Meakins-Christie Laboratories 50th Anniversary Symposium and Respiratory Research Day

SPEAKER ABSTRACT BOOK

Wednesday, May 17 – Thursday, May 18, 2023

InterContinental Hotel, Old Montreal
360 Saint-Antoine St. West, QC, H2Y 3X4

Diaphragm dysfunction in the critically ill: of mice, men, beer and gym

Alexandre Demoule[1]

[1]Sorbonne University, France

ABSTRACT:

Diaphragm weakness is observed in the vast majority (circa 75 %) of patients undergoing mechanical ventilation in the intensive care unit (ICU). It may exist prior to ICU admission and may precipitate the need for mechanical ventilation. This is typically the case of sepsis-induced diaphragm dysfunction, a phenomenon that was first described in 1985 in an animal model by Sabah Hussain in 1985. Interested in this topic, I joined in 2003 Basil Pretrof's lab at Meakins as a research fellow. With Maziar Divangahi, who taught me how to perform basic molecular biology experiments, we made a great team. Here, we showed that constitutive and lipopolysaccharide-induced proinflammatory gene expression were exaggerated in the diaphragm compared with limb muscles, suggesting the diaphragm may be relatively predisposed to proinflammatory responses. This could explain why the diaphragm was more susceptible to sepsis-induced weakness than limb muscles. Back to France, I set my own lab. We studied humans and we evidenced for the first time that diaphragm weakness was present on ICU admission in two third of mechanically ventilated patients, that sepsis was a major risk factor for diaphragm weakness and that diaphragm weakness was associated with higher mortality. Still in humans, we also showed that, although severe, sepsis-induced diaphragm weakness was reversible.

Diaphragm weakness may also develop during ICU stay. One of the major risk factors of ICU-acquired diaphragm weakness is mechanical ventilation, which rests the diaphragm and triggers a variety of mechanisms (oxygen free radicals, proteosynthesis proteolysis imbalance) that damage the diaphragm. This ventilation-induced diaphragm dysfunction was also one of the major research topics of Basil Petrof's lab that was fascinating me during my fellowship at the Meakins. However, it was all about animal models. Back to France, I conducted the first large study that evidenced this phenomenon in ICU patients. I also showed that diaphragm dysfunction was associated with poor outcomes including increased ICU mortality, difficult weaning, and prolonged duration of mechanical ventilation. In addition, in an animal model, we showed that mechanical ventilation and sepsis had additive deleterious effects on diaphragm strength.

Our challenge is now to improve the detection of diaphragm weakness in humans and to find non-invasive tools to assess diaphragm structures in critically ill patients. It is also to find inspiratory muscle training and pharmacological interventions may improve diaphragm strength. Diaphragm neurostimulation could be one of these.

BIOGRAPHY:

Alexandre Demoule is professor of intensive care medicine at the Sorbonne University Medical Centre in Paris. He is also the director of a medical intensive care unit and a weaning center within in La Pitié-Salpêtrière hospital in Paris.

He was trained as a pulmonologist and then as an intensivist. During his PhD program, he spent in the early 2000's one year and a half at the Meakins Christie Laboratories under the supervision of Basil Petrof. The Maekins is a very special and a fantastic place that had a lot of influence on his professional life, but not only. Here, he met great people and friends. The typical working day was starting by an early morning intense training session at the gym under the tough (if not sadistic) supervision of Maziar, who was his co-PhD student. So the Meakins changed not only Alex mind, but also his body shape (no worries, he pretty lost everything). Beer was not only at the mythic Tuesday seminar, but also at night at the bar on Fridays, but sometimes also on Thursday, and even on Saturday.

Today, Alex's main research field is patient-ventilator interactions in critically ill mechanically ventilated patients. It involves specific research topics such as respiratory muscles, the impact of mechanical ventilation on respiratory sensations and comfort, and brain-ventilator interactions.

Today, when he drafts a manuscript, Alex still remembers these precious words from Basil Petrof: "Alex, now we have all these data, it's time to write a story. So, what's the story?".

2003-04: Postdoctoral fellow under the supervision of Dr Basil Petrof

Airway imaging and the developmental origins of COPD

Benjamin Smith[1]

[1]McGill University

ABSTRACT:

The human airway tree serves as the conduit for gas-exchange and is our first line of defense against inhaled noxious aerosols such as tobacco smoke and air pollution. Over the past 150 years, airway tree structure has been mainly studied using small autopsy series and casting techniques (e.g., Abey, Ewart, Boyden, Weibel, Yamashita). More recently, high resolution *in vivo* imaging has facilitated the study of native airway tree structure and its relationship to respiratory function and disease risk in the general population. In this talk, I will try to convince you that, contrary to what our anatomy textbooks tell us, there is significant variation in native airway tree structure. This variation is established early in life and is a major determinant of disease susceptibility later in life - on par with tobacco smoking. Some etiologic factors underlying resilient vs. susceptible airway tree structure and the mechanisms of increased disease risk will be explored.

BIOGRAPHY:

Ben is a scientist and respirologist at the McGill University Health Centre Research Institute. His academic training is in respiratory medicine, physiology and epidemiology from McGill and Columbia Universities. His research program support includes CIHR, NIH and FRQS and is focused on understanding why some people develop chronic lung disease and other people do not. His recent work investigates the remarkable variation in native lung structure and its relationship to disease susceptibility across the lifespan.

Got your head in the clouds?

Carolyn Baglole[1]

[1]McGill University

ABSTRACT:

E-cigarettes consist of a rechargeable battery, an atomizer (or heating element/coil) and a liquid that contains a solvent (usually propylene glycol [PG] and vegetable glycerin [VG]), nicotine and various additives including flavors. Vaping is the act of inhaling into the lungs the vapor or aerosol that is produced by an e-cigarette. Pod-style e-cigarettes are the most popular type of device and includes brands like JUUL, Vuse, and STLTH. These brands use nicotine salts to deliver greater nicotine concentrations to the lungs, but each brand differs in their proprietary e-liquid formulations. Moreover, these brands come in many popular flavors such as fruit and menthol/mint that are especially appealing to youth. Flavor appeal, in conjunction with curiosity and lifestyle messaging, has led to a dramatic increase in vaping among youth and young adults in Canada, an age demographic where there are few that currently smoke cigarettes. However, there is exceedingly little information of the lung health effects of pod-style e-cigarettes in tobacco-naïve individuals. We therefore hypothesized that vaping would cause inflammation and oxidative stress concomitant with lung damage and further predicted that different flavors of e-cigarettes from these popular brands would have varying levels of lung damage. After establishing that our preclinical mouse model of e-cigarette exposure mimics light-moderate human e-cigarette use patterns, we exposed mice to JUUL aerosols and assessed inflammation and oxidative stress responses and performed RNA-sequencing and LC-MS/MS analysis of lung samples. Our results show that a low level of JUUL aerosol exposure elicits pulmonary immunologic, transcriptomic, and proteomic changes. Thus, e-cigarettes are not inert and may cause lung damage when inhaled for prolonged periods.

