

**IMO5**

**WORKSHOP**

**NOVEMBER 8-13, 2015**



**IMMUNE CANCER**

**[IMO5.eventbrite.com](http://IMO5.eventbrite.com)**



# Integrated Mathematical Oncology

On behalf of the department of Integrated Mathematical Oncology we welcome you to the 5th annual workshop, “Immune Cancer”. It is widely assumed that all clinical cancers must overcome the predator-like effects of the immune system during the course of their development and that harnessing the immune response to tumors could be an effective therapy. However, only in the last few years has immunotherapy begun to fulfill its promise as new agents and strategies are beginning to elicit significant tumor responses. Unfortunately, like other tumor treatments, immunotherapy is typically defeated by the tumor evolutionary response. This workshop will consider all aspects of the immune-tumor interaction through a range of cancers and treatments. Most cancers have at least a few effective therapies, but even these few produce a huge therapeutic parameter space of drug combination and dose schedules. An obvious challenge then is how to combine therapies that exploit an immune response, whilst maximizing tumor response and minimizing immune toxicity and treatment resistance. This will be the central theme of our workshop this year.

This workshop is designed to motivate and facilitate a hands-on modeling experience focused on the role of the immune system in cancer. The workshop will divide into four teams integrating clinical, experimental and theoretical members to develop and implement a mathematical model focussed on the role of the immune system in cancer progression and treatment. The teams are expected to come up with a model, analyze it and give a presentation all within 4.5 intense days. The color of the dot on your badge indicates the team that you have been allocated. These colors continue throughout the timetable to indicate where each team should go for there breakout sessions.

● RED

● GREEN

● Yellow

● Blue

The primary goals of each team are to (i) Cultivate interdisciplinary collaboration to promote the exchange of ideas and develop novel approaches to understanding the tumor-immune dialogue (ii) Focus on a specific question relevant to this dialogue (iii) Develop a mathematical/computational model to facilitate answering this question (iv) Utilize this model in a practical manner and (v) Produce an integrated coherent presentation. Critical to the success of each team and the workshop as a whole is participation, so please attend as much of the meeting as possible, the teams cannot function otherwise.

The logo for Integrated Mathematical Oncology (IMO) features the letters 'i', 'M', and 'O' in a stylized, white, blocky font. The 'i' has a dot, the 'M' has a central vertical bar, and the 'O' is a solid circle. To the right of the 'O' is a large, white, stylized number '5' with a curved tail that loops back to the right. The entire logo is set against a black background.

# Integrated Mathematical Oncology


The workshop format has evolved over the years, based on the feedback we received from each year, and has converged on what you will experience this week. Each team independently will begin with short introductory presentations from the team leaders to motivate each team and give relevant information. We will have 2 updates that bring the teams together on Monday and Thursday. The 1st one is the Question presentation: by the afternoon break today, each team needs to have already agreed upon a question. The 2nd is to have a single specific aims page that serves as part of the pilot grant application and must be sent to me by 4pm on Thursday. These aims will also need to be presented to the greater group during the Thursday afternoon break. These presentations can be done by any member(s) of the team and should be oral only for the question and a 1-2 slides for the specific aims.

Please remember this is a competition and we have a number of judges who will view your closing presentation: Bob Gatenby, P. K. Burnette, Shari Pilon-Thomas and Me. Each year we award the team leaders of the winning team a \$50,000 pilot grant. The primary purpose of this grant will be to facilitate model validation and subsequent collaboration. In addition, every active member (as defined by the team leaders) of the winning team will receive a \$75 Amazon gift voucher. Judges will be scoring several criteria, including (i) Importance of the question, (ii) Originality of the approach, (iii) Degree of success, (iv) Quality of presentation, (v) Degree of integration. Depending on how close the runner-up team is in score to the winning team we will also award every active member (as defined by the team leaders) of the runner-up team a \$25 Amazon gift voucher. After the winning team has been chosen a more formal budget will be requested before the funds can be released. Each of the three winning team leaders will be considered joint PIs with the contact PI being an IMO member.

We hope you enjoy this intense experience and learn to communicate across disciplines, by helping provide the tools and skills required to approach the complexities of cancer with broader perspectives, and create a truly integrated and collaborative environment for all the investigators involved in the study of cancer.

Good luck and happy model building!

