**ISHLT ACADEMY**
**CORE COMPETENCIES IN BASIC SCIENCE AND TRANSLATIONAL RESEARCH**
**APRIL 21, 2020**
**MONTRÉAL, CANADA**

**Scientific Program Committee**

Chair: Tereza Martinu, MD, Toronto General Hospital, Toronto, Canada
Co-Chair: Esme Dijke, PhD, University of Alberta, Edmonton, Canada
Co-Chair: John Greenland, MD, PhD, University of California San Francisco, San Francisco, CA, USA

**Faculty**

Carla Baan, PhD, University Hospital Rotterdam, Rotterdam, The Netherlands
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Esme Dijke, PhD, University of Alberta, Edmonton, Canada
Eric Epailly, MD, Centre Hospitalier de l'Université de Strasbourg, Strasbourg, France
Christine Falk, PhD, Hannover Medical School, Hannover, Germany
Andrew Gelman, PhD, Washington University, St. Louis, MO, USA
John Greenland, MD, PhD, University of California San Francisco, San Francisco, CA, USA
Stephen Juvet, MD, PhD, University of Toronto, Toronto, Canada
Joren Madsen, MD, DPhil, Massachusetts General Hospital, Boston, MA, USA
Tereza Martinu, MD, Toronto General Hospital/UHN, Toronto, Canada
Federica Meloni, MD, PhD, Policlinico San Matteo, Pavia, Italy
Ciara Shaver, MD, PhD, Vanderbilt University Medical Center, Nashville, TN, USA
Simon Urschel, MD, University of Alberta, Edmonton, Canada
Stijn Verleden, PhD, KU Leuven, Leuven, Belgium
Glen Westall, MD, PhD, Alfred Hospital, Melbourne, Australia

**Educational Goals**

The educational goals of this activity are to provide a concise review of basic concepts in transplant-related immunology and molecular biology, to define and promote the clinical relevance of basic science and translational research related to heart and lung transplantation, and to encourage interaction between basic scientists, translational researchers and clinicians.

**Target Audience**

This course is primarily designed to be of benefit for clinicians, allied health professionals, and researchers who are in the early stages of their careers, or who are in training and/or are part of a new program, or desire an update on the current state of the field. The information presented covers core competencies and is intended to provide a strong foundation of the overarching principles pertinent to basic science and translational research in thoracic transplantation, rather than as a detailed update for those who are already proficient experts in the field.

**Learning Objectives**

At the conclusion of this meeting, participants will have improved competence and professional performance in their abilities to:

1. Discuss basic concepts in transplant-related immunology and molecular biology;
2. Recognize key analytical techniques and models used in transplantation research;
3. Understand basic mechanisms of immunosuppression;
4. Recognize key contributions from basic research in transplantation that improved clinical outcomes in heart and lung transplantation;
5. Recognize how clinical questions may inspire basic research;

6. Improve effective communication between research scientists and clinicians and health care professionals.

**Disclosure**

Current guidelines state that participants in CME activities must be made aware of any affiliation or financial interest that may affect the program content or a speaker's presentation. Planners, Faculty and Chairs participating in this meeting are required to disclose to the program audience any real or apparent conflict(s) of interest related to the content of their presentations or service as Chair/Planner. These disclosures will be distributed at the meeting. Additionally, all speakers have been asked to verbally disclose at the start of their presentation if a product they are discussing is not labeled for the use under discussion or is still investigational.

**Accreditation Statement**

The International Society for Heart and Lung Transplantation (ISHLT) is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

**Credit Designation Statement**

ISHLT designates this live activity for a maximum of 7.50 *AMA PRA Category 1 Credits*™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

**Nurses and Pharmacists**


In support of improving patient care, this activity has been planned and implemented by Amedco LLC and ISHLT. Amedco LLC is jointly accredited by the Accreditation Council for Continuing Medical Education (ACCME), the Accreditation Council for Pharmacy Education (ACPE), and the American Nurses Credentialing Center (ANCC), to provide continuing education for the healthcare team.