BIOGRAPHY:

Dr. Carolyn Baglole received her BSc and MSc from the University of Prince Edward Island and PhD in Physiology and Pharmacology at the University of Calgary. She then went on to post-doctoral training at the University of Rochester in the Department of Environmental Medicine before joining McGill and the Meakins-Christie Laboratories as an Assistant Professor in 2010. Dr. Baglole is also Director of the McGill Research Centre for Cannabis and has published more than 90 peer-reviewed papers in journals such as FASEB, AJP-Lung, Frontiers in Immunology, and Journal of Cellular Physiology. Dr. Baglole is funded through CIHR and NSERC and is currently a Fonds de recherche du Québec Senior Research Scholar. She also sits on a number of journal editorial boards and government advisory panels.

Dr. Baglole's research focuses on the how environmental exposures drive the pathogenesis of chronic lung diseases, including COPD. Her translational research program utilizes preclinical models of exposure to tobacco smoke as well as new and emerging threats to lung health including inhalation of various types of cannabis products as well as the use of e-cigarettes. Her main research focus is to understand at the cellular and molecular levels, how these environmental exposures contribute to pathogenic mechanisms such as chronic inflammation that drive the development of disease.

Host-pathogen interactions in chronic Pseudomonas aeruginosa infections

Dao Nguyen[1]

[1]McGill University

ABSTRACT:

Chronic *Pseudomonas aeruginosa* airway infections occur in the majority of adult individuals with cystic fibrosis, and are associated with accelerated lung function decline and increased mortality. During chronic infections, *P. aeruginosa* evolves and adapts to the CF lung environment, incurring genetic mutations that alter its phenotypes, including its ability to cause host damage and inflammation. How this genetic adaptation alters host-pathogen relationships and contributes to the progression of CF lung disease remains poorly understood. Using in vitro and mouse infection models, our group has demonstrated how common *P. aeruginosa* variants are not simply markers of disease, but promote immune evasion or induce exaggerated inflammation, and thus contribute to the pathogenesis of chronic CF infections.

BIOGRAPHY:

Dao completed her MD (’97) and respirology fellowship (2002) at McGill, a post-doctoral research training at the University of Washington (2008), before returning to McGill and the MUHC as a clinician scientist in 2009, and joining the Meakins in 2015. She is an Associate Professor in medicine, a respirologist at the MUHC and the director of the McGill AMR Center. She is a recipient of a FRQS chercheur de mérite, and past recipient of the Burroughs Wellcome Fund Career Award, Vertex Research Innovation Award and Cystic Fibrosis Canada Scholar award.

Building a lung from scratch: a new frontier to study human disease and to generate transplantable tissue units

Darcy Wagner[1]

[1]Lund University

ABSTRACT:

The ability to manufacture customizable and on-demand lung or airway tissue in the laboratory provides multiple opportunities to develop new therapies for patients with acute and chronic lung diseases. On the one hand, humanized tissue models allow for the study of pathomechanisms and potential compounds in 3D and in human cells and tissues. In addition, bioengineered tissues which are designed with immunologically compatible materials and cells offer a future hope for use in the clinic to treat diseases where the existing lung and airway tissue is beyond repair with current therapies. This talk will focus on the recent advances being made in this exciting area which combines biomaterials, stem cell biology and biomanufacturing. In particular, this talk will highlight recent advances in bioprinting as well as 3D imaging techniques which provide information at subcellular resolution, all of which can be used to design the next generation of therapies using bioengineering.

BIOGRAPHY:

Darcy Wagner is a Senior Lecturer and Wallenberg Molecular Medicine Fellow in Regeneration and Repair in the Respiratory System at the Department of Experimental Medical Sciences ad Lund University where she heads the group ‘Lung Bioengineering and Regeneration.’ She is a principal investigator in the strategic research areas at the Lund Stem Cell Center and NanoLund. Her lab aims to build lung tissue in the lab as next generation models of lung homeostasis, injury and repair as well as for manufacturing transplantable tissue.

She conducted her PhD at the University of Toledo in Biomedical Engineering with a focus on synthesizing novel materials and scaffolds for orthopedic tissue engineering. She conducted her first postdoctoral research period at the University of Vermont under Dr. Daniel Weiss in the Vermont Lung Center on deriving scaffolds for lung bioengineering. Her work was among the first to obtain decellularized whole lungs from porcine and human lungs. The Vermont Lung Center was headed by Dr. Charles Irvin at that time, a former member of the Meakins, and she collaborated with other former principal investigators of the Meakins at her time in Vermont (e.g. Jason Bates). She started her lab in 2017 in Sweden where her lab is funded by a European Research Council Grant, the Swedish Research Council, and the Swedish Innovation Agency VINNOVA.

A new player in alveolar macrophages development: neutrophils

Erwan Pernet[1]

[1]University of Quebec - Trois-Rivieres

ABSTRACT:

Alveolar macrophages (AM), the lung resident-tissue macrophages (RTM), reside in the airways where they play an essential function in the maintenance of pulmonary homeostasis and immunosurveillance. Compared to monocyte-derived interstitial macrophages, AM arise from fetal precursors and are maintained by local self-renewal. Although cytokines have been extensively studied in AM maturation and function, the developmental signals shaping their longevity remain largely unknown. Here we investigated the role of the host bioactive lipids, the eicosanoids, in programming AM self-renewal capacities. We demonstrated in mice genetically deficient in 12/15-LOX (*Alox15*$^{-/-}$) that neonatal neutrophil-derived 12-HETE was required for self-renewal and maintenance of alveolar macrophages (AM) during lung development. Although the seeding and differentiation of AM progenitors remained intact, the absence of 12-HETE led to a significant reduction of AM in the adult lungs and enhanced senescence due to increased prostaglandin E_2 production. A compromised AM compartment resulted in increased susceptibility to respiratory infections by pulmonary influenza A virus and SARS-CoV-2 infections. Collectively, our results highlight the complexity of prenatal RTM programming and reveal their dependency on *in trans* eicosanoid production by neutrophils for lifelong self-renewal.

BIOGRAPHY:

I grew up in France where I obtained a Master in Microbiology in University of Rennes 1 before moving to the Institut Pasteur in Paris for my doctoral studies on pulmonary infections. After completing my PhD, I moved to Montreal to join the laboratory of Pr. Maziar Divangahi at the Meakins-Christie Laboratories as a postdoctoral fellow. During my stay in Pr. Divangahi's lab, I studied how the eicosanoids determine pulmonary macrophages development and functions. I recently became an assistant professor at the University of Québec at Trois-Rivières where I continue my studies on respiratory diseases, with a special focus on neonatal immunity.

