

ISHLT ACADEMY
CORE COMPETENCIES IN BASIC SCIENCE AND TRANSLATIONAL RESEARCH
FINAL SCIENTIFIC PROGRAM

BASIC SCIENCE | 7 February 2022 | 1:00-4:30 p.m. EST
TRANSLATIONAL RESEARCH | 9 February 2022 | 1:00-4:30 p.m. EST

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, Erasmus Medical Center, Rotterdam, The Netherlands
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Esme Dijke, PhD, University of Alberta, Edmonton, Canada
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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, University of Antwerp, Antwerp, Belgium
Glen Westall, MD, PhD, Alfred Hospital, Melbourne, Australia

Educational Goals

The course is designed 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 heart and lung 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.

Acknowledgement of Financial Commercial Support

No financial commercial support was received for this educational activity.

Acknowledgement of In-Kind Commercial Support

No in-kind commercial support was received for this educational activity.

Accreditation and Credit Designation Statements

Physicians

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 6.75 *AMA PRA Category 1 Credits™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Nurses and Pharmacists



Accreditation Statement – In support of improving patient care, this activity has been planned and implemented by Amedco LLC and International Society for Heart and Lung Transplantation. 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.

Nurses (ANCC) Credit Designation Statement – Amedco LLC designates this live activity for a maximum of 6.75 ANCC contact hours.

Nurses Practitioners Credit Designation Statement – The American Association of Nurse Practitioners (AANP) recognizes the Accreditation Council for Continuing Medical Education (ACCME) and the American Nurses Credentialing Center (ANCC) as approved accreditors and allow reciprocity for AANPCP continuing education credit.

Pharmacists and Pharmacy Technicians (ACPE) Credit Designation Statement – Amedco LLC designates this activity for a maximum of 6.75 knowledge-based CPE contact hours.

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.

1:00 – 1:10 PM

WELCOME AND OVERVIEW

Tereza Martinu, MD MHS, University of Toronto, Toronto, Ontario, Canada

1:10 PM – 2:10 PM

SESSION 1: ADAPTIVE IMMUNITY IN THORACIC TRANSPLANTATION

Chair: Esme Dijke, PhD, University of Alberta, Edmonton, Alberta, Canada

1:10 PM - Overview of Adaptive Immunity in Transplantation: Attack of the Clones (15 minutes)

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

1:25 PM - T cells: They Pity the Fool that Don't be Cool (15 minutes)

Carla Baan, PhD, Erasmus Medical Center, 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

1:40 PM - B cells: You too Can be a B-liever (15 minutes)

Simon Urschel, MD PhD, University of Alberta, Edmonton, Alberta, 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)

1:55 PM - Panel Discussion - What cell is most important in acute rejection? (15 minutes)

2:10 PM – 2:15 PM– Break

2:15 PM – 3:45 PM

SESSION 2: INNATE IMMUNITY IN THORACIC TRANSPLANTATION

Chair: John Greenland, MD PhD, UCSF, San Francisco, CA, USA

2:15 PM - Overview of Innate Immunity in Transplantation: Every Body Needs a Hero (15 minutes)

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.

2:30 PM - Neutrophils: The First Responders (15 minutes)

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

2:45 PM - Macrophages and Dendritic Cells: The Usual Suspects (15 minutes)

Stephen Juvet, MD PhD, University of Toronto, Toronto, Ontario, 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

3:00 PM - Innate Lymphoid Cells: The Unusual Suspects (15 minutes)

Christine Falk, PhD, Hannover Medical School, Germany

Teaching/Discussion Points

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

3:15 PM - Panel Discussion – What cell is most important to PGD? (15 minutes)

3:30 PM – 4:30 PM

SESSION 3: FIBROSIS AND TRANSPLANTATION TOOLS OF THE TRADE

Chair: Tereza Martinu, MD MHS, University of Toronto, Toronto, Ontario, Canada

3:30 PM - Transplantation Endgame: Fibrosis Pathways (15 minutes)

Stijn Verleden, PhD, University of Antwerp, Antwerp, 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)

3:45 PM - Cellular Assays: The Sixth Sense (15 minutes)

Carla Baan, PhD, Erasmus Medical Center, 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

4:00 PM - Mouse Modeling in Thoracic Transplantation: Secrets of NIMH (15 minutes)

Stephen Juvet, MD PhD, University of Toronto, Toronto, Ontario, 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.

4:15 PM - Q&A Discussion (10 minutes)

4:25 PM – 4:30 PM

CLOSING REMARKS

Tereza Martinu, MD MHS, University of Toronto, Toronto, Ontario, Canada

1:00 PM – 1:05 PM

WELCOME

John Greenland, MD, PhD, University of California San Francisco, San Francisco, CA, USA

1:05 PM – 1:45 PM

SESSION 1: TRANSPLANTATION TOOLS OF THE TRADE

Chair: John Greenland, MD, PhD, University of California San Francisco, San Francisco, CA, USA

1:05 PM - Clinical Transplant Medicine: More than Just a Band Aid... (15 minutes)

Ciara Shaver, MD PhD, Vanderbilt University Medical Center, Nashville, Tennessee, 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.

1:20 PM - Design and Analysis of Cohorts for Translational Research: Full House (15 minutes)

Edward Cantu III, MD MSCE, University of Pennsylvania, Philadelphia, Pennsylvania, 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

1:35 PM - OMICS: Ralph Breaks the Internet (15 minutes)

Edward Cantu III, MD MSCE, University of Pennsylvania, Philadelphia, Pennsylvania, 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

1:50 PM - Q&A with Speakers (10 minutes)

2:00 PM – 3:00 PM

SESSION 2: INFECTION AND IMMUNITY IN THORACIC TRANSPLANTATION

Chair: Esme Dijke, PhD, University of Alberta, Edmonton, Alberta, Canada

2:00 PM - They Came from the Swamp: Microbiome (15 minutes)

Tereza Martinu, MD MHS, University of Toronto, Toronto, Ontario, 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.

2:15 PM - Streetlight Effect: How to Monitor Post-Transplant Immune Responses (15 minutes)

John Greenland, MD PhD, UCSF, 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.

2:30 PM - Scylla and Charybdis: How Infections Potentiate Rejection (15 minutes)

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.

2:45 PM - Q&A with Panel (15 minutes)

3:00 PM – 3:05 PM - Break

3:05 PM – 4:20 PM

SESSION 3: THERAPEUTICS IN THORACIC TRANSPLANTATION

Chair: Tereza Martinu, MD MHS, University of Toronto, Toronto, Ontario, Canada

3:05 PM - Mechanisms of Immunosuppression: The Empire Strikes Back (15 minutes)

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

3:20 PM - Novel Agents in the Pipeline: A New Hope (15 minutes)

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

3:35 PM - Infinity Wars: Will Tolerance Prevail? (15 minutes)

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

3:50 PM - Cell Therapy in Transplantation: The Force Awakens (15 Minutes)

Daniel Chambers, 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?

4:05 PM - Q&A with Panel (15 minutes)

4:20 PM – 4:30 PM

SUMMARY / EVALUATION

John Greenland, MD PhD, UCSF, San Francisco, CA, USA