Credit Designation Statement – Amedco LLC designates this live activity for a maximum of 7.50 contact hours for nurses and 3.0 knowledge-based contact hours for pharmacists. Learners should claim only the credit commensurate with the extent of their participation in the activity.

**ISHLT ACADEMY**
**CORE COMPETENCIES IN BASIC SCIENCE AND TRANSLATIONAL RESEARCH**
**PRELIMINARY SCIENTIFIC PROGRAM SCHEDULE**

**7:00 AM – 8:00 AM**
**REGISTRATION & MORNING COFFEE**

**8:00 AM – 8:10 AM**
**WELCOME AND OVERVIEW**
Tereza Martinu, MD, MHS, University of Toronto, Toronto, Canada

**8:10 AM - 9:00 AM**
**SESSION 1 – BRIDGING CLINICAL AND BASIC SCIENCE**
**Chair:** Tereza Martinu, MD, MHS, University of Toronto, Toronto, Canada

**8:10 AM** ***Basic Transplant Immunology: It's All Greek To Me…***
Esme Dijke, PhD, University of Alberta, Edmonton, Canada

**Teaching/Discussion Points**

a. Overview of an immune response in general
b. Allorecognition and HLA
c. Mechanisms of rejection: T cell mediated / B cell mediated responses

**8:30 AM Q&A**

**8:35 AM** ***Clinical Transplant Medicine: More than Just a Band Aid…***
Ciara Shaver, MD, PhD, Vanderbilt University Medical Center, Nashville, TN, USA

**Teaching/Discussion Points**

a. Clinical overview for the basic scientists covering the life of the allograft from donor to patient.
b. Clinical presentation of ischemia-reperfusion injury, acute cellular rejection, antibody-mediated rejection, chronic rejection; Compare and contrast heart and lung-specific concepts.

**8:55 AM Q&A**

**9:00 AM – 10:00 AM**
**SESSION 2 – ADAPTIVE IMMUNITY IN THORACIC TRANSPLANTATION**
**Chair:** Esme Dijke, PhD, University of Alberta, Edmonton, Canada

**9:00 AM** ***Overview of Adaptive Immunity in Transplantation: Attack of the Clones***
Federica Meloni, MD, PhD, Policlinico San Matteo, Pavia, Italy

**Teaching/Discussion Points**

a. T/B cell receptors, diversity of specificities
b. Antigen presentation: Intracellular and extracellular antigens and direct versus indirect alloimmunity
c. Compare pathology and epidemiology of acute cellular and antibody-mediated rejection in heart and lung transplant

**9:15 AM** ***T cells: They Pity the Fool that Don't be Cool***
Carla Baan, PhD, University Hospital Rotterdam, Rotterdam, The Netherlands

**Teaching/Discussion Points**

a. Thymic development and T cell signaling
b. Why are there alloreactive T cells in the first place?
c. Major T cell types and their roles: CD8, CD4, Tregs, central/effector memory, tissue resident vs. lymphoid
d. Cytokines and their associated helper T cell subsets and their roles: Th1, Th2, Th17
e. T cell Metabolome

**9:30 AM** ***B cells: You too Can be a B-liever***
Simon Urschel, MD, University of Alberta, Edmonton, Canada

**Teaching/Discussion Points**

a. How does antibody-mediated rejection happen?
b. From co-stimulation to complement and antibody-dependent cellular cytotoxicity, with attention to therapeutic targets
c. B cells in antigen presentation
d. Immune protection from B cells (suppression, cytoprotection, immune regulation)

**9:45 AM** ***Q&A with Panel***

**10:00 AM – 10:30 AM**
**COFFEE BREAK**

**10:30 AM – 11:45 AM**
**SESSION 3 – INNATE IMMUNITY IN THORACIC TRANSPLANTATION**
**Chair:** John Greenland, MD, PhD, University of California San Francisco, San Francisco, CA, USA

**10:30 AM** ***Overview of Innate Immunity in Transplantation: Every Body Needs a Hero***
Glen Westall, MD, PhD, Alfred Hospital, Melbourne, Australia

**Teaching/Discussion Points**

a. The various barriers of innate immunity (physical, chemical and cellular)
b. Signaling pathways (TLR, PRR, DAMPs, PAMPs)
c. Interaction of complement and innate immune cells with adaptive immunity
d. The role of innate immunity in ischemia-reperfusion injury
e. Contrast lung versus heart-specific concepts.