2014-2019: Postdoctoral fellow under the supervision of Drs. Maziar Divangahi and Christine McCusker
2019-2020: Research Assistant in Dr. Divangahi's lab
2020-2022: Research Associate in Dr. Divangahi's lab

Differential clinical phenotypes in bronchiectasis patients: evidence from cluster analysis

Esther Barreiro[1]

[1]Hospital del Mar Medical Research Institute, Spain

ABSTRACT:

Bronchiectasis is a chronic respiratory disease characterized by a permanent dilatation of the airways of different etiology. Bronchiectasis is a very heterogeneous and complex disease, in which patients experience recurrent exacerbations mainly due to bronchial infection. Exacerbations negatively impact on the patients' quality of life and disease prognosis. The immune response against infections is crucial in bronchiectasis patients. Neutrophilic inflammation is the predominant phenotype in these patients. In response to bacterial loads, neutrophils are recruited to the lungs, where they secrete antimicrobial peptides to fight against infection. However, other inflammatory cell types such as eosinophils are also involved in the pathobiology of bronchiectasis, particularly in the response to different biological agents as well as to inhaled corticosteroids. Lymphocytic infiltration was also demonstrated to take place in bronchiectasis. On the other hand, nutritional abnormalities and systemic inflammation are common in patients with chronic respiratory diseases including bronchiectasis. Phenotypic clustering has been defined in a large-cohort of patients with bronchiectasis (RIBRON, Spanish online registry). During the presentation an overview of the main results corresponding to the different analyses were provided. Differences between female and male patients were also analyzed as to the systemic manifestations including inflammation and muscle function. Additionally, using a data mining approach, five different clusters of bronchiectasis patients were identified in an initial stage. A refined analysis allowed us to merge a few of the clusters into three clinically different ones, whose specific clinical features were analyzed from different standpoints including systemic inflammation and nutritional abnormalities. Disease severity differed across the clusters. Two distinct clinical phenotypes of stable patients with non-CF bronchiectasis of a wide range of disease severity were also established on the basis of blood eosinophil counts using a biostatistical approach. Patients classified within the above-threshold cluster were those exhibiting a mild disease, significantly better clinical outcomes, lung function parameters, nutritional status, while showing lower levels of systemic inflammatory parameters. Low levels of eosinophils revealed a specific phenotype that was associated with poorer clinical outcomes such as disease severity and hospitalizations. Moreover, on the basis of blood neutrophil counts using a biostatistics approach two distinct clinical phenotypes of stable patients with bronchiectasis of a wide range of disease severity were also established. Patients classified within the above-threshold cluster were those exhibiting a severe disease, significantly worse clinical outcomes, lung function parameters and nutritional status, while showing greater levels of systemic inflammatory parameters. Clustering analyses of systemic blood parameters defined differential clinical phenotypes of bronchiectasis patients that were further confirmed by a logistic regression. Cluster analysis of systemic parameters offers a powerful tool to better characterize patients with bronchiectasis. These results have clinical implications in the management of the complexity and heterogeneity of these patients.

BIOGRAPHY:

Dr. Esther Barreiro (factor-H 62) is a Pulmonologist (Consultant 3) with clinical, research, and teaching activities. She is the director of the Research Group on Muscle Wasting and Cachexia in Chronic Respiratory Diseases and Lung Cancer, Hospital del Mar-IMIM and Pompeu Fabra University in Barcelona, Spain. Dr. Barreiro is also the coordinator of group CB06/06/0043 of the CIBER of the Spanish Respiratory Network of Excellence (CIBERES). Dr. Barreiro completed her medical studies at the *Universitat de Barcelona*, where she graduated in 1989 and became specialist in Respiratory Medicine (1994). Subsequently, she obtained her Master of Science degree at McGill University (Montreal, Canada, 2001) and her Ph.D. degree at *Universitat Pompeu Fabra* (Barcelona, 2002), under the supervision of Professors Sabah Hussain and Sheldon Magder. Dr. Barreiro

worked in the Meakins-Christie Labs (Royal Victoria Hospital facilities) at McGill University from September 1998 to September 2001. She enjoyed very much her stay at McGill over those three years. That was a great opportunity to acquire an incredible amount of knowledge, while also having fun with many colleagues and friends in Montreal's life. Dr. Barreiro has published almost 300 scientific articles including original research papers, reviews, and book chapters. She has also received financial support to carry out a great variety of research projects from public agencies, the pharmaceutical industry, and scientific societies, which reinforces the visibility and transferability of the results of her research. She is currently the Editor-in-Chief of the international journal *European Respiratory Journal Open Research* (European Respiratory Society), and has been Editor-in-Chief of the journals *Archivos de Bronconeumología* and *Open Respiratory Archives* of the Spanish Respiratory Society, she is also Associate Editor of the international journals *The Journal of Applied Physiology* and *European Respiratory Journal*, and is a member of the editorial board of the international journals *American Journal of Respiratory and Critical Care Medicine*, *Journal of COPD* and other journals. Dr. Barreiro also seats in many different national and international panels where research grants are assessed. She is a member of the scientific societies: Spanish Respiratory Society (SEPAR), European Respiratory Society (ERS), American Thoracic Society (ATS) and American Physiological Society (APS).

1999-2001: MSc, she obtained her Master of Science degree at McGill University (Montreal, Canada) 2002: Ph.D. degree at *Universitat Pompeu Fabra* (Barcelona, under the supervision of Professors Sabah Hussain and Sheldon Magder).Dr. Barreiro worked in the Meakins-Christie Labs (Royal Victoria Hospital facilities) at McGill University from September 1998 to September 2001.

Trained immunity in infectious and non-infectious pulmonary diseases

Eva Kaufmann[1]

[1]Queens University

ABSTRACT:

A hallmark of the adaptive immune system is its specific memory function. However, more than 95% of species rely solely on innate immunity for host defense. Nevertheless, they are better protected against re-encounter of pathogens through an epigenetically mediated trait called "innate immune memory" or "trained immunity". Not surprisingly, such an advantageous trait has been retained during the evolution of vertebrates. This recent discovery brings tremendous potential to better understand non-specific vaccine effects but also disease pathogeneses.

While the mechanistic advances of epigenetic imprinting and metabolic reprogramming in trained immunity have been described, its induction, duration, and maintenance are still under intense investigation. We envision that the long-lived induction of trained immunity through either direct infection of cells, pathogen-associated molecular patterns, or cytokine signaling, occurs centrally in the bone marrow, at the level of hematopoietic stem cells (HSCs), and peripherally at the tissue-resident level. Recently, we have demonstrated that the vaccine BCG and beta-glucan can generate protective trained immunity through HSCs reprogramming. In contrast, virulent *M. tuberculosis* induces reprogramming that renders the host more susceptible to the infection.

