



Towards defining graft rejection with the help of AI

2023 NephroCAGE Symposium

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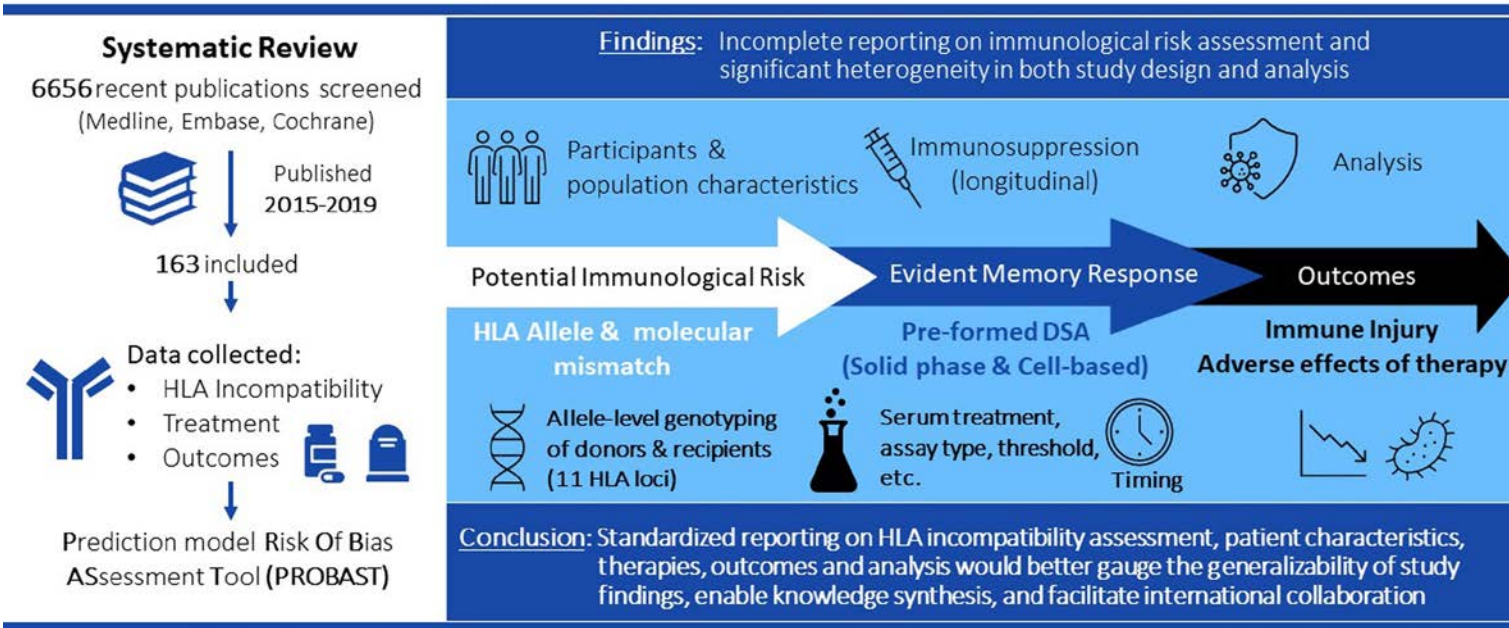
“Seeking Standardized Definitions for HLA-incompatible Kidney Transplants”

Banff Antibody-Mediated Injury Working Group



Seeking Standardized Definitions for HLA-incompatible Kidney Transplants: A Systematic Review

Jatana et al.
Transplantation (2023)

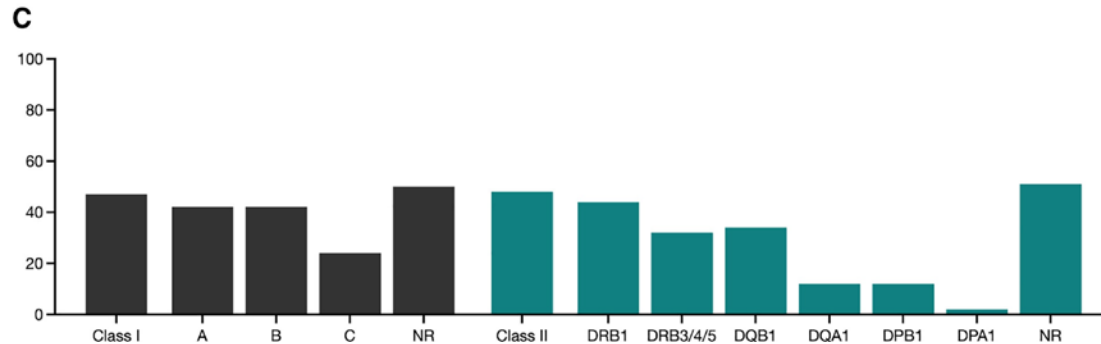
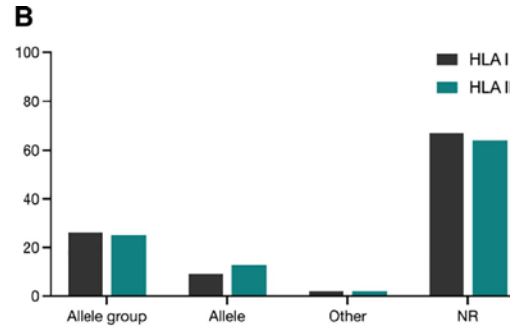
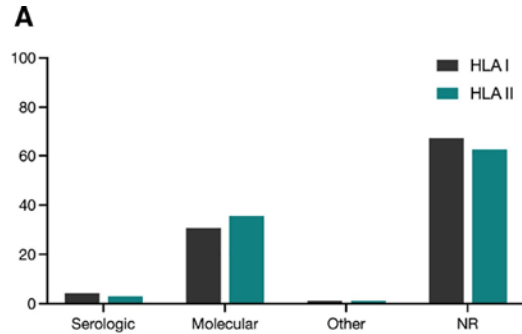


