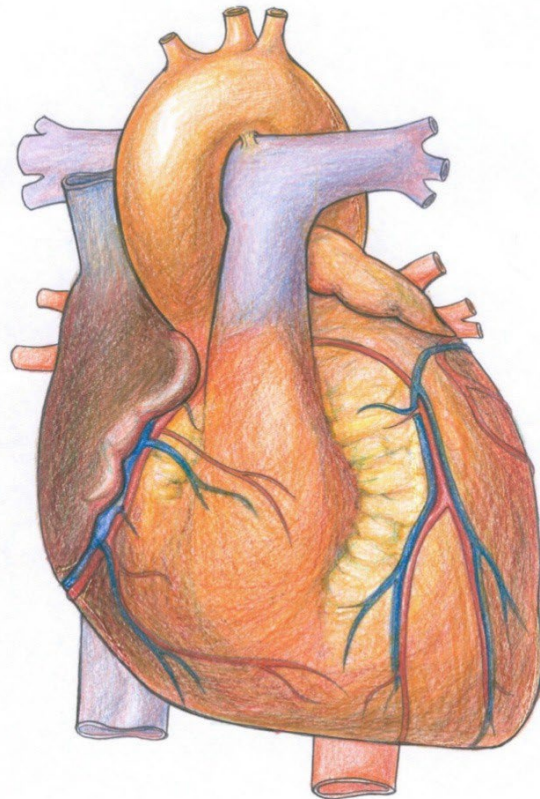


Regenerative Medicine Scholarly Pathway 2022



**Course Director:
Lina Shehadeh, PhD**

[Inside Our Labs: Behind
the Scenes of
Regenerative Medicine](#)

Regenerative Medicine Scholarly Pathway Course

03/15/22 through 05/17/22

Course Module Director: Lina Shehadeh, PhD

I. Introduction

The faculty involved with the teachings of the Regenerative Medicine Scholarly Pathway Course want to welcome you to the next seven weeks of stimulating learning. This marks a major transition in your medical education! The Regenerative Medicine Scholarly Pathway is one of 22 scholarly pathways that NextGen medical students get the chance to enroll in and pursue as a research track during their entire medical education journey. Our primary goals are for you to develop a strong foundation of regenerative medicine and develop a research knowledge base that allows you to understand and appreciate related research articles, and enroll in a UM research laboratory and perform cutting edge research under the mentorship of one of our best regenerative medicine faculty.

II. Course Description

The structure of the regenerative medicine scholarly pathway course allows the students to develop a basic understanding of the evolution of regenerative medicine and its application to vast variety of diseases. Importantly, the structure of the course will help the students understand and discuss research on stem cell application. Attendance and participation is required for all 9 sessions as this is the best opportunity to solidify your self-directed learning and of course ask questions. Multiple faculty members from different disciplines and subspecialties will be involved in these teachings. We plan to record all the 9 in-class and zoom sessions. Specific objectives for all teaching activities are clearly stated in this syllabus along with supplemental content and reading material.

Content Flow

This course is 9 sessions in total that aims to meet the learning goals on 1) Gene Therapy, 2) Cell Transplantation, 3) Transplantation Immunology, and Induced Pluripotent Stem Cells (IPSCs) – each detailed below under Course Objectives. Throughout the course, we will discuss a group of research articles that are focused on lentiviral gene therapy using hematopoietic stem cells (HSCs) for treatment of sickle cell disease (SCD). This is a fascinating story from bench to bedside with successes in clinical trials and a most recent 2021 halt on the trials because of a suspected leukemia side effect. The distribution of the student presentation will be throughout the course to make these discussions integrated with the teaching material presented by the faculty. Also throughout the course, the students will work on their other assignments listed below.

Dr. Shehadeh will be available throughout the course to help you stay oriented and direct you when necessary. We can have a class representative to establish effective and accurate communications throughout the course. The faculty involved in the teaching of the course and the research mentors (listed in the faculty roster below) are available to

discuss your interests and answer questions. Please reach out to them by email and you can schedule 1:1 meetings with them.