**Sandy Anderson.**



# monday

NOVEMBER 9, 2015

8:00 am

-

Registration

SRB

9:00 am

Breakfast

Atrium

9:00 am

-

Introduction  
Sandy Anderson

SRB

Ferman

10:30 am

2014 Winning team Presentation

10:30 am

-

Working Group  
Session I

PI-2

PI-3

Atrium 4

Collaboratorium

1:00 pm

1:00 pm

-

Lunch

SRB

Atrium

1:45 pm

PI-2

PI-3

Atrium 4

Collaboratorium

1:45 pm

-

Working Group  
Session II

4:00 pm

4:00 pm

-

Question Presentation

SRB

Ferman

4:30 pm

PI-2

PI-3

Atrium 4

Collaboratorium

4:30 pm

-

Working Group  
Session III

7:00 pm



# tuesday

NOVEMBER 10, 2015

8:30 am

–

9:00 am

BREAKFAST

SRB  
Atrium

9:30 am

–

1:00 pm

Working Group  
Session IV

Atrium 2

Collaboratorium

PI-3

Atrium 4

1:00 pm

–

1:45 pm

LUNCH

SRB  
Atrium

1:45 pm

–

4:00 pm

Working Group  
Session V

Atrium 2

Collaboratorium

PI-3

Atrium 4

4:00 pm

–

4:30 pm

BREAK

SRB  
Atrium

4:30 pm

–

7:00 pm

Working Group  
Session VI

Atrium 2

Collaboratorium

PI-3

Atrium 4

# wednesday

NOVEMBER 11, 2015

8:30 am

-

9:00 am

BREAKFAST

SRB  
ATRIUM

9:30 am

-

1:00 pm

Working Group  
Session VII

Collaboratorium

Atrium 2

Atrium 3

PI-3

1:00 pm

-

1:45 pm

LUNCH

SRB  
Atrium

1:45 pm

-

4:00 pm

Working Group  
Session VIII

Collaboratorium

Atrium 2

Atrium 3

PI-3

4:00 pm

-

4:30 pm

BREAK

SRB  
Atrium

4:30 PM

-

7:00 PM

Working Group  
Session IX

Collaboratorium

Atrium 2

Atrium 3

PI-3

# thursday

NOVEMBER 12, 2015

8:30 am

–

9:00 am

Breakfast

SRB  
Atrium

9:30 am

–

1:00 pm

Working Group  
Session X

PI-3

Atrium 4

Collaboratorium

Atrium 3

1:00 pm

–

1:45 pm

Lunch

SRB  
Atrium

1:45 pm

–

4:00 pm

Working Group  
Session XI

PI-3

Atrium 4

Collaboratorium

Atrium 3

4:00 pm

–

4:30 pm

SPECIFIC AIMS PRESENTATION

SRB  
Ferman

4:30 pm

–

7:00 pm

Working Group  
Session XII

PI-3

Atrium 4

Collaboratorium

Atrium 3



# friday

NOVEMBER 13, 2015

8:30 am

-

9:00 am

Breakfast

SRB  
atrium

9:00 am

-

11:30 am

Final Presentations MUST  
be submitted to Sandy before 9am

SRB  
ferman

9:00 am

red team

9:35 am

green team

10:10

yellow team

10:45

blue team

11:30

-

noon

Judging

noon

-

1:30

Lunch

SRB Atrium

Award Presentation



# Red



**Dr. Sungjune Kim, MD, PhD** As the section chief for hematologic malignancy in the department of radiation oncology, Dr. Kim's clinical interests are treatment of patients with lymphoma and leukemia with radiation therapy. He is conducting a number of clinical research projects to improve management of lymphoma patients. Additionally, he has non-site specific interest in combining radiation therapy with immunotherapy, in particular melanoma, Merkel cell carcinoma and CNS malignancies.



**Dr. Marco Davila, MD, PhD** is a medical oncologist that specializes in the treatment of patients with hematologic malignancies. He received his medical degree from Duke University and medical training at the New York Presbyterian Weill Cornell Medical Center and Memorial Sloan Kettering Cancer Center. His clinical focus is on diseases such as chronic lymphocytic leukemia, B cell Acute Lymphoblastic Leukemia (B-ALL), and Acute Myeloid Leukemia. His clinical management includes the use of chemotherapies and/or cell therapies. He is appointed as an Associate Member in the Blood and Marrow Transplantation and Immunology Departments. As a translational physician-scientist, he is engaged in both clinical and laboratory research involving cancer. His research has helped usher in a new field of medical oncology by developing a novel cell engineered therapy for B-ALL that has been featured in the New York Times and Wall Street Journal. His work has been recognized with awards from the American Society of Hematology, American Society for Clinical Investigation, and Damon Runyon Cancer Research Foundation. It is now Dr. Davila's intent to develop similar engineered cell therapies here at Moffitt.