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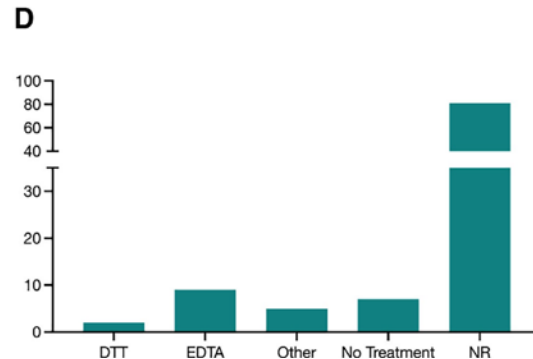
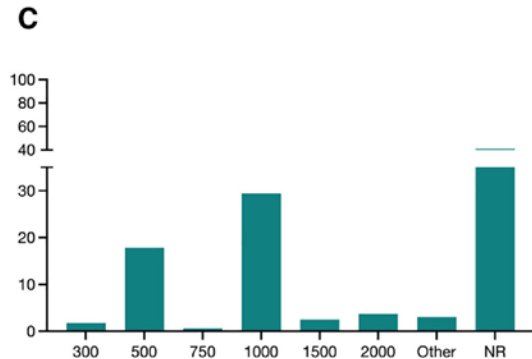
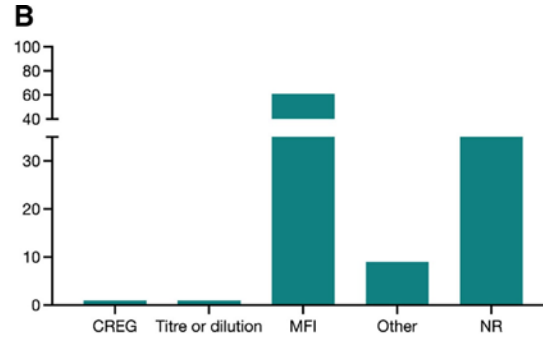
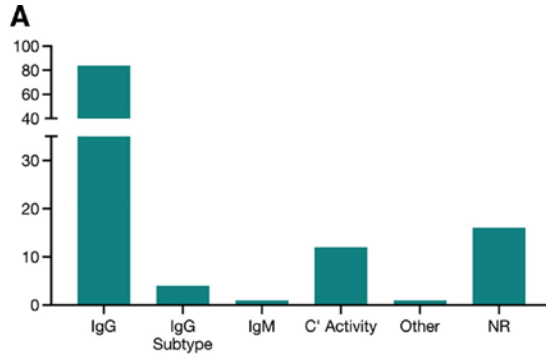
Reporting on HLA typing



Jatana et al.
Transplantation (2023)

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Preformed DSA by solid-phase assays



Jatana et al.
Transplantation (2023)

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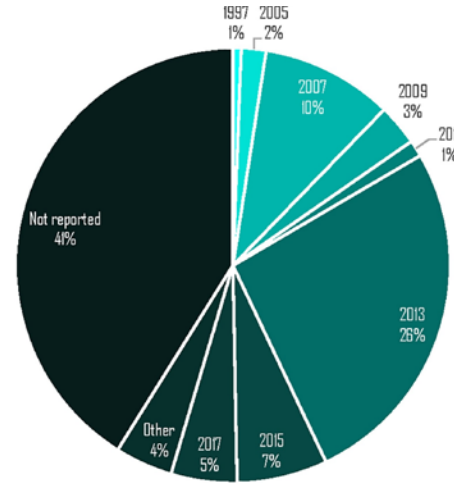
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Banff rejection data

A, Banff classification.

A



Jatana et al.
Transplantation (2023)

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Describe⁸:

- source of data
- study design
- criteria for participant selection
- sensitizing events
- demographics (e.g., age, sex, self-reported ethnicity)
- separately consider first-transplant and retransplant recipients

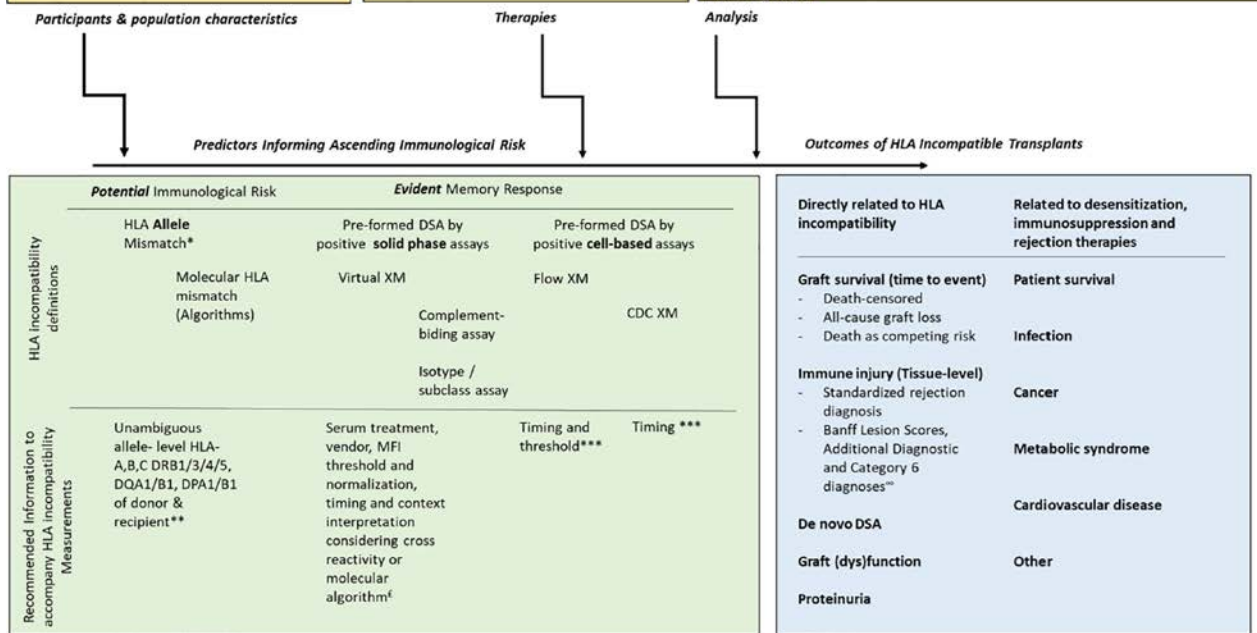
Describe:

- desensitization protocols & timing
- induction immunosuppression
- maintenance immunosuppression
- longitudinal therapeutic drug monitoring and drug adjustments
- therapies for rejection events