III. **Research Articles and Presentations**

The theme of the research articles studied and discussed in this course will be on lentiviral gene therapy using hematopoietic stem cells (HSCs) for treatment of sickle cell disease (SCD). This is a fascinating story from bench to bedside with successes in clinical trials and a most recent 2021 halt on the trials because of a suspected leukemia side effect. **Eight research papers are posted on Blackboard** and will be used for article discussions and presentations.

IV. **Interview with a Physician Scientist**

Each student will interview one of our successful physician scientists at UM and present the interview to the class. The goal of this activity is to learn from the various experiences of UM physician scientists who can be role models for the the MD students. After planning with Dr. Shehadeh, each student will reach out to the physician scientist and schedule the date of the interview and the date of presenting to the class.

V. **Stock Market Analysis of a Regenerative Medicine Company**

The goal of this exercise is to understand the link between science, discoveries, publications, clinical trials on one hand and the value of regenerative medicine companies on the stock market on the other hand. After planning with Dr. Shehadeh, each student will chose one pharmaceutical company and summarize to the group its history and value in relation to preclinical and clinical studies.

VI. **Scholarly project proposal:** The culmination of this course will be the development of a scholarly project proposal that states the scholarly (research) question that will be examined in the mentoring project, and an outline of the scholarly project activities that will take place in June – July 2022. Pathways may specify a more detailed format, but the general format will be a 1-page background section that contains a statement of the scholarly question, and a 1-2 page outline of the components of the scholarly project plan (organized as specific aims, deliverables or milestones, or project components or elements, depending on the discipline of study). The pathway director and mentor will evaluate the sufficiency of this proposal. A general rubric for the evaluation is provided on Blackboard.

At the end of the course, students who performed less than satisfactory will be notified in **TWO WAYS**. Each student will receive a letter signed by the coordinators with a copy sent to Dean Chrisfouad Alabiad. Each student will also be notified by the student e-mail address. These students are then **required** to notify Dr. Shehadeh, by e-mail at lshehadeh@miami.edu. A meeting will be scheduled with Dr. Shehadeh to discuss options.

VII. **Nine SESSIONS:**

There are **nine** mandatory sessions during the 9 week module. The schedule shown below is updated in Blackboard with room numbers and zoom links. **Please use Blackboard as the most updated version of the schedule.**

These sessions consist of some lectures, and small group sessions. These 9 sessions are listed below and will be labeled mandatory on the posted schedule. The first session will take place in the 4th floor auditorium and all the remaining sessions are via zoom. The plan is to record all 9 sessions.

All absences, whether excused or unexcused, will be monitored and tracked. Too many could result in a **PIRS**. This includes both excused and unexcused absences. Please refer to the “Medical Student Rights and Responsibilities Handbook 2019 - 2020” pages 12-14 for more information on this.

Nine Sessions

	Date	Time	Title	Faculty	Objectives
Tuesday	3/15/22	2:00-4:00 (Zoom-Recorded)	Introduction to Regenerative Medicine Pathway	Lina Shehadeh, PhD	
Tuesday	3/22/22	2:00-4:00 (Zoom-Recorded)	Induced pluripotent stem cells in disease modeling and therapy	Derek Dykxhoorn, PhD	Meet Pathway Goal #4 on IPSCs
Tuesday	3/29/22	2:00-4:00 (Zoom-Recorded)	Cardiovascular Gene Therapy: Past, Present and Future	Roberto Vazquez, PhD	Meet Pathway Goal #1 on Gene Therapy
Tuesday	4/5/22		Spring Break		
Tuesday	4/12/22	2:00-4:00 (Zoom-Recorded)	Bringing the Next Generation of Medicine to the Cellular and Genetic Levels	Chunming Dong, MD	Meet Pathway Goal # 2 and understand the biology of adult stem cell senescence
Tuesday	4/19/22	2:00-4:00 (Zoom-Recorded)	Alphabet Soup: The Basic Immunobiology of Transplantation	Asha Pillai, MD	Meet Pathway Goal #3 (i-iii) on Transplantation Immunology
Tuesday	4/26/22	2:00-4:00 (Zoom-Recorded)	Graft-versus-host disease, Graft-versus-leukemia effect, and immunotherapy	Asha Pillai, MD	Meet Pathway Goal #3 (iv-vi) on Transplantation Immunology
Tuesday	5/3/22	2:00-4:00 (Zoom-Recorded)	Research Article Discussion	Lina Shehadeh, PhD	
Tuesday	5/10/22	2:00-4:00 (Zoom-Recorded)	Assignment Presentations	Lina Shehadeh, PhD	
Tuesday	5/17/22	2:00-4:00 (Zoom-Recorded)	Assignment Presentations	Lina Shehadeh, PhD	