**Dr. Arturo Araujo** is a Postdoctoral fellow who joined IMO in August of 2012. He used to be a particle physicist and then turned into a modeler of biological complexity at University College London's brilliant CoMPLEX program where he focused on modeling aneuploidy in cancer for his PhD. At Moffitt he works together with David Basanta and the Lynch Lab, to tackle prostate to bone metastasis at the interphase between mathematics, biology and the clinic. He deals with complex systems and emergent behaviors and has recently been awarded a prestigious Department of Defense Prostate Cancer Research fellowship, to continue his work on developing an integrated multiscale computational model of prostate cancer metastases in the bone..

# Green



**Dr. Frederick Locke, MD** is a medical oncologist in the Department of Blood and Marrow Transplant at Moffitt Cancer Center and an assistant professor of oncology at the University of South Florida. Dr. Locke's research interests include autologous and allogeneic hematopoietic stem cell transplantation for lymphoma and myeloma and post-transplant immunotherapy. He is also a collaborator on research using survivin vaccine in myeloma patients and on the role of myeloid derived suppressor cells following allogeneic stem cell transplant. A graduate of Wayne State University School of Medicine, Dr. Locke completed his residency at Detroit Medical Center-Wayne State University, where he was chief medical resident. He did his fellowship in hematology/oncology at the University of Chicago Medical Center. Dr. Locke has received numerous academic and research awards, including the American Society of Clinical Oncology Foundation Young Investigator Award and the Cancer Education Consortium Award for Molecular and Translational Research. During his undergraduate years at Michigan State University, he was an All-Big Ten Conference Academic Athlete and gold medal award winner. Before joining Moffitt in 2010, Dr. Locke was an instructor of medicine at the University of Chicago Medical Center. He has been published in numerous peer-reviewed publications and is a member of several professional associations, including the American Society of Blood and Marrow Transplant.



**Kim Luddy**, is an experimental cancer immunologist. She has been at Moffitt Cancer Center for 11 years. She spent the bulk of her training in a translational immunology/immunotherapy lab working on preclinical and clinical research under Dr. Scott Antonia. In 2013 she transferred to Dr. Robert Gatenby where she now applies ecology and evolutionary concepts to standard immunology research methods. Her research interests include examining how the tumor evolves under pressure of the immune system and how the immune system reacts to these changes. Additionally she works on combining theoretical and computational models with experimental systems, with emphasis on T cell trafficking, phenotypic plasticity, and adaptive therapy protocols.



**Dr. Chandler Gatenbee, PhD** is a post-doctoral fellow who joined IMO in May, 2012. He has an M.S. in Biological Anthropology (University of Utah) and a Ph.D in Biology (University of Louisville) and has focused on applying evolutionary theory to understand human health and disease. As a Ph.D student, Chandler worked with Paul Ewald to develop probability and agent based models that examine the role of mutation and JC Virus in colorectal cancer. At the IMO, Chandler would like to continue to apply evolutionary theory to develop mathematical and computational models that explore how cellular competition within the micro-environment can favor the evolution of aggressive metastatic cancer cells. If we can understand how tumor cells evolve naturally and in response to treatment, we should gain a better understanding of what initiates and drives tumor progression and resistance. He joined the IMO because it provides an environment in which modelers are able to work closely with clinicians to develop realistic models that can lead to novel and intelligent methods to treat, and ideally, prevent cancer.



# Yellow



**Dr. Daniel Abate-Daga, PhD** is research is focused on the development of T cell-based immunotherapies for the treatment of cancer, and the translation of those preclinical findings into clinical application. The effort in my lab spans a wide process: starting with the identification of tumor-associated antigens, generation of the appropriate targeting receptor for genetic modification of T cells, in vitro and in vivo validation of immune receptors, and, ultimately, the implementation of those treatments in phase I clinical trials. A special emphasis is put on the use of gene therapy technologies, involving the expression of chimeric antigen receptors (CAR) and traditional T-cell receptors (TCR) to "train" the patient's own immune system to detect and kill cancer cells. The gene transfer of immune receptors is accomplished by retroviral transduction of primary human lymphocytes, and has proven efficacious in the induction of clinical remissions of patients with B cell malignancies. Beyond its therapeutic potential, this technology can be used in the laboratory setting to pursue basic scientific research leading to a better understanding of tumor and immune cell biology. Active and prospective projects in the laboratory include the study of antigen recognition, by tumor-infiltrating T cells from pancreatic cancer, bladder cancer and melanoma, geared towards the isolation of TCRs that recognize cancer/testis antigens of therapeutic interest.