Describe⁸:

- numbers of participants, candidate predictors, outcome events and events per candidate predictor;
- model development (modelling, predictor selection, and risk group definition);
- internal and external model validation;
- model performance;
- participants excluded from the analysis;
- missing data and outcomes as well as methods used to handle missing data

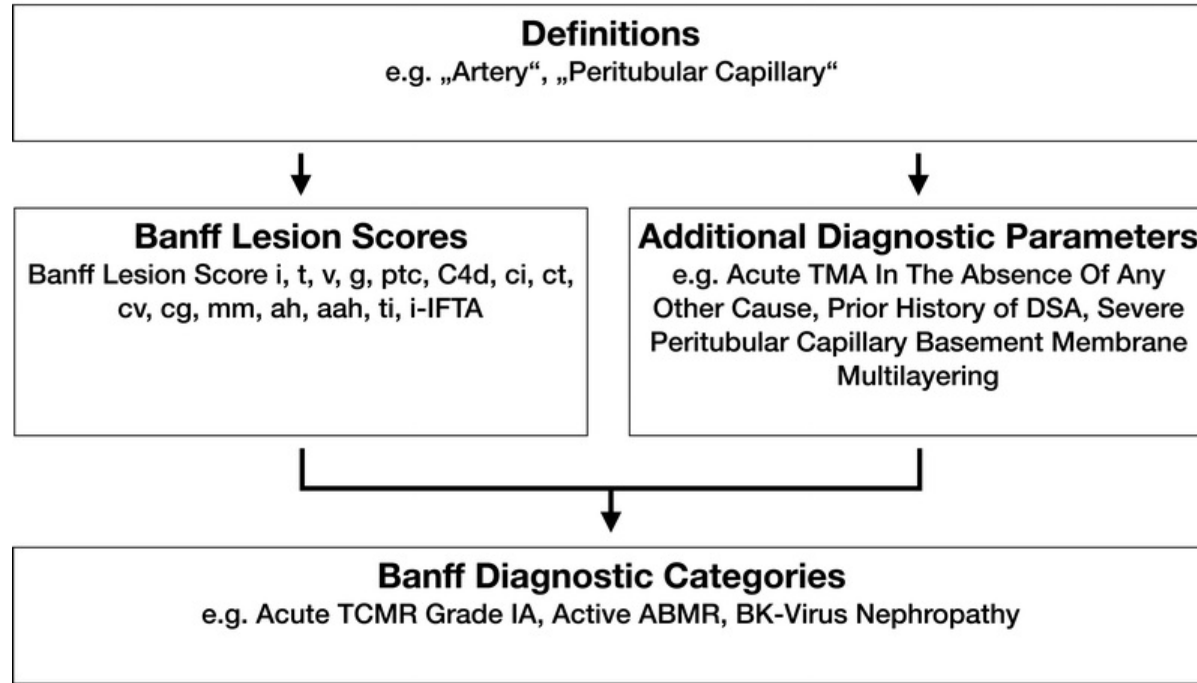
Jatana et al.
Transplantation (2023)



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BANFF-IT, Computer-Assisted Reporting of Banff Classification of Kidney Allograft Biopsies

Content of the Banff Classification of Renal Allograft Pathology



Roufousse et al.
Transplantation (2018)

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Banff-IT

- **Data dictionary** –
 - Template of minimal set of variables, including Banff Lesion Scores, Additional Diagnostic Parameters and Category 6 diagnoses
- **Algorithm** –
 - Assigns Category 1 to 6 diagnoses utilizing minimal dataset by sequentially applying rules
 - Developed in R software and adaptable to other software
 - Assesses dataset quality
 - Rapid execution time
 - Handles longitudinal datasets
- **Applications** –
 - Diagnostic aid for expert nephrologists
 - Standardized rejection diagnoses for transplant outcome prediction (survival models & AI)

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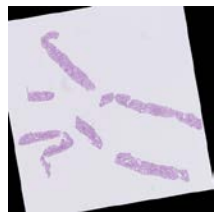
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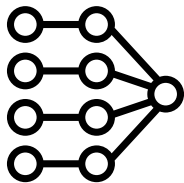
Application of AI in Nephropathology

Slides courtesy of Dr. Jan Becker, Hien V. Nguyen, and Chandra Mohan

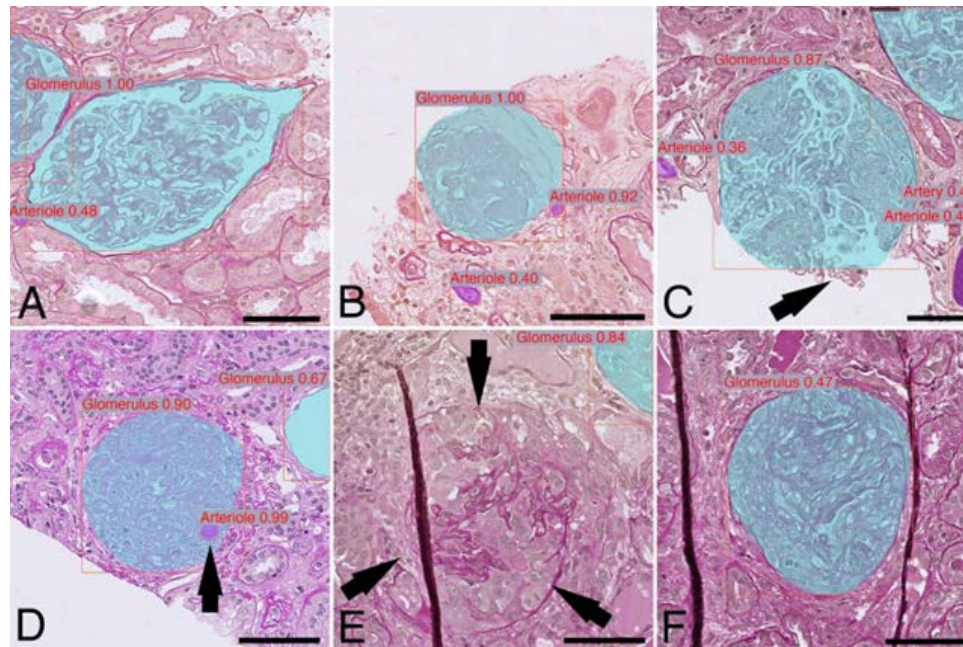
GN Classification – Machine learning in image analysis & histopathology