**10:45 AM** ***Neutrophils: The First Responders***
Andrew Gelman, PhD, Washington University, St. Louis, MO, USA

**Teaching/Discussion Points**

a. Characteristics of neutrophils and role in inflammation
b. Neutrophil extracellular traps (NETs)
c. The role of neutrophils in transplantation

**11:00 AM** ***Macrophages and Dendritic Cells: The Usual Suspects***
Stephen Juvet, MD, PhD, University of Toronto, Toronto, Canada

**Teaching/Discussion Points**

a. Characteristics of macrophages and DCs
b. Phagocytosis, antigen processing and presentation
c. The role of DCs and macrophages in inflammation and transplantation

**11:15 AM** ***Innate Lymphoid Cells: The Unusual Suspects***
Christine Falk, PhD, Hannover Medical School, Hannover, Germany

**Teaching/Discussion Points**

a. Characteristics of ILCs, NK cells and γδT cells
b. The role of ILCs, NK cells and T cells in inflammation and transplantation
c. Immune memory in innate immunity

**11:30 AM** ***Q&A with Panel***

**11:45 AM - 12:30 PM**
**SESSION 4 –FIBROSIS AND TOLERANCE IN THORACIC TRANSPLANTATION**
**Chair:** Tereza Martinu, MD, MHS, University of Toronto, Toronto, Canada

**11:45 AM** ***Transplantation Endgame: Fibrosis Pathways***
Stijn Verleden, PhD, KU Leuven, Leuven, Belgium

**Teaching/Discussion Points**

a. The roles and manifestations of fibrosis in chronic rejection of the heart and lung
b. Triggers of fibrosis
c. Injury and dysregulated repair
d. Pro-fibrotic factors; Fibroblast phenotypes
e. Extracellular matrix; Origins of fibroblasts (local proliferation and migration, fibrocytes, epithelial-mesenchymal transition)

**12:00 PM** ***Infinity Wars: Will Tolerance Prevail?***
Joren Madsen, MD, Dphil, Massachusetts General Hospital, Boston, MA, USA

**Teaching/Discussion Points**

a. Operational definitions of tolerance
b. Types of regulatory cells
c. Current strategies to achieving tolerance in pre-clinical and clinical thoracic transplantation

**12:15 PM** ***Q&A with Panel***

**12:30 AM – 1:45 PM**
**LUNCH BREAK** (a box lunch is included in the registration fee)

**1:45 PM – 2:45 PM**
**SESSION 5 – INFECTION AND IMMUNITY IN THORACIC TRANSPLANTATION**
**Chair:** Esme Dijke, PhD, University of Alberta, Edmonton, Canada

**1:45 PM** ***Scylla and Charybdis: How Infections Potentiate Rejection***
Andrew Gelman, PhD, Washington University, St. Louis, MO, USA

**Teaching/Discussion Points**

a. Bacterial activation of pathogen-specific responses (PAMPs, DAMPs)
b. Specific case of pseudomonas
c. Viral effects on antigen presentation and interferon-dependent immunity
d. Heterotopic immune responses.

**2:00 PM** ***Streetlight Effect: How to Monitor Post-Transplant Immune Responses***
John Greenland, MD, PhD, University of California San Francisco, San Francisco, CA, USA

**Teaching/Discussion Points**

a. Strategies to assess immunosuppression level and infection vs. rejection risk
b. Elispots (CMV, EBV, TB, allo-reactive etc.)
c. Immunoknow; Cell-free DNA
d. Microvesicles/cross-dressing
e. BAL immunophenotyping/cytokines.

