of British Columbia

sturvey@cw.bc.ca

Translational, interdisciplinary and unique in its focus on understanding the role of innate immunity in infectious and inflammatory diseases of childhood. Starting with a population of children with a defined infectious or inflammatory disease phenotype to determine the underlying cellular, molecular and genetic abnormalities responsible for the disease through detailed immunological, genomic and proteomic analysis.

Tania Watts
Director

Toronto Human Immunology Network
Professor,
Department of Immunology
University of Toronto

tania.watts@utoronto.ca

Research Interests:

- Immune reaction during to persistent viral infection
- Mechanisms that control the persistence of memory T cells as well as the survival of immune related cancer cells.
- T cell immunity to viruses, including HIV and influenza virus, in humans.

Lori West
Professor of Pediatrics

Surgery and Immunology
Director, Canadian National Transplant Research Program
University of Alberta

ljwest@ualberta.ca

The overarching goal of the Heart Transplant Research Program is the development of a comprehensive research focus encompassing specific projects related to cardiac transplantation. These projects range from molecular level 'gene therapy' and cell biology investigations in murine models through to clinical projects that include patient and population outcomes, quality-of-life studies and clinical drug trials.

Ola Winqvist
Senior Researcher

Department of Medicine
Karolinska Institutet (Sweden)
Vice-Chair
ENTIRE

Ola.Winqvist@ki.se

In a multidisciplinary approach, ENTIRE concentrates the specialised expertise of the participating centres to define a minimal set of functional tests for immunotype profiling validate, standardize and implement the panels for immunotype profiling define the immunotypes in normals and in disease cohorts using these panels use these panels in the context of clinical trials with targeted therapies give guidelines and advice to clinicians, authorities and industry train a new generation of translational/ interventional immunologists dissemination and outreach by publications, website, and congresses/workshops.

Xi Yang
Professor

Department of Immunology
University of Manitoba

yangxi@cc.umanitoba.ca

The current research program in my laboratory focuses on the cellular and molecular basis of immune responses to allergens and infectious agents and on the development of immunoprophylactic approaches for allergy and infectious diseases.

Hygiene hypothesis related to allergy/asthma.

Protective immunity and immunopathology to chlamydial infection.

Development of vaccines for human chlamydial infection.

Rae Yeung
Professor

Dept. of Paediatrics,
Immunology and Institute of
Medical Science
University of Toronto

rae.yeung@sickkids.ca

Towards understanding the path from systemic inflammation to localized coronary artery disease, we have identified key molecules involved in disease pathogenesis. Using both *in vitro* and *in vivo* methods involving genetically modified mice, we have identified critical mechanisms involved in vessel wall breakdown. The ultimate goal of these studies is to identify key molecules to target for development of new therapeutic agents in treatment of Kawasaki disease.

Juan Carlos Zúñiga-Pflücker
Professor and Chair

Department of Immunology,
University of Toronto

jczp@sri.utoronto.ca

Research interests:

- Identifying the role of several activating lymphokines in creating a proper growth environment for T cell development;
- Defining the stages at which T cell commitment occurs and establishing the lymphokines produced by the thymic stroma
- Isolation of a thymocyte sub-population with NK and T cell precursor potential.
- To identify the molecular events that are induced following the pre-T cell receptor complex formation

Tuesday, November 25th, 2014 – Room Collingwood

Time	Description	Lead
09:00	Continental Breakfast – Muskoka I Room	
10:00	Welcome and Introduction of Steering group	Isabelle Létourneau
10:10	Presentation of the initiative on Human Immunology	Marc Ouellette
10:20	Workshop overview: Goals and Objectives	Megan Levings
10:30	HIPC: The Human Immunology Project Consortium	Ellis Reinherz
11:00	**Theme 1. Transformational therapeutics and diagnostics** • Pamela Ohashi: *Making cancer immunotherapy a reality in Canada* • Scott Tebbutt: *Biomarkers: the road from discovery to implementation* • Jan Dutz: *Innovations in the use of biologics to treat autoimmunity*	Rae Yeung
11:45	Lunch – Muskoka I Room	
12:45	**Theme 1. Roundtable** • *What therapeutic approaches are close to clinical testing? Of these which ones would have the biggest impact?* • *Are there opportunities to test current/emerging immune therapies in new indications and/or patient populations?* • *What diagnostic/patient stratification methods have the greatest potential to advance diagnosis/treatment of immunological diseases?* • *Are there immunological diseases for which Canada is uniquely poised to have a significant research impact?*	

Tuesday continued...

13:30	**Theme 1. Report back from roundtable**	
14:15	**Theme 2. Barriers and opportunities** • Quim Madrenas: *Lessons learned from the Canadian Human Immunology Network* • Kent HayGlass: *Dating tips: Practical strategies for building effective interdisciplinary collaborations* • Michael Burgess: *Biobanking and cohort studies: the critical role of public engagement*	Hani El-Gabalawy
15:00	Heath Break – Collingwood Foyer	
15:30	**Theme 2 Roundtable** • *What barriers prevent/hinder human immunology research in Canada?* • *What non-traditional collaborations need to be fostered to enable the discovery and development of cutting edge therapies and diagnostics?* • *What training and mentoring is lacking in different fields to support growth in human immunology?* • *What is the role of the public/patients in promoting and participating in human immunology research?*	
16:15	**Theme 2. Report back from roundtable**	
17:00	**Theme 3. Technology and partnerships** • Felix Breden: *Repertoire profiling* • Denis-Claude Roy: *CellCAN* • Jim Richards: *The National Research Council, facilities and opportunities for collaboration*	Philip Sherman
17:45	Networking reception – MacIntosh Foyer	
19:00	Dinner – MacIntosh Room	

Wednesday, November 26th 2014 – Room Collingwood

Time	Description	Lead
07:30	Breakfast – Algonquin Room	
8:15	Highlights of Day 1	Megan Levings
8:30	ENTIRE: European Network for translational immunology Research Education	Ola Wingvist
9:00	**Theme 3 Roundtable** • *List major technological innovations that are, or are poised to, impact human immunology. Comment on how soon each is likely to be used in clinical applications* • *What facilities are available in Canada that could be leveraged to advance human immunology?* • *What unique areas of expertise in Canada could be leveraged to advance human immunology?* • *Which key national and international partners (academic, government, NGO, private sector) need to be involved and how can they be engaged?*	
9:45	**Theme 3 Report back**	
10:30	Health Break – Collingwood Foyer	
11:00	**Theme 4. Funding mechanisms and impact** • Deborah Marshall: *Measuring value in personalized medicine* • Lori West: *The CNTRP: a new way of doing research* • Helen Loughrey: *Collaboration with industry, what do they expect* • Isabelle Létourneau: *Funding mechanisms at CIHR*	Marc Ouellette
12:00	Lunch – Algonquin Room	

Wednesday continued...

12:45	**Theme 4 Roundtable** • *What funding mechanisms would best catalyze human immunology research? List the pros and cons of various options.* • *What key partners are needed to enable different funding mechanisms?* • *What outcomes would you expect in the short (3 years), medium (5 years) and long term (beyond 5) and how can they be measured?* • *What are the "low hanging fruit" in human immunology*	
13:30	**Theme 4 report back**	
14:15	Concluding remarks	Steering committee
14:30	Departure for workshop participants	
14:30	Health break – Collingwood Foyer	
14:40-16:30	Steering committee meeting – planning the next step	