Input:
PAS Whole Slide
Images

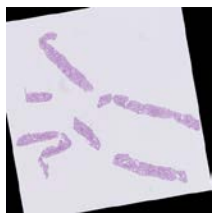


Module 1:
Glomerular
Segmentation Model

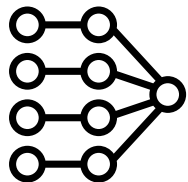


Cicalese et al.
in preparation (2023)

GN Classification – Machine learning in image analysis & histopathology



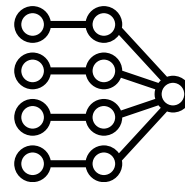
Input:
PAS Whole
Slide Images



Module 1:
Glomerular
Segmentation
Model



"Bag" of
Glomerular
Crops



Module 2:
MILxFormer
Classification
Model

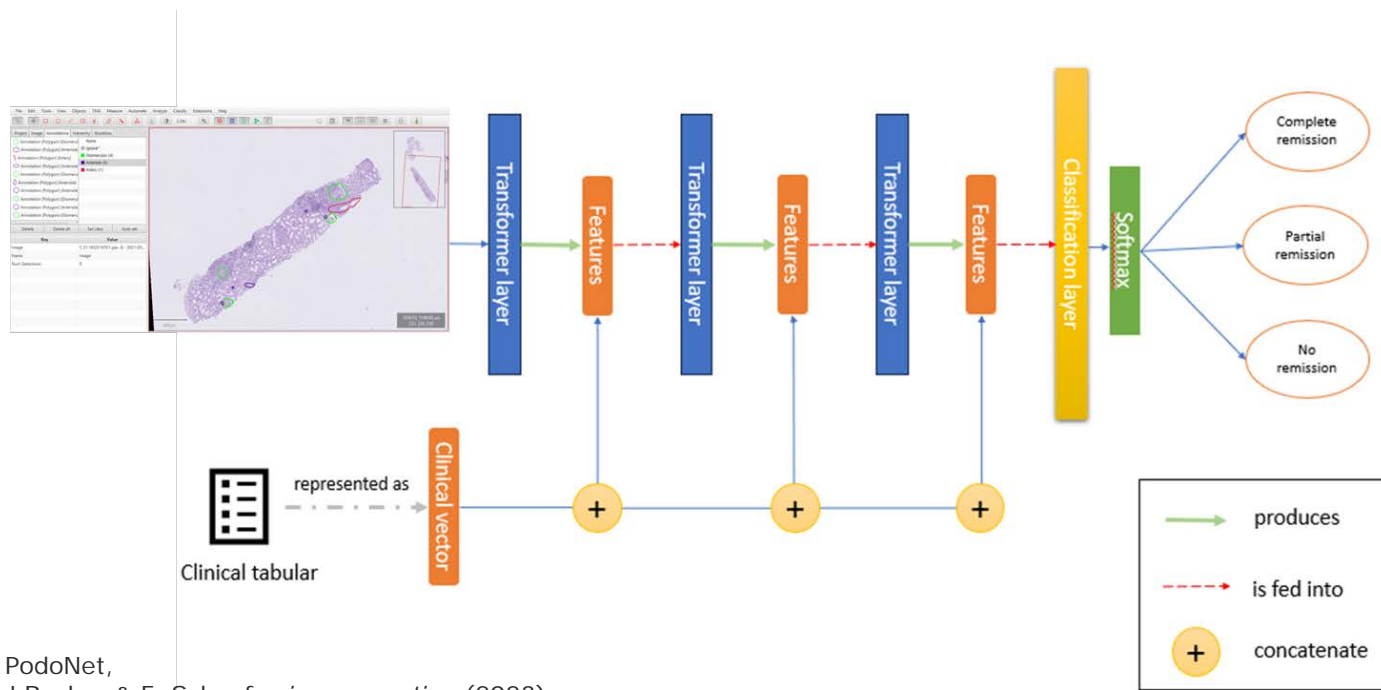
Rank	Predicted Class	Confidence
Top-1	Membranous	44%
Top-2	IgAGN	26%
Top-3	ANCA	15%

Output:
Bayesian Classification
(example)

Cicalese et al.
in preparation (2023)

Integration of Clinical Data

Response to intensified immunosuppression in steroid resistant nephrotic syndrome



PodoNet,
J Becker & F. Schaefer *in preparation* (2023)

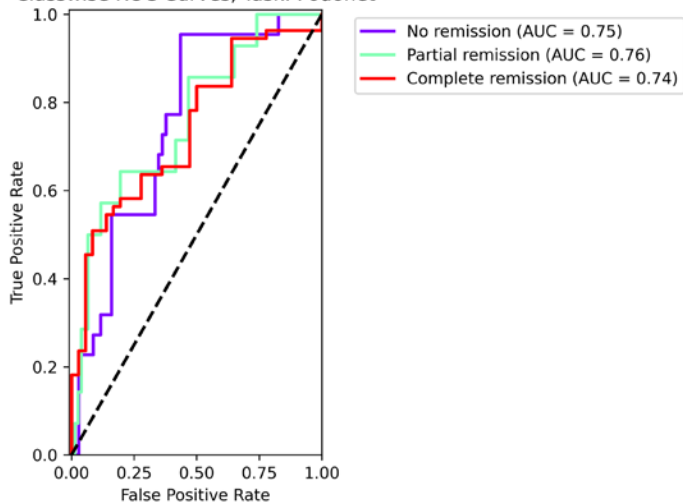
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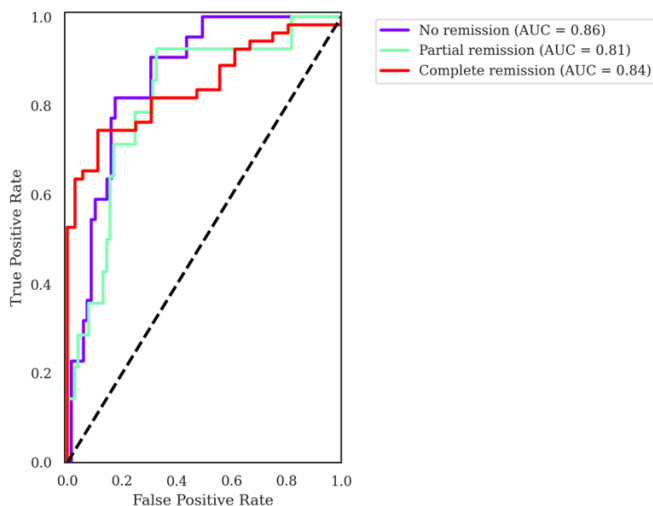
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MILxFormer for theranostics (steroid resistant nephrotic syndrome)