VIII. GRADING:

The final grade is the sum of points earned from the participation, research paper presentation, scholarly project proposal, interview of a physician scientist, and stock market analysis of a regenerative medicine company.

Participation: 3% x 8 sessions = 24%

Research Paper Presentation = 26%

Scholarly Project Proposal = 30%

Interview with a Physician Scientist = 10%

Stock Market Analysis of a Regenerative Medicine Company = 10%

- a) **Passing Grade:** It is anticipated that a **passing grade** for the module will be a **score of 70%**; however, the cutoff point will, of course, depend upon the final grade distribution. The course director will review the distribution of grades and make a determination regarding the lowest possible passing score for the module.
- b) **Failing Grade:** < 70% (unless adjusted as discussed above)
- c) **D Grades:** Depending upon the final grade distribution, a grade of D may be assigned by the module coordinators to students whose performance is close to a failing grade. This could result in a recommendation for the student to perform remedial work. Unless altered by the class grade distribution, **students scoring 70%-74% will receive a D grade.** The promotions committee will make the final decision regarding this issue.
- d) **Remedial Work:** Permission to perform remedial work and the date for the remediation must be approved by both the course director and the Freshman Promotion Committee.

Any student with special circumstances must meet with the coordinators so appropriate accommodations can be made. The course director needs to know about these special circumstances before missing a deadline.

In the event of a personal emergency, the course director and the Office of Student Affairs must be notified of the absence as soon as possible. Missed deadlines will be rescheduled at the discretion of the course director. Unexcused absences will result in a grade of zero (0) for the missed work.

IX. Syllabus

The syllabus contains the seven-week course schedule, lecture objectives, assignments, reference to papers posted on Blackboard, grade breakdown, course directions when applicable, faculty roster, and the list of available mentors and a short description of their research programs. Pertinent information and handouts will be provided as required on Blackboard. The student is urged to keep up-to-date with the syllabus.

X. Attendance

Student attendance is mandatory for all 9 interactive sessions. We look forward to these seven weeks of exciting interactions.

From "our heart to yours."
Lina Shehadeh, PhD

Faculty Roster

Includes faculty office locations and phone numbers. Faculty e-mail addresses can be located in the University of Miami Miller School of Medicine's e-mail address book. Students are encouraged to discuss any problems or concerns with the course director and seek out individual faculty if desired.

Faculty	Email	Department	Address
Chunming Dong, MD	cdong3@med.miami.edu	Medicine	BRB 812
Derek Dykxhoorn, PhD	DDykxhoorn@med.miami.edu	Human Genetics	BRB 406
Joshua Hare, MD	jbarrett@miami.edu	Medicine	BRB 910
Robert Levy, PhD	rlevy@med.miami.edu	Microbiology	RMSB 3123A
Asha Pillai, MD	asha.pillai@med.miami.edu	Pediatrics	BCRI 745
Lina Shehadeh, PhD	lshehadeh@med.miami.edu	Medicine	BRB 818
Roberto Vazquez-Padron, PhD	rvazquez@med.miami.edu	Surgery	RMSB 1048
Karen Young, MD	KYoung3@med.miami.edu	Pediatrics	BCRI 345

Regenerative Medicine Scholarly Pathway Course Objectives

Pathway Goals:

#1 Gene Therapy

After the course, the students should be able to:

1. Explain mechanisms that are involved in viral gene integration in mammalian cells.
2. Apply their knowledge in molecular biology to genetic modification of mammalian cells. This means they should be able to develop cloning strategies for your gene of interest into a viral vector and propose a strategy for *in vivo* genetic manipulation.
3. Apply their knowledge in single gene disorders and develop treatment schemes for patients with these disorders using gene therapy.