**Jason B. Brayer, MD, PhD**, My research interests include: Exploring the therapeutic potential of HDAC11 inhibitors in the treatment of multiple myeloma. Exploring the potential for selective HDAC11 inhibitors to enhance T cell responses in the context of immunotherapy, including vaccine-based and cellular adoptive therapeutic approaches. Defining the functional significance of the interaction between HDAC11 and IRF4 and its impact as a regulator of CD8 T cell function. Defining the functional significance of the interaction between HDAC11 and IRF4 as it relates to myeloma cell development and survival.



**Dr. Heiko Enderling, PhD** is a computer scientist turned mathematical biologist, who is interested in mathematical and computational models of cancer dynamics, with focus on cancer stem cells and cell-cell as well as tumor-microenvironment interactions. Primarily he uses agent-based models and differential equations to describe single cell and population level dynamics and simulate diffusion of soluble factors used by cells to grow and communicate with each other. The aim of Dr. Enderling's work is to thoroughly investigate physiological development as well as tumor growth and progression to understand how and why some tumors remain benign and do not advance into malignancy - a state called dormancy. As we understand the kinetics underlying tumor dormancy, novel treatments might be developed that prevent aggressive growth and keep tumors in a non-clinical stage. As a second major research interest, Dr. Enderling develops mathematical models of radiotherapy to predict the response of single cells and the tumor population as a whole to irradiation. The ultimate aim will then be to perform in silico clinical trials to design treatment schedules that best counteract tumor progression. The radiotherapy model has been applied to conventional, experimental, and hypothetical treatment protocols for early stage breast cancer as well as glioblastoma multiforme.

# Blue



**Dr. Cliona O'Farrelly, PhD** is Professor of Comparative Immunology at Trinity College Dublin (TCD) since 2007 and has been researching human gut and liver immunology with a particular focus on cancer for over three decades. A recipient of the Irish Research Scientists' Association Gold Medal, the Graves Medal, the Conway Medal, the Isla Haliday Award and the 2014 Nature Mentoring Award, Cliona was President of the Irish Society of Immunology from 2000-2007 and on the Board of the Irish Cancer Society from 2008-2013. She currently serves on the Boards of Trinity College Dublin, the Science Gallery at TCD, the Royal Dublin Society and the editorial board of Transactions B of the

Royal Society London. After completing a primary degree in Microbiology at TCD, Cliona graduated with a PhD in Immunology, also from TCD, in 1982, undertook postdoctoral research at St. James's Hospital Dublin and Sussex University in the UK, before becoming Lecturer on Biology at Harvard University in 1987. On returning to Ireland, Cliona was Wellcome Research Fellow before becoming Director of the Research Laboratories at St. Vincent's University Hospital, home to the National Liver Transplant Centre, Dublin. There, Cliona was instrumental in developing one of the world's first research programmes into human liver immunology which, with metastatic liver disease, remains her main research focus. She has published over 200 papers, reviews and book chapters, has raised more than 12 million Euro in grant funding and has graduated 32 PhD students, 7 MD and 4 MCh students. She designed and directs a new MSc in Immunology at TCD, now in its fourth year. She is passionate about public understanding of science and is academic lead for TCD's Discover Research Dublin, an event which attracts >6000 members of the public to TCD's research labs and institutes.



**Dr. John E Mullinax, MD** is a Fellow in Complex General Surgical Oncology at Moffitt Cancer Center. During my General Surgery training I spent two years completing a Surgical Oncology Research Fellowship in the Surgery Branch at the NCI. My research focus is on developing novel immunotherapy approaches, including adoptive cell therapy, for treating patients with advanced soft tissue sarcoma. I will join the Sarcoma Division at Moffitt Cancer Center as an attending surgeon in July 2016 upon completion of my fellowship.



**Dr. Jacob G. Scott, MD** is a faculty member of the Moffitt Cancer Center as Clinical Instructor in the Department of Radiation Oncology as of June 29, 2015. Dr. Scott has a secondary appointment in the Department of Integrated Mathematical Oncology. Dr. Scott received his MD from Case Western Reserve University School of Medicine in Cleveland, Ohio. He recently completed a Post-Doctoral Fellowship in the Department of Integrative Mathematical Oncology at Moffitt Cancer Center, and a Radiation Oncology Residency from the University of South Florida here at Moffitt Cancer Center. He is currently completing his D.Phil. in Mathematical Biology at the University of Oxford. Dr. Scott's clinical area of focus will be patients with primary and metastatic sarcoma.



# IMMUNE CANCER



## SPECIAL THANKS

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