Classwise ROC Curves, Task: Podonet



Gaussian naive Bayes classifier
Clinical data only (e.g, **mutation** yes/no)



MILxFormer
Histology only (arteries, arterioles, glomeruli)

Podonet,
 J Becker & F. Schaefer
in preparation (2023)

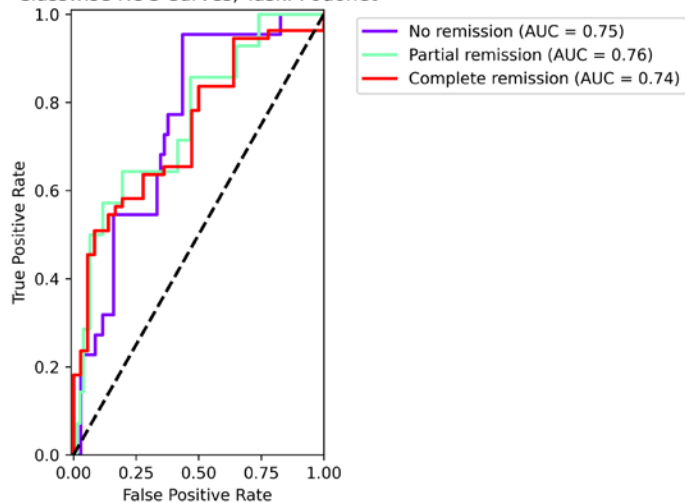
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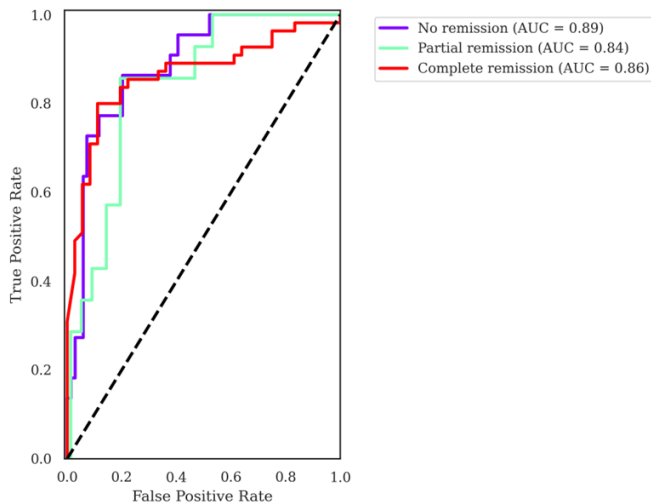
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MILxFormer for theranostics (steroid resistant nephrotic syndrome)

Classwise ROC Curves, Task: Podonet



Gaussian naive Bayes classifier
Clinical data only (e.g., **mutation** yes/no)



MILxFormer
Histology + **clinical** data (e.g., **mutation** yes/no)

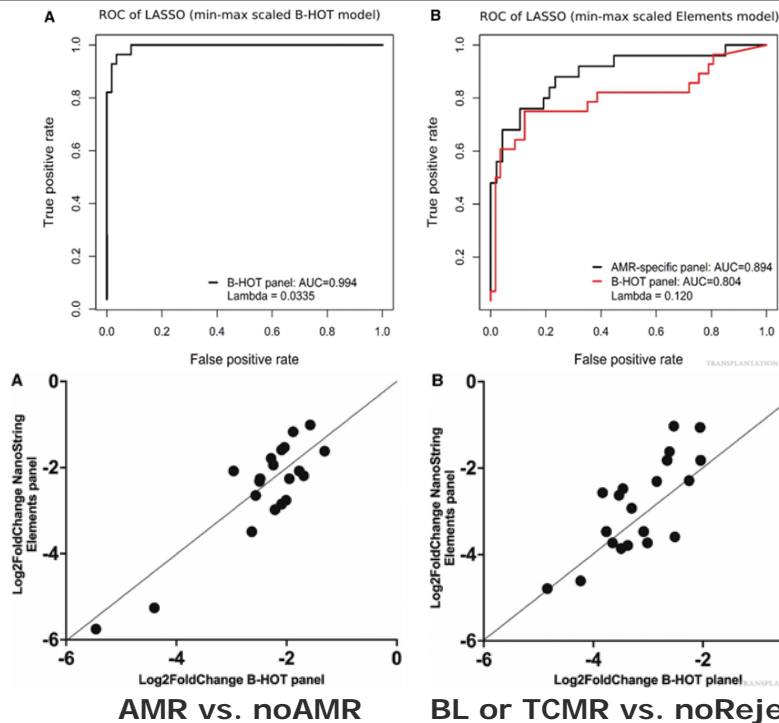
Podonet,
 J Becker & F. Schaefer
in preparation (2023)

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Active AMR Diagnosis by Nanostring



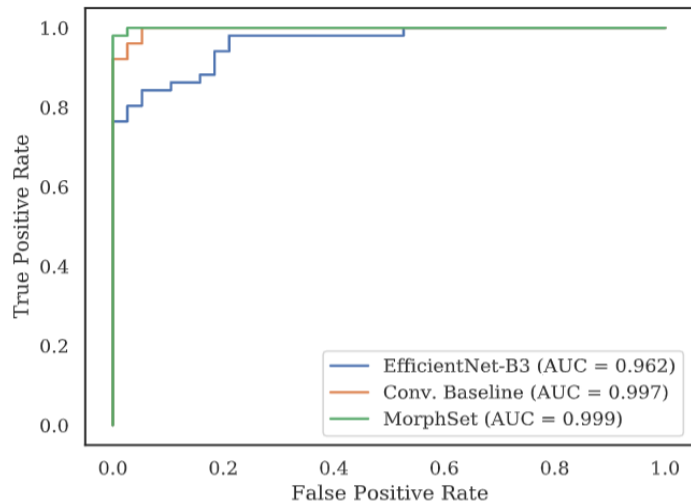
Varol et al. Transplantation (2022)

