

Vascular Remodeling Research Fellowship Jewish General Hospital-McGill University

Name of Institution: Jewish General Hospital/Lady Davis Institute for Medical Research

Type of Fellowship: Clinical/Research Fellowship

Length of Fellowship: Two years

Number of Fellowship Positions: 1-2 per year

Academic Affiliation: McGill University

Name of Hospitals Involved in Training: Jewish General Hospital-100%

Research Activity:

Mark Lipman, MD

T-cell rearrangements of graft infiltrating lymphocytes.

Cytokine gene expression in protocol renal biopsies

Mediators of phosphate homeostasis in chronic kidney disease.

Dr. Lipman is Chief of the Division of Nephrology at the JGH. He has a longstanding research interest in renal transplantation immune-biology but has also made important contributions in the area of phosphate homeostasis. He was the first to clone the full-length human PHEX gene, a key regulator of phosphate excretion.

Dr. Lipman is a graduate of McGill University Faculty of Medicine and did his post-graduate research fellowship training at Harvard University.

S. Nessim, MD

The role of Vitamin D in the management of patients with chronic kidney disease.

Predictors of peritonitis in the peritoneal dialysis population.

Dr. Nessim is a newly recruited nephrologist who just completed her Master's degree in Clinical Epidemiology and has strong interests in clinical research. She has specific expertise in the peritoneal dialysis population and general interest in the management of metabolic bone disease in patients with chronic kidney disease.

Dr. Nessim is a graduate of McGill University Faculty of Medicine and did her post-graduate research fellowship training at the University of Toronto.

A. Karaplis, MD, PhD

Osteogenic transformation of vascular smooth muscle cells.

Dr. Karaplis is an endocrinologist and a world renowned expert in bone biology. He was the first to describe the physiological role for PTHrp in normal bone/chondrocyte

development. He has made numerous seminal contributions to this field of study over the past 20 years.

Dr. Karaplis is a graduate of McGill University Faculty of Medicine and did his post-graduate research fellowship training at Harvard University and the Massachusetts Institute of Technology.

Ernesto Schiffrin, MD, PhD

Vascular remodeling of resistance arterioles in disease states.

Dr. Schiffrin is Chairman of the Department of Medicine at the JGH and Vice-Chairman (Research) for the Department of Medicine of McGill University. He is a world renowned expert in hypertension and vascular remodeling having pioneered the technique for the study of small resistance arteries. His scientific contributions to his field of research span over 3 decades and are legion.

Requirements

- 1) Completion or anticipation of completion of clinical training in nephrology, cardiology, or internal medicine.
- 2) Good academic standing.
- 3) One or two reference letters from previous supervisors.
- 4) Complete C.V. submission.
- 5) Working knowledge of French or English.
- 6) Interview by Training Program Director.
- 7) The candidate must be successful in obtaining fellowship funding from one of the following agencies: FRSQ, CIHR, Heart and Stroke, Kidney Foundation, etc. Foreign candidates who have funding from their local agencies will be considered.

Mission

The purpose of this fellowship is to develop expertise in the study of the pathogenesis of arterial disease. Emphasis is placed on the structural and functional changes that occur in arteries in several disease states including hypertension and diabetes. However, there is a specific focus on the vasculopathy that develops in patients with progressive renal insufficiency.

The cardiovascular complication event rate is dramatically elevated in patients with renal disease and is attributable to both the traditional and non-traditional risk factors in

this population. The former includes hypertension, diabetes, hyperlipidemia, smoking, male gender, etc. The latter includes a state of chronic inflammation, hemodynamic lability, vascular calcification, etc. Together, these risk factors contribute to a cardiovascular complication rate in patients with advanced chronic kidney disease (CKD) that can be up to 100-fold higher than age-matched controls with normal renal function.

The fellowship will provide in-depth teaching on the qualitative changes in the vasculature that transpires in CKD. Postulated pathogenic mechanisms that contribute to these changes will be reviewed critically.

The fellow will master many of the state-of-the-art techniques for evaluating arterial changes. For the larger arteries this will include developing expertise with equipment that can measure pulse wave velocity (PWV), aortic augmentation index, arterial compliance. For the medium-sized arteries, techniques to measure carotid artery parameters (intimal-medial thickness, carotid diameter) will be acquired. Finally, for smaller arteries a biopsy technique will be taught to procure resistance arterioles. Additionally, the fellow will learn how to evaluate these arteries using bench-side laboratory myogenic measurements and assays of endothelial function.

Combined, these techniques will provide the fellow with a comprehensive set of skills with which to evaluate arterial structure and function. The fellow will apply these techniques in the context of a clinical research project that will be designed by the fellow with the support and advice of the principal teachers. The expectation is that the fellow will design an experimental protocol that will contribute to the understanding of vascular remodeling in patients with CKD. The project must be of the scope that it can be completed in no more than two years. The project will respect all the norms and standards of clinical research that are in place at the Jewish General Hospital.

As this is a research intensive fellowship, there are no mandated clinical or teaching responsibilities in this program. However, the fellow will participate in all academic conferences and rounds throughout the tenure of the fellowship period.

The candidate will be encouraged to apply for a Master's degree in experimental science or clinical epidemiology. This will afford the candidate a better understanding of clinical research methodology and biostatistics.

The expectations for the candidate are to design and carry out a clinical research project with relevance to vascular remodeling using the technical tools and research methods acquired. Data that is accrued will be analyzed by the candidate and presented in abstract form at a national or international scientific meeting. When merited, the data will be submitted in the form of a manuscript for publication in a peer-reviewed journal and may be used as part of a thesis if the candidate has enrolled in Master's program.

The anticipated time line is for the fellow to acquire the technical and laboratory skills within the first 3-4 months of fellowship. During this time the clinical research project will be conceived and designed. Research protocols and patient consent forms will be

finalized and approval will be obtained from the hospital's Research and Ethics Committee. The research project will run for the next 6-18 months followed by a period of 2-3 months for data analysis and preparation of abstract/manuscript.

Specifically the candidate will be evaluated on:

- 1) Ability to perform the non-invasive arterial testing and to interpret the data generated.
- 2) Ability to perform subcutaneous biopsies to harvest resistance arteries and to apply the appropriate laboratory techniques for assessing the structure and function of these vessels.
- 3) Ability to conceive, design and carry out a relevant clinical research project on vascular remodeling.
- 4) Ability to analyze the results and to write a scientific abstract and/or manuscript.

The fellow's successful completion of the program will be evaluated by the teaching faculty named below.

Name of Fellowship Program Director: Dr. Mark Lipman

Names of Teaching Faculty: Dr. Ernesto L. Schiffrin, Dr. Mark Lipman, Dr. Andrew Karaplis.

Publication references available upon request.