During the last decade, and particularly through the work carried out at Meakins-Christie-Labs, we have learned a lot about the impact of infections and vaccinations on immune training. Nevertheless, the implications of trained immunity in sterile inflammation, such as allergies, and the induction of innate immune memory through allergens, are still largely unknown and subject to my research program as Meakins alumnus. Defining the signatures of innate immunity during infectious and allergic airway diseases will enable us collectively to develop novel targeted immunotherapies against respiratory diseases.

BIOGRAPHY:

I am a tenure-track Assistant Professor in the Department of Biomedical and Molecular Sciences at Queen`s University in Kingston, Ontario, Canada. I am interested in the evolutionary concept of trained immunity, which describes epigenetic reprogramming in hematopoietic stem cells (HSC) leading to adaptations in innate immune cells, and thereby shaping the host response to infection and inflammation. Specifically, my research program focuses on the role of trained immunity in respiratory infection and allergic airway diseases. A better understanding of the mechanistic basis of trained immunity generation in asthma will improve our understandingof the pathogenesis of allergic diseases and has tremendous translational potential in the development of new therapeutic and preventive treatments.

To date, I have published 17 scientific articles, including first authorship manuscripts in Cell, Nature Immunology, and Cell Reports. In my lab at Queen’s University, I currently supervise one graduate and two undergraduate students, with one more grad student and one postdoc expected to join shortly. In addition to my supervised students, I am Thesis Committee Member of six further graduate students at Queen’s University in the Department of Biomedical and Molecular Sciences and in the Department of Medicine. Over the last 6 years, I established multiple productive collaborations that now range within Queen’s, across Canada, in the US, and abroad to Europe, including experts in trained immunity, immunology, respiratory infections, asthma, HSC research, animal models, and computational biology. At Queen’s, I am a committee member for the biweekly Plenary Seminar Series, inviting outstanding international researchers for presentation of their research, and connecting with students and faculty. Additionally, I am the faculty lead of the new DBMS flow cytometry core facility. With expertise in small animal and human cell-based models, I bridge basic and clinical research through selection from numerous established animal and humanized models to increase the translational relevance. Eva completed her postdoctoral fellowship under the supervision of Maziar Divangahi between 2016-2022.

Respiratory mechanics - in”sights” into respiratory function

Geoffrey Maksym[1]

[1]Dalhousie University

ABSTRACT:

When it is difficult to breathe, this is usually from abnormal respiratory mechanics. Airflow is impeded by mucous, airway narrowing from airway smooth muscle constriction and airway remodelling as occurs in asthma. Or the tissues can weaken through tissue and airway loss and the loss of alveolar tethering in emphysema, impeding exhalation. Or conversely the lung can become too stiff, through fibrosis and scarring, or from the loss of accessible lung volume from either atelectasis or obstructed airways. Can we discern these many different factors from lung function measures? Oscillometry has emerged as a tool that is sensitive to changes due to lung disease and helps us better understanding of the impact of disease on lung function but can be challenging to interpret. For example, resistance to oscillatory flow during breathing increases with airway narrowing and is usually inversely frequency dependent in disease in humans, thought to assess abnormal heterogeneity in small airways, but frequency dependence is also present in health in the very young and in small animals. Low frequency reactance from oscillometry is an index of elastance which is associated with stiffening of lung tissue, but can also increase in magnitude with tissue loss, causing loss of accessible airspaces and lung volume in COPD. This presentation will describe my experience with oscillometry, show normal and abnormal examples of oscillometry coupled with functional image data from asthma, COPD, ILD and lung transplant, and show how measurements, modelling and imaging have aided our understanding of lung disease and evolved our understanding of how disease affects lung mechanics, but also, how these in turn have aided our understanding of our measurements of oscillometry.

BIOGRAPHY:

Geoff Maksym first arrived at the Meakins-Christie joining the laboratory of Dr Jason Bates in 1991, spending six wonderful years there measuring and modelling lung mechanics, completing a master’s in electrical engineering and then one of the first doctorates in Biomedical Engineering at McGill. After a post-doc at the Harvard School of Public Health measuring airway smooth muscle cell mechanobiology, he started at Dalhousie in 2000 where he is now a Professor in the School of Biomedical Engineering, serving as Director for 11 years, and heads the respiratory cell and lung mechanics laboratory. He develops tools to probe the properties of the lung from the cell to the patient, including developing magnetic twisting cytometry, oscillometry for lung mechanics and he is cofounder of Thorasys, Montreal which commercialized the tremoflo Oscillometer. His research interests include measurement and computational modeling of respiratory mechanical function, as well as combining these with imaging methodologies including MRI and SPECT/CT from asthma, COPD, lung transplant and recently lung cancer. He has served on programming committees and as track and assembly chairs for the Biomedical Engineering Society and the Respiratory Structure Function Assembly of the American Thoracic Society, serving as grant review panel member for the Canadian Thoracic Society, Canadian Institutes of Health Research, NSERC and the Nova Scotia Health Research Foundation and Lung Association of Nova Scotia, and is an Associate Editor for the Journal of Applied Physiology.

1991-93: MSc under the supervision of Dr. Jason Bates1993-97: PhD under the supervision of Dr. Jason Bates

Understanding lung disease using agent-based models

Jason Bates[1]

[1]University of Vermont, USA

ABSTRACT:

Agent-based modeling (ABM) is a computational technique that creates a virtual reality mapping to actual reality without the intermediary of mathematical equations. ABM is ideally suited to the computational exploration of cellular behavior because it represents individual cells as discrete agents following rules of behavior presumed to correspond those exhibited by real cells. Accordingly, ABM relies on biologic expertise as much as on the technical skills of coders, and thus affords a means by which biomedical and mathematical/computational scientists can collaborate on an equal footing. In this talk, I will describe how I and my colleagues have used ABM to gain insights into the way that allergic inflammation may be controlled, the morphogenesis of pulmonary fibrotic lesions, and the strategies that nature uses to maintain biologic tissue throughout life and to repair it when injured.

BIOGRAPHY:

Jason H.T. Bates, PhD, DSc, is a respiratory biomedical engineer and physiologist working predominately in the field of lung mechanics with a focus on the biophysical mechanisms of airways responsiveness and the pathophysiology of ventilator-induced lung injury. Dr. Bates received a bachelors degree with first-class honors in physics from the University of Canterbury, New Zealand in 1978 and a PhD in medicine from the University of Otago in 1981. In 1983 he joined the Meakins-Christie Laboratories as a post-doctoral researcher under the mentorship of Dr. Joseph Milic-Emili, and in 1986 he became a research director at the Meakins-Christie Labs and joined the academic faculty of McGill in the Departments of Medicine and Biomedical Engineering until 1999. He is currently a Professor of Medicine, Molecular Physiology & Biophysics, and Electrical & Biomedical Engineering at the University of Vermont. From 2010-14 he also served as Interim Director of the University of Vermont School of Engineering. Dr. Bates has co-authored more than 330 peer-reviewed scientific papers as well as numerous other articles. In 2009 he authored a book published by Cambridge University Press entitled “Lung Mechanics. An Inverse Modeling Approach”. Dr. Bates is a Fellow of the American Institute for Medical & Biological Engineering, a Fellow of the Biomedical Engineering Society, a Fellow of the American Thoracic Society, and a Senior member of the Institute of Electrical & Electronic Engineers.