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AMR Diagnosis with Machine Learning

- Semi-supervised training (binary biopsy label: AMR vs. noAMR)
 - n=89 biopsies, n=51 AMR, n=38 noAMR
 - Only glomeruli on PAS whole slide images
 - n=1655 glomerular crops, expert annotated
- Three experimental models:
 - EfficientNet-B3-Encoder with fully supervised training vs. expert consensus label
 - Semi supervised ConvNet model
 - Morphset model



Cicalese et al. MICCAI (2020)

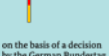
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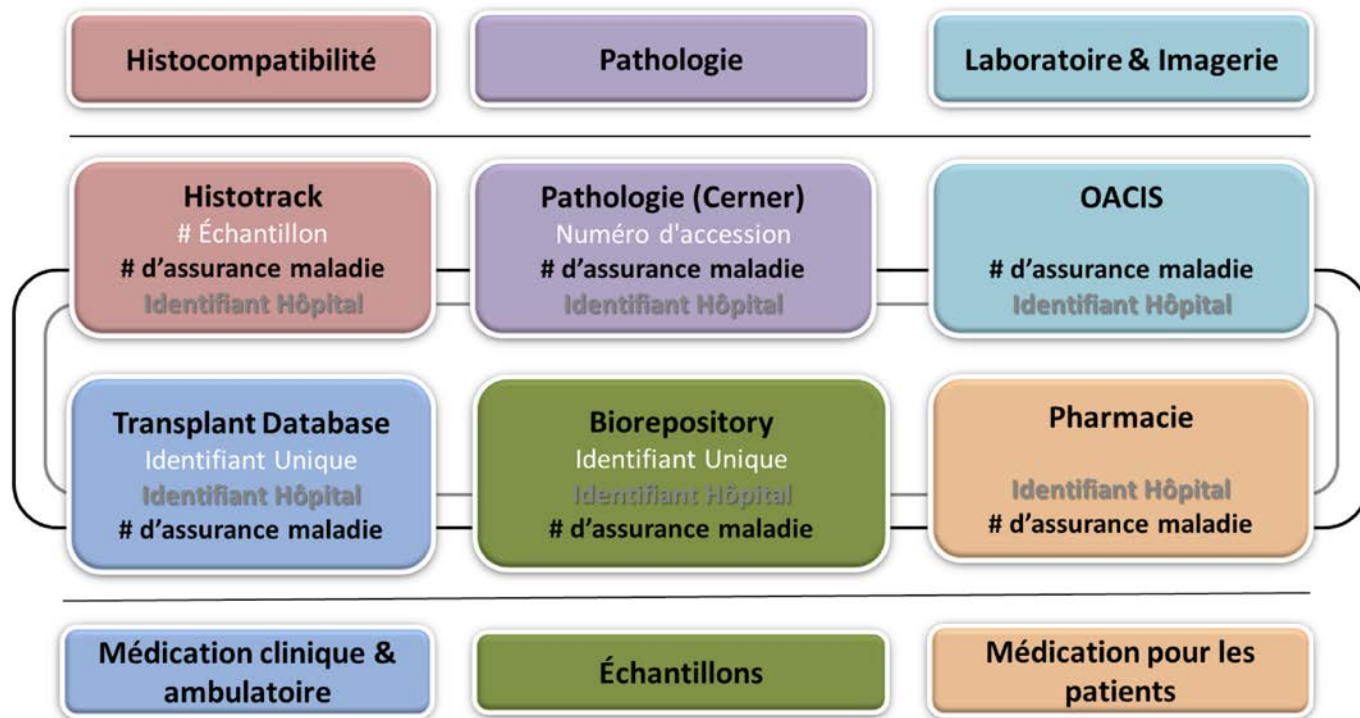
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Digital Pathology & AI

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Sources de données et plan de liaison pour les centres du Québec (NephroCAGE)



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Computation pathology Infrastructure



Slide scanner with full time research assistant



Local server housed in research institute (50Tbs/250Tbs)



Renal Transplant Pathology
(scanning retrospective cases
125 patients; 690 digital files)



Welcome Dr. Pierre-Olivier Fiset

Local AI computer with
dual RTX A1000 GPUs

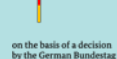


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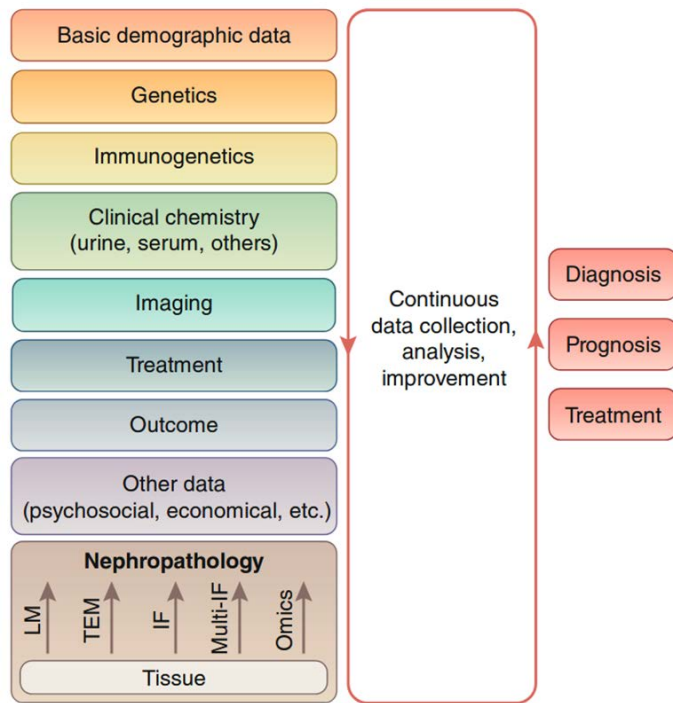
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Nephropathology, Big Data, AI, and Precision Medicine