#2 Cell Transplantation

After the course, the students will be able to:

1. Describe the basics of stem cell biology, different types of stem cells and the immunological mechanisms behind engraftment and rejection, and how tolerance develops after transplantation.
2. Extract and integrate information from state-of-the-art lectures in combination with overview articles and literature searches on the internet within the research field.

#3 Transplantation Immunology

After the course, the students are expected to be able to:

1. Discuss immunological principles of relevance to transplantation and relate those to normal immunological reactions.
2. Relate relevant methods used for investigations and diagnosis in relation to stem cell and organ transplantation.
3. Discuss the cutting-edge of preclinical transplantation research.
4. Discuss diagnostic principles before and after transplantation that are under development.
5. Give a historical perspective of clinical and preclinical transplantation.
6. Reflect over the future of clinical transplantation immunology.

#4 Induced Pluripotent Stem Cells (iPSCs)

After the course, the students are expected to be able to understand how:

1. Patient-specific iPSCs, and the differentiated products, can help to better understand pathogenic mechanisms that underlie disease.
2. Patient-specific iPSCs can serve as a source of autologous cells for transplantation therapies.

Introduction to Regenerative Medicine Pathway

Lina Shehadeh, PhD

March 15, 2022

2:00 – 4:00pm

Zoom Session

Learning Objectives:

- A. Go over syllabus.
- B. Meet each other and learn about each other's interests.
- C. Plan paper discussions and presentations.
- D. Plan the interviews and other assignments.
- E. Plan and assign deadlines.
- F. Help identify research mentor and plan pathway research project.
- G. Update on mentor-mentee matches.

Induced pluripotent stem cells (iPSCs) in disease modeling and therapy

Derek Dyxhoorn, PhD

Tuesday March 22, 2022

2:00 – 4:00pm

Zoom Session

Learning Objectives:

- A. Patient-specific iPSCs, and the differentiated products, can help to better understand pathogenic mechanisms that underlie disease.
- B. Patient-specific iPSCs can serve as a source of autologous cells for transplantation therapies

Cardiovascular Gene Therapy: Past, Present and Future

Roberto Vazquez-Padron, PhD

Tuesday March 29, 2022

2:00 – 4:00pm

Zoom Session

Learning Objectives:

- A. Explain mechanisms that are involved in viral gene integration in mammalian cells.
- B. Apply their knowledge in molecular biology to genetic modification of mammalian cells. This means they should be able to develop cloning strategies for your gene of interest into a viral vector and propose a strategy for in vivo genetic manipulation.
- C. Apply their knowledge in single gene disorders and develop treatment schemes for patients with these disorders using gene therapy.

Bringing the Next Generation of Medicine to the Cellular and Genetic Levels

Chunming Dong, MD

Tuesday April 12, 2022

2:00 – 4:00pm

Zoom Session

Learning Objectives:

- A. Describe the basics of stem cell biology, different types of stem cells and the immunological mechanisms behind engraftment and rejection, and how tolerance develops after transplantation.
- B. Extract and integrate information from state-of-the-art lectures in combination with overview articles and literature searches on the internet within the research field.
- C. Understand the biology of adult stem cell senescence.

Alphabet Soup: The Basic Immunobiology of Transplantation #1

Asha Pillai, MD

Tuesday April 19, 2022

2:00 – 4:00pm

Zoom Session

Learning Objectives:

- A. Discuss immunological principles of relevance to transplantation and relate those to normal immunological reactions.
- B. Relate relevant methods used for investigations and diagnosis in relation to stem cell and organ transplantation.
- C. Discuss the cutting-edge of preclinical transplantation research.

Graft-versus-host disease, Graft-versus-leukemia effect, and immunotherapy #2

Asha Pillai, MD

Tuesday April 26, 2022

2:00 – 4:00pm

Zoom Session

Learning Objectives:

- A. Discuss diagnostic principles before and after transplantation that are under development.
- B. Give a historical perspective of clinical and preclinical transplantation.
- C. Reflect over the future of clinical transplantation immunology.

Research Article Presentation and Discussion

Lina Shehadeh