1983-86: Research Fellow under Dr. J. Milic-Emili1986-99: Research Director at the MCL1995-98: Associate Director, MCL

Metabolomic biomarkers in COPD and its phenotypes

Joaquim Gea[1]

[1]Universitat Pompeu Fabra, Hospital del Mar, Spain

ABSTRACT:

COPD is a highly prevalent disorder with heterogeneous clinical presentations. Many attempts have been made in the last decade to group COPD patients in different phenotypes, or even better treatable traits, according to their characteristics. These groups are probably associated with distinct pathophysiological factors and mechanisms. However, our present knowledge on these mechanisms still does not allow us to offer a more personalized management to the patients. The use of biological markers seems to be the most appropriate way of identifying these mechanisms, and assigning each patient to a more specific subgroup. Different 'omic sciences', including metabolomics (study of the metabolites and their corresponding pathways), can help in this objective. Numerous metabolomic changes have been already described in the blood and other biological samples of COPD. Probably those markers obtained from blood are the most relevant due to the ease of obtaining samples, which may allow their use in clinics. The main changes that have already been observed in COPD include different amino acid, lipids (mainly phospholipids and eicosanoids) and components of nucleic acids. We hypothesize that the present most accepted phenotypes could evidence diverse metabolomic profiles, which could help to differentiate them. Therefore, we have studied blood samples from two cohorts of patients with COPD (one of relatively young individuals and the other including older subjects) of both sexes and including a wide spectrum of clinical characteristics, performing transcriptomic, proteomic and metabolomic studies. Our results indicate that the metabolomic signatures of COPD patients share many common elements, but they also differ on others, which appear to be related to age, sex, and their clinical phenotypes.

BIOGRAPHY:

Joaquim Gea obtained his MD (1979) and PhD (1989, Directors: Robert Rodríguez-Roisin and Peter D. Wagner) degrees at the University of Barcelona, being specialist in both Internal Medicine (1981) and Pneumology (1985). He has been Head of the Pneumology Department at Hospital del Mar (2005-21), and is Full Professor of Human Physiology at the Pompeu Fabra University in Barcelona (2009), having also served as the Dean of the Faculty of Medicine (2011-23). Joaquim was Visiting Professor at McGill University (Montreal, Canada, 1994-95), and more specifically at the Meakins-Christie Laboratories, where he conducted studies on changes in the molecular and fibrillar composition of respiratory muscles in an animal model of COPD, under the direction of Prof. Alejandro Grassino and Prof. Quatyba A. Hamid. He has already participated in the former events of the 25th and 40th anniversaries of these laboratories. Joaquim has also completed a 7-month stay, linked to metabolomics studies in COPD under the direction of prof. Eyal Gottlieb, at the Technion Institute of Israel (2022-23). On the other hand, he has also been Associate Professor at the John's Hopkins University School of Medicine (Fall Institute, 2009-10) and Deputy Director of the Spanish Network of Excellence in Research in Respiratory Diseases (CIBERES, 2011- 2015). Dr. Gea has also been president of the Commission for Residents' training (1992-94) and the Research Commission both at Hospital del Mar (2007-2012). He has been funded by 73 competitive grants, including 5 projects from the European Commission, having directed 25 doctoral theses and 5 master's theses. Finally, Joaquim has published over 340 original articles and reviews in peer-reviewed journals, as well as 57 book chapters. His main areas of work are chronic airway diseases, and specifically nutrition and muscle function, as well as potential blood biomarkers in these disorders.

1994-95: Visiting Professor under the supervision of Drs. Alex Grassino and Qutayba Hamid

Lung research in a computational laboratory

Jun Ding[1]

[1]McGill University

ABSTRACT:

The emerging single-cell multi-omics datasets present unrivaled opportunities to understand complex biological processes from comprehensive perspectives, but the distinct feature spaces associated with different modalities pose challenges in data integration and downstream analyses. Here we report scCross, an algorithm based on the combination of a variational autoencoder and generative adversarial network (VAE-GAN) that can integrate the features from different modalities to learn joint cell embeddings. We applied scCross to integrate and analyze various single-cell multi-omics data, including dual-omics and triple-omics data integration. scCross is able to map all data modalities to a shared latent space, allowing for various downstream data analytic tasks. scCross outperforms existing methods for data integration of single-cell multi-omics data and is able to generate single-cell data across modalities. Moreover, scCross can infer intra-modal and inter-modal perturbations to manipulate the cellular states, which can be leveraged to discover interventions and therapeutics against various diseases.

BIOGRAPHY:

Jun Ding (https://www.meakinsmcgill.com/ding/) is an assistant professor in the Department of Medicine, McGill University Health Centre since March 2021. Before that, he was trained as a postdoc at the Computational Biology Department, School of Computer Science, Carnegie Mellon University, under the supervision of Dr. Ziv Bar-Joseph. In 2016, he received his PhD. in Computer Science from the University of Central Florida. His research focuses on developing machine learning methods to drive biological discoveries and medical innovations by analyzing and modeling large-scale biomedical data, especially single-cell genomics data. Jun had published ~30 papers in leading computational biology journals such as genome research and cell stem cell, over 10 of which are about machine learning approaches for cell identification and trajectory inference from single-cell datasets. Many of the computational models that Jun developed had led to significant biomedical advances. Currently, Jun is particularly interested in developing computational models and visualizations to decode cellular dynamics in a variety of biological processes, particularly in pulmonary diseases (e.g., cell differentiation and disease progression) from single-cell multimodal measurements.

A personal journey from mucus rheology and mucociliary clearance to Indigenous respiratory health and disease

Malcolm King[1]

[1]University of Saskatchewan

ABSTRACT:

I spent 11 wonderful years at the Meakins-Christie Labs, from Oct 1974 to Nov 1985. This included a postdoctoral fellowship with Dr. PT Macklem (MRC Centennial Fellow 1975-78); two years as a Lecturer; and then five years as an Asst. Professor and MRC Scholar 1980-85. I then went on to Univ. Alberta, where I rose to the rank of Professor and member of the Pulmonary Research Group. I returned to the Meakins-Christie for a sabbatical year 1996-97, hosted by Dr. Eidelman.