Nephropathology, Big Data, AI, and Precision Medicine

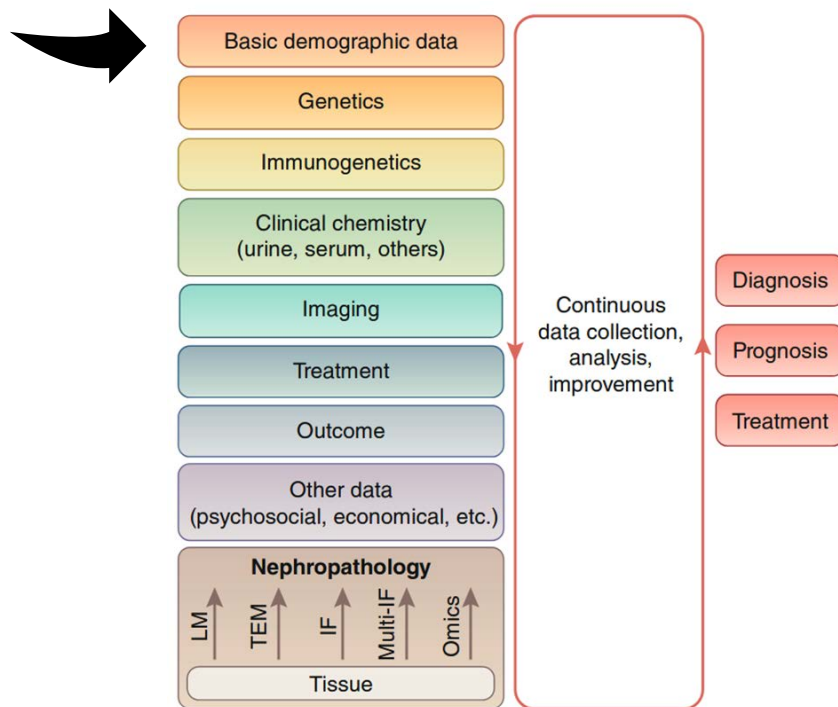


Becker et al. KI (2020)

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Nephropathology, Big Data, AI, and Precision Medicine

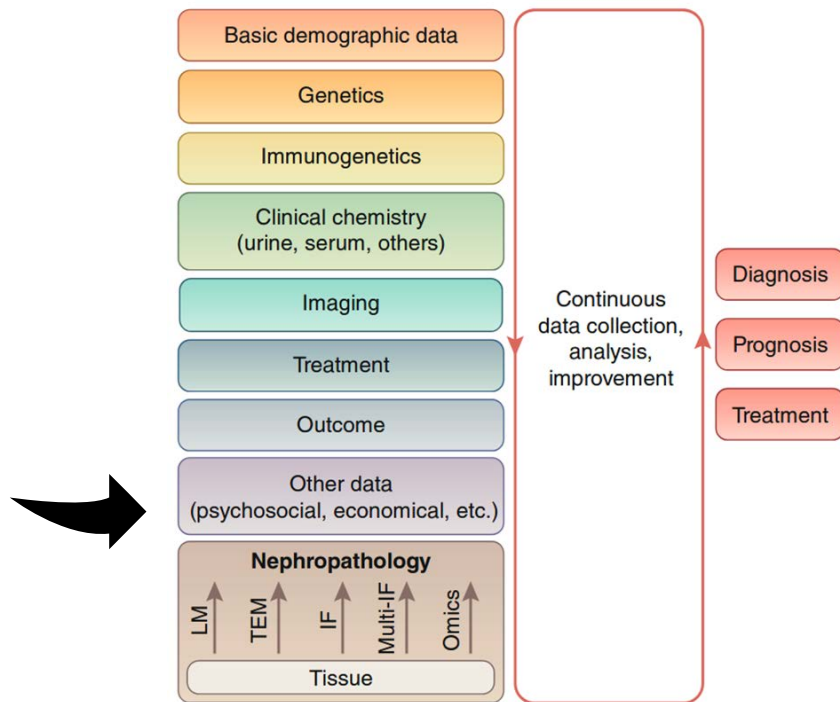


Becker et al. KI (2020)

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Nephropathology, Big Data, AI, and Precision Medicine

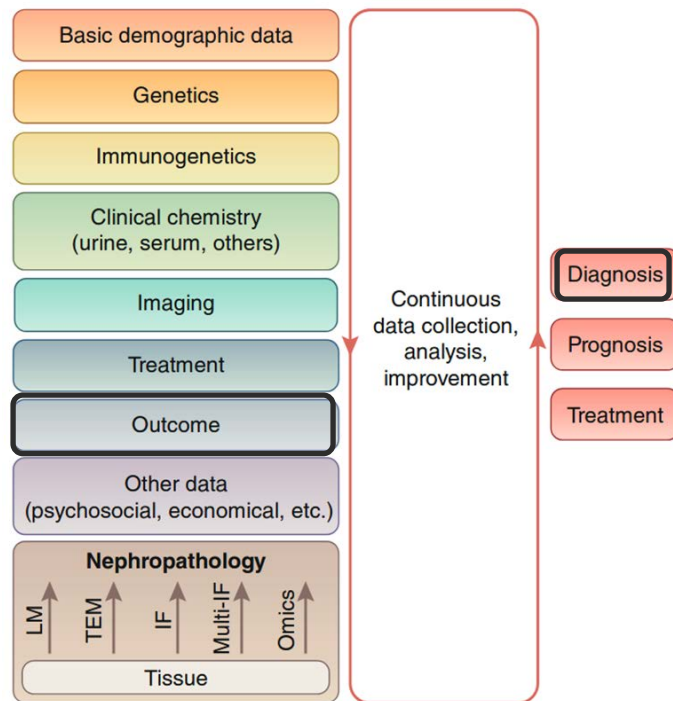


Becker et al. KI (2020)