**2:15 PM** ***They Came from the Swamp: Microbiome***
Tereza Martinu, MD, MHS, University of Toronto, Toronto, Canada

**Teaching/Discussion Points**

a. Gut and lung microbiome
b. Effects of microbiota on immune responses
c. Role of microbiome in transplantation
d. Microbiome-derived metabolite effects on the immune system.

**2:30 PM** ***Q&A with Panel***

**2:45 PM - 3:45 PM**
**SESSION 6 – THERAPEUTICS IN THORACIC TRANSPLANTATION**
**Chair:** Tereza Martinu, MD, MHS, University of Toronto, Toronto, Canada

**2:45 PM** ***Mechanisms of Immunosuppression: The Empire Strikes Back***
Eric Epailly, MD, Centre Hospitalier de l'Université de Strasbourg, Strasbourg, France

**Teaching/Discussion Points**

a. Molecular pathways and specific cell types targeted by current immunosuppressants
b. How these mechanisms play into the effects of immunosuppression

**3:00 PM** ***Novel Agents in the Pipeline: A New Hope***
Glen Westall, MD, PhD, Alfred Hospital, Melbourne, Australia

**Teaching/Discussion Points**

a. New agents being developed for immunosuppression or immunomodulation and their mechanisms of action

**3:15 PM** ***Cell Therapy in Transplantation: The Force Awakens***
Daniel Chambers, MBBS, MRCP, FRACP, MD, The Prince Charles Hospital, Brisbane, Australia

**Teaching/Discussion Points**

b. Current state on cell therapy in transplantation
c. Different types of cell therapy; Future directions
d. Can cell therapy make use of ex-vivo organ perfusion?

**3:30 PM** ***Q&A with Panel***

**3:45 PM - 4:15 PM**
**COFFEE BREAK**

**4:15 PM - 5:45 PM**
**SESSION 7 – TRANSPLANTATION TOOLS OF THE TRADE**
**Chair:** John Greenland, MD, PhD, University of California San Francisco, San Francisco, CA, USA

**4:15 PM** ***OMICS: Ralph Breaks the Internet***
Edward Cantu III, MD, MSCE, University of Pennsylvania, Philadelphia, PA, USA

**Teaching/Discussion Points**

a. Genomics, Transcriptomics, Proteomics, Metabolomics
b. Considerations for Big Data analysis
c. Focus on the use of these tools for the study of ischemia-reperfusion injury

**4:30 PM** ***Cellular Assays: The Sixth Sense***
Carla Baan, PhD, University Hospital Rotterdam, Rotterdam, The Netherlands

**Teaching/Discussion Points**

a. Describe the concepts behind high parameter flow cytometry and mass cytometry, Seahorse assay, confocal and intravital microscopy
b. Focus on the use of these tools for the study of acute cellular rejection

**4:45 PM** ***Design and Analysis of Cohorts for Translational Research: Full House***
Edward Cantu III, MD, MSCE, University of Pennsylvania, Philadelphia, PA, USA

**Teaching/Discussion Points**

a. Describe approaches to designing cohorts for translational studies in thoracic transplantation
b. What controls should be considered
c. Sources of bias
d. Statistical Power
e. Survival Analysis (censoring and competing risks)
f. Focus on the use of these tools for the study of antibody-mediated rejection

**5:00 PM** ***Mouse Modeling in Thoracic Transplantation: Secrets of NIMH***
Stephen Juvet, MD, PhD, University of Toronto, Toronto, Canada

**Teaching/Discussion Points**

a. Describe approaches to designing mouse model-based studies
b. What controls need to be considered
c. Genetically-engineered mice
d. Focus on the use of these tools for the study of chronic rejection.

**5:15 PM** ***Q&A with Panel***

**5:35 PM SUMMARY / EVALUATION**
Tereza Martinu, MD, MHS, University of Toronto, Toronto, Canada
Esme Dijke, PhD, University of Alberta, Edmonton, Canada
John Greenland, MD, PhD, University of California San Francisco, San Francisco, CA, USA

**5:55 PM**
**ADJOURN**