I subsequently became President of the Canadian Thoracic Society 1999-2000 (first PhD President of CTS, as well as first Indigenous President). I became more involved in Indigenous health research at the University of Alberta, seeing the need for Indigenous people to achieve equity, which required increasing participation of Indigenous people in research and professional training. My research increasingly turned to health issues of importance to Indigenous communities. This included not only chronic lung disease and tuberculosis, but also diabetes and chronic kidney disease, equitable access to health services, and mental wellness. I served the Indigenous community as Scientific Director of the CIHR Institute of Indigenous Peoples' Health 2009-2016. I currently serve as Scientific Director of the Saskatchewan Centre for Patient-Oriented Research. I also work with several First Nation and Métis communities on research to help them achieve wellness.

My presentation outlines some of the highlights of my time a the Meakins-Christie Labs. I reveal to the audience what was really important to me in my subsequent years as a researcher and administrator - not so much the research findings but the ways of working with colleagues, trainees and communities. My years at the Meakins-Christie Labs were very important in shaping the subsequent years of my career.

BIOGRAPHY:

Professor Malcolm King is a member of the Mississaugas of the Credit First Nation in Ontario and a health researcher at the University of Saskatchewan. Prof. King served as Scientific Director of the CIHR Institute of Aboriginal Peoples' Health from 2009 to 2016, and is currently the Scientific Director of the Saskatchewan Centre for Patient-Oriented Research. His research is aimed at improving wellness and achieving health equity for First Nations, Métis and Inuit through strengths-based approaches that respect self-determination and privilege Indigenous ways of knowing. Honoured with a National Aboriginal Achievement Award in 1999, he was elected a Fellow of the Canadian Academy of Health Sciences in 2016 and a Fellow of the Royal Society of Canada in 2021.

Malcolm spent a total of 12 years at the Meakins-Christie Labs, from Oct 1974 to Nov 1985, and then 1996-97. He was first a postdoctoral fellow with Dr. Peter T Macklem, then a Lecturer and finally Assistant Professor and MRC Scholar 1980-85. He returned in 1996 for a year's sabbatical.

1974-1978: Fellow under the supervision of Dr. Peter Macklem
1999-2000: Visiting Scholar under Dr. David Eidelman

Unlocking the power of innate immunity against pulmonary infections

Maziar Divangahi[1]

[1]McGill University

ABSTRACT:

Respiratory infections cause more than 4 million deaths per year, with influenza virus, *Mycobacterium tuberculosis* (*Mtb*), and now SARS-CoV-2, being major causes of mortality and morbidity worldwide. *The overarching focus of our research program* is to investigate the regulatory mechanisms involved in innate and adaptive immunity against these old (TB and Influenza) and new (COVID-19) pandemics and to broadly understand critical differences between protective and deleterious immune responses. More specifically, our studies seek to understand the full spectrum of two evolutionarily conserved host defense strategies, “disease tolerance” and “trained immunity” against these major pulmonary infections. Related to these research foci, we are investigating the contribution of hematopoietic stem cells (HSCs) to innate immune memory (trained immunity) as a platform for developing new host-directed immunotherapies or vaccines against infections.

BIOGRAPHY:

Dr. Maziar Divangahi is a Professor of Medicine at McGill University. Dr. Divangahi is the Associate Director of the Meakins-Christie Laboratories, past Co-Leader of the Respiratory Program at the Research Institute of the McGill University Health Centre, and an Associate Director of the McGill International TB Centre. He is an internationally recognized pulmonary immunologist and the overarching focus of his research program is to investigate the regulatory mechanisms involved in host resistance and disease tolerance against major pulmonary bacterial (Mycobacterium tuberculosis) and viral (influenza virus and SARS-CoV2) pathogens. He is currently investigating how to harness the power of innate immunity in vaccine via reprogramming of hematopoietic stem cells. Throughout his career, he has been a proliferative investigator publishing in outstanding journals and received numerous awards, including a CIHR New Investigator Award, FRQS Award, and the CIHR Foundation grant. His scholarly work has been recognized by election to the Royal Society of Canada. He is currently holding the Strauss Chair in Respiratory Diseases.

Clinical and translational respiratory research at the Chang Gung Memorial Hospitals: A Taiwanese perspective

Meng-Chih Lin[1]

[1]Chang Gung University, Taiwan

ABSTRACT:

Chang Gung Medical Foundation is the largest private medical and hospital network in Taiwan. Since its establishment in 1973, it has comprised a total of 10 branch hospitals and three universities. I went to study at Meakins-Christis Laboratory (MCL) of McGill University in Canada in 1996 and was the first international research fellow of Dr. Basil Petrof. We carried out experiments to explore the pathophysiology of diaphragmatic injury during sepsis or mechanical ventilation under supervision of Prof. Petrof. The research knowledge and experimental skills I had learned during this year enabled me to improve my research capability after returning to Taiwan. Over the past 25 years, I have been able to contribute what I have learned and lead the respiratory research of the different Chang Gung hospitals I have served to a better status.

The content of my speech will include sharing the experience and outcome of respiratory research at Chang Gung hospitals that I participated in and led in the past, and also introducing the administrative management system that encourages and evaluates medical research in Chang Gung. Though most of our respiratory research is clinical research, translational research has been conducted in different topics. All research results were always aimed for clinically use. We are also very much looking forward to having the opportunity to collaborate with international medical institutions.

BIOGRAPHY:

Education: Chung Shan Medical University, Taichung, Taiwan 1978-1985

Post-graduate Education: McGill University, Montreal, Canada 1996-1997

Academic Appointments: Professor, Chang Gung Memorial Hospital 2010-Professor, Tsing-Hua University, Beijing, China 2011-2017Professor, Chang Gung University 2011-Member, Education Committee, Asia Pacific Society of Respirology 2017-Member, Planning and Acting Committee, Asia Pacific Society of Respiratory 2021-

Research Interests: Obstructive Sleep Apnea, Lung Cancer, Respiratory failure, Airway diseases

1996-97: Postdoctoral fellow under Dr. Basil Petrof

Influence of the Meakins-Christie on respiratory research in Japan

Michiaki Mishima[1], Satoru Ebihara[2]

[1]Kyoto University, [2]Tohoku University

ABSTRACT:

The first fellow from Japan to Meakins-Christie laboratory (MCL) is Yoshinosuke Fukuchi, Professor Emeritus at Juntendo University. In 1974-1976, he studied under the supervision of Prof. Macklem. After that, fellows from Japan went to study at MCL one after another, and now there are more than 50 fellows in total, and they have played a major role in the respiratory disease research community in Japan. While the number of people who had studied at MCL in Japan was accumulating, in 2001, Prof. Fukuchi held the Annual Assembly of the Japanese Respiratory Society and invited many directors, including the president of MCL at that time, Prof. Martin. At the same time, a big reunion party of MCL Japanese Fellows was held. Since then, the MCL Fellow Alumni Reunion has been held every year at same timing with the annual meetings of the Japanese Respiratory Society, and has continued to this day. Communication there has often inspired new research and led to creative joint research. Under the pandemic of COVID-19, it was held remotely and continued without interruption. A number of leading professors of respiratory disease in Japan have been produced from this MCL alumni. In this symposium, we would like to introduce some of them and their recent research.