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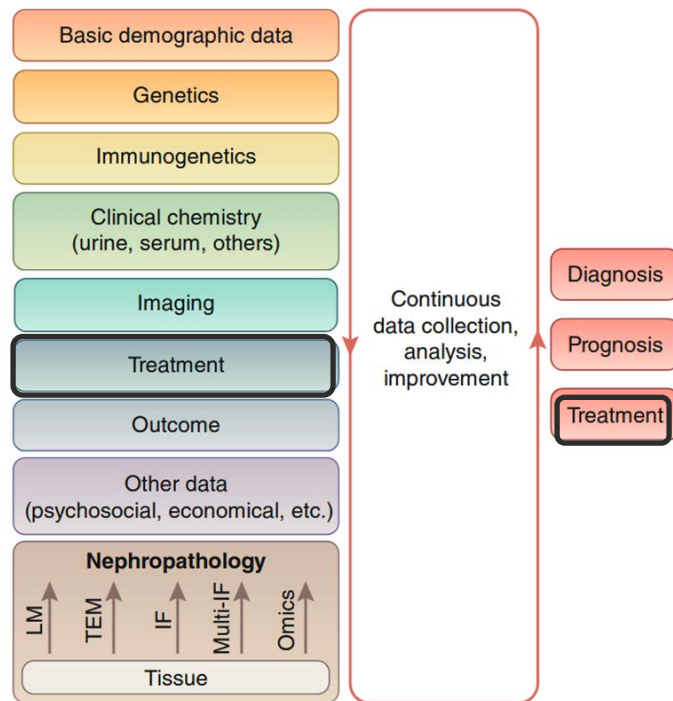


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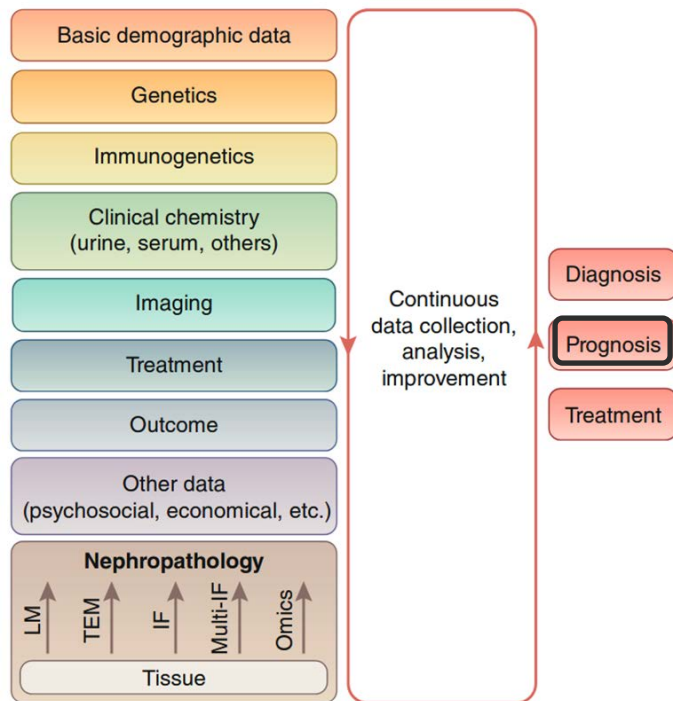


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Banff-Antibody-Mediated Injury Working Group

LM Bow, E Cozzi, I Batal, T Horak, A Amar-Zifkin, C Schinstock, M Askar, DM Dadhania, M Cooper, M Naesens, ES Kraus.
Drs. SS Jatana, H Zhao, and Z Song

Pathology (MUHC, CHUM, HMR & CHUQ)

Dr. Pierre-Olivier Fiset
Dr. Chantal Bernard
Dr. Rene Michel

Banff Rules and Dissemination Working Group

Dr. Jan Becker
Dr. Candice Roufousse

Research Team

Dr. Samuel El Bouzaidi Tiali (Maelstrom Research)
Edden Gitelman, BSc
Dr. Mohammed Kaouache (Biostats platform)



Precision Medicine **CanPrevent** Antibody-Mediated Rejection

Co-leads: Drs. Keown, Sapir-Pichhadze, Caulfield, Bryan

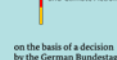
Co-applicants:

Dr. Rene Duquesnoy
Dr. Derek Middleton
Dr. Steven Marsh
Dr. Jiannis Ragoussis
Dr. Marcel Tilanus,
Dr. Karim Oualkacha
Dr. Kathryn Tincam
Dr. Robert Liwski
Dr. Patricia Campbell
Dr. Heloise Cardinal
Dr. Sacha DeSerres
Dr. Lenka Allan
Dr. Chee Loong Saw
Dr. Michael Mengel

Dr. Banu Sis
Dr. Frans Claas
Dr. Henry Erlich
Dr. Howard Gebel
Dr. Gerhard Opelz
Dr. Eric Weimer
Dr. Karen Sherwood
Dr. Eric Wagner
Dr. Noureddine Berka
Dr. Bruce McManus
Dr. Robert McMaster
Dr. Marie-Josée Hebert
Dr. Leonard Foster
Dr. Fabio Rossi

Dr. Christoph Borchers
Dr. Ciro Piccirillo
Dr. Constantin Polychronakos
Dr. Raymond Ng
Dr. Michael Oellerich
Dr. Anthony Jevnikar
Dr. Pieter Cullis
Dr. Guido Filler
Dr. Harvey Wong
Dr. Teun van Gelder
Dr. Pierre Marquet
Dr. Bruce Kaplan
Dr. Gilbert Burckart
Dr. Bethany Foster

Dr. John Gill
Dr. Joseph Kim
Dr. Lee Anne Tibbles
Dr. Atul Humar
Dr. James Lan
Dr. Steven Shechter
Dr. Prosanto Chaudhury
Dr. Nicolas Fernandez
Dr. Elizabeth Fowler
Dr. Bryce Kiberd
Dr. Karthik Tennankore
Dr. Jagbir Gill
Dr. Marie-Chantal Fortin
Dr. Scott Klarenbach
Dr. Carlo Marra
Dr. Zoltan Kilo
Dr. Seema Mittal
Dr. Istanu Musca
Dr. David Sorrow
Dr. Calvin Stiller OC
Dr. Rylan Parekh
Dr. Lucie Richard
Dr. Lynne Senecal



M[i]⁴ Interdisciplinary Initiative in Infection and Immunity

Centre universitaire de santé McGill
Institut de recherche



McGill University
Health Centre
Research Institute



GenomeCanada



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



kidney
Foundation
Canada



GenomeQuébec

Fonds de recherche
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Fondation
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