BIOGRAPHY :

Michiaki Mishima, MD, PhD:
1977 M.D. Cum laude, Faculty of Medicine, Kyoto University, Japan
1986 Ph.D., Graduate School of Medicine, Kyoto University, Japan
1992-1994 Visiting Researcher, Meakins-Christie laboratories. Supervisor: Prof. Jason Bates.
2001-2016 Professor and Chairman, Department of Respiratory Medicine, Graduate School of Medicine, Kyoto University, Kyoto, Japan.
2011-2015 Director, Kyoto University Hospital, Kyoto, Japan
2022-presnt President, Osaka Saiseikai Noe Medical Welfare Center, Osaka, Japan

Satoru Ebihara, MD, PhD:
1990 MD, School of Medicine, Tohoku University, Sendai, Japan
1994 PhD, Tohoku University Graduate School of Medicine, Sendai, Japan
1996-2000 Post-doctoral Fellow, Meakins-Christie laboratories. Supervisor: Prof. Basil J .Petrof.
2014-2021 Professor, Department of Rehabilitation Medicine, Toho University Graduate School of Medicine, Tokyo, Japan
2022-present Professor and Chairman, Department of Internal Medicine and Rehabilitation Science, Tohoku University Graduate School of Medicine, Sendai, Japan

The past is a foreign country - Life lessons from the Meakins-Christie

Peter Calverley[1]

[1]University of Liverpool, UK

ABSTRACT:

In this presentation I will review some of the many life lessons I learned from my time at the Meakins. Included in these were the need to look carefully at your original data as illustrated by our studies on sleep-disordered breathing in Duchenne muscular dystrophy and to challenge received wisdom as we did in systematically exploring the limits of bronchodilator reversibility testing in COPD. Other important lessons include being prepared to accept setbacks as the inhaled corticosteroids in COPD saga illustrates and to remember old physiological ideas which come in useful later like oscillatory lung mechanics. Finally I learnt that what goes around , comes around as with the concept of the Lung in Transition between Health and Disease which we have now revisited in a new UK cohort study of younger smokers.

BIOGRAPHY:

Peter Calverley is Emeritus Professor of Respiratory Medicine at the University of Liverpool, UK and continues to work in the Institute of Life Courses and Medical Science. He trained at the University of Edinburgh, was a travelling fellow at the Meakins-Christie Laboratories at McGill University, Montreal 1982-3 and subsequently moved to Liverpool, becoming a full professor in 1995. His research interests focus on the patho-physiology and management of chronic obstructive pulmonary disease He has published over 500 papers and several textbooks as well as lecturing widely on these topics.

Professor Calverley was Associate Editor of *Thorax* till 2010 and Associate Editor of the American Journal of Respiratory and Critical Care Medicine until 2022. He is currently Editor in Chief of the European Respiratory Monograph. He has chaired the scientific committee of the British Lung Foundation, the British Sleep Society and the Clinical Physiology Assembly of the ERS and was a member of the ERS Executive Committee. He was a founder member of the GOLD initiative for COPD and chaired its Dissemination Committee and Scientific Committee. He was President of the British Thoracic Society in 2006, co-chaired the External Reference Group advising Ministers on the content of the COPD Clinical Service Strategy and chaired the Respiratory Specialty groups of the UK Comprehensive Clinical Research Network until 2015. He currently Chairs the UK BEACON study (British Early COpd Network) researching the origins of COPD in young adults.

He is a Fellow of both the London and Edinburgh Colleges of Physicians and was elected to the Fellowship of the Academy of Medical Sciences in 2011, the European Respiratory Society in 2014, the American Thoracic Society and The Association of Physicians of Great Britain and Ireland in 2020.

1982-83: Research fellow under the supervision of Dr. Joseph Milic-Emili

IL5 from discovery to clinical implication

Qutayba Hamid[1]

[1]McGill University, University of Sharjah

ABSTRACT:

IL-5 is an essential cytokine for the activation, recruitment and survival of Eosinophils. Eosinophilic inflammation is one of the main features of asthmatics. The expression of IL-5 in Asthma was reported in the early nineties using in situ hybridization and was followed by describing the predominance of Th-2 cytokine in allergy and asthma. The initial report of possible involvement of IL-5 in Asthma was followed by many papers to support its role in vitro and in vivo using animal models. Further studies confirmed IL-5 upregulation in human tissue. Initial clinical trials failed to show the value of monoclonal antibodies against IL-5 in antigen induced asthma in human. However, the discovery of asthma phenotypes and the use of biomarker including the level of eosinophil in sputum and blood has shown the efficacy of using monoclonal antibodies to IL-5 or its receptor in steroid hypo-responsive, severe asthmatic and currently there are 3 medications available to target IL-5 with similar results.

Recently, we have demonstrated that IL-5 receptors are expressed on fibroblasts of airways of normal and asthmatics and found that IL-5 could induce the fibroblast to proliferate and produce extra-cellular matrix and suggest a possible role of Anti IL-5 in regulating subepithelial fibrosis that is one of the features of severe asthma and COPD. These experimental data support initial report of the ability of Anti-IL 5 modulating airway remodeling via the down-regulation of extra cellular matrix proteins.

BIOGRAPHY:

Dr Hamid is Professor of Medicine, Vice Chancellor for Medical & Health Sciences Colleges, and Dean of College of Medicine at the University of Sharjah. He was until 2016 the Strauss chair of Respiratory Medicine, James McGill Professor and the Director of the Meakins Christie labs at McGill University, Canada.

Dr. Hamid has published over 590 scientific articles in prestigious international journals and has contributed more than 150 chapters and review articles. He is the editor of 2 textbooks for Respiratory Cell and Molecular Biology and Respiratory Physiology. He has been a visiting professor worldwide at Universities in Japan, USA and Europe, Dr. Hamid has served in many advisory committees in Canada and the UAE.

In addition to obtaining a PhD from the Imperial College, University of London, Dr Hamid is a member Royal College of Physicians (MRCP), London, UK, , Fellow of the Royal College of Pathologists (FRCPath) and a Fellow of the Royal College of Physicians (FRCPC), Canada.

Dr Hamid has received many awards including Best Clinical Scientist in Canada award, Distinguished Respiratory scientist award in the USA and was to be a Fellow of Royal Society. He recently received Hamdan Bin Rashid Medical Prize and Mohammed Bin Rahsid Medal for life achievement.

Dr Hamid is well known internationally for his work in the area of Asthma and COPD.

Discovery of new autophagy genes regulating skeletal muscle health

Sabah Hussain[1]

[1]McGill University

ABSTRACT:

Autophagy is a critical process in the regulation of muscle mass, function and integrity. The molecular mechanisms regulating autophagy are complex and still partly understood. Here, we identify and characterize a novel FoxO dependent gene, d230025d16rik which we named Mytho (Macroautophagy and YouTH Optimizer), as a regulator of autophagy and skeletal muscle integrity in vivo. Mytho is significantly up-regulated in various mouse models of skeletal muscle atrophy. Short term depletion of MYTHO in mice attenuates muscle atrophy caused by fasting, denervation, cancer cachexia and sepsis. While MYTHO overexpression is sufficient to trigger muscle atrophy, MYTHO knockdown results in a progressive increase in muscle mass associated with a sustained activation of the mTORC1 signaling pathway. Prolonged MYTHO knockdown is associated with severe myopathic features, including impaired autophagy, muscle weakness, myofiber degeneration, and extensive ultrastructural defects, such as accumulation of autophagic vacuoles and tubular aggregates. Inhibition of the mTORC1 signaling pathway in mice using rapamycin treatment attenuates the myopathic phenotype triggered by MYTHO knockdown. We conclude that MYTHO is a key regulator of muscle autophagy and integrity.

BIOGRAPHY:

Graduated from Medical School, University of Baghdad in 1978. Joined the Meakins-Christie Laboratories 1982 as a PhD student, Department of Physiology, McGill University. Graduated in 1989 with a PhD degree in Physiology. Spent one year post-doctoral fellowship at the Division of Critical Care, Department of Medicine, McGill University. Obtained an Assistant Professor position at the Department of Medicine, McGill University in 1990. Joined the Meakins-Christie Laboratories as a Research Director in 1990. Promoted to Associate Professor and Professor in 1996 and 2094, respectively. Promoted to James McGill Professor of Medicine in 2005. Promoted to Distinguished James McGill Professor of Medicine in 2019.

Breathe with your brain, think with your lungs: the Meakins-Christie as a beacon for out-of-the-box navigation

Thomas Similowski[1]

[1]Inserm-Sorbonne University, France

ABSTRACT:

Vital functions are autonomous. Thus, a heart can continue to beat outside the body. Breathing represents a singular exception to this rule: it depends on skeletal muscles answering commands that originate in the central nervous system rather than in the respiratory system itself. Take the lungs outside the body: nothing happens. Furthermore, and also in contrast with other vital functions, breathing can be decoupled from the body's homeostatic needs (*Peter Macklem would have chastised homeostatic and preferred homeokinetic, because"Thomas, life if anything but static"*). Indeed, the brainstem central pattern generators (CPGs) that produce and regulate metabolic breathing can be temporarily superseded by respiratory-related corticospinal circuits. They allow the voluntary control of breathing and the use of the respiratory system for non-respiratory actions. These circuits exert a tonic facilitatory activity on automatic breathing during wakefulness. They can be "recruited" to maintain ventilation when the brainstem CPGs are defective. For example, a respiratory-related cortical activity is associated with the maintenance of ventilation in patients with congenital central alveolar hypoventilation (CCAH) due to PHOX2B mutations (Ondine's curse syndrome). But the human cerebral cortex does not like to share. When it is engaged to help CCAH patients breathe, mobilizing it to perform cognitive tasks can disrupt breathing to the point of hypoventilation. Reciprocally, CCAH patients can exhibit better cognitive performance when mechanically ventilated. These observations characterize dual-tasking. The respiratory-related cortical circuits also engage in the presence of respiratory muscle loading, respiratory muscle weakness, or their combination, contributing to maintaining adequate alveolar ventilation. A convergent body of experimental data in healthy humans indicates that respiratory-related cortical activity is associated with various types of cognitive impairment. This can result from competition for cortical resources, dyspnea-related attentional diversion, or both. In addition, preliminary clinical data suggest that initiating non-invasive ventilation in patients with chronic respiratory failure can rapidly improve cognitive performance. From this, two conclusions (*I can hear Milic, almost Yoda-like, booming something like "Tômâ, if you conclude, conclude! There can be only one conclusion"*): 1) we need our brain to breathe right and good lungs to think straight; 2) cognitive testing should become an outcome of dyspnea-relieving interventions.

BIOGRAPHY:

Thomas Similowski is 62, married, and the father of 4. His medical background combines respiratory medicine, intensive care medicine, and clinical physiology. He worked as a research fellow with Milic during a Paris sabbatical in 1987. He then stayed at the Meakins in 1988 and 1989 (namely 35 kilos ago), working with Milic, Jason Bates, François Bellemare, Peter Macklem, and many others, some of whom unusual characters, but all fondly remembered. Specializing in respiratory neurophysiology, a research domain that he has pioneered, Thomas likes to present himself as the respiratory physician who knows less about the lungs (but most about the brain). He currently heads a large hospital structure that includes a respiratory medicine department, an intensive care medicine one, a pulmonary function testing lab, a sleep medicine structure, and a pulmonary rehabilitation facility. Thomas also leads a research unit that covers respiratory neurophysiology with approaches ranging from molecular biology to physiology, psychophysiology, and humanities. He likes connections, disorder, and divergence. And to play scrabble (in French).

1988-89: Postdoctoral fellow under the supervision of Drs. Joseph Milic-Emili and Peter Macklem

Lessons in mentorship and career development

Tony Eissa[1]

[1]University of California at Irvine, USA

ABSTRACT:

Research training at Meakins-Christie laboratories was my first introduction to research. It was a great opportunity for me to work side by side with a large group of brilliant scientist and great mentors. I was fortunate to train under the guidance of Dr. Joseph Milic-Emili. Dr. Milic was very generous with his time and guidance. My time at Meakins was very productive and that helped my career trajectory afterwards. Following my training at Meakins, I received further training in molecular and cell biology. My post-Meakins research career was mostly molecular and quite different from the type of training I received at Meakins. However, the research tools I learned at Meakins were instrumental in my post-Meakins career. In this presentation, I list some of the lessons I learned and I applied it in my career.

BRIEF BIOGRAPHY:

Associate Chief of Staff for research and development at the Long Beach Veterans Affairs (LBVA) and as the Associate Dean for VA research at UCI. Dr. Eissa's research has focused on the molecular mechanisms of inflammation and innate immunity and translational therapeutics for lung disease. Dr. Eissa has broad background in physiology, immunology, molecular cell biology and clinical research. His research program is credited for several key discoveries in the field of gene therapy, nitric oxide, regulation of misfolded proteins, lung inflammation, host pathogen interactions and autophagy. He has served on many study sections for NIH, American Heart Association, Alpha One Foundation, Department of Defense and March of Dimes.

1989-91: Postdoctoral fellow under the supervision of Dr. Joseph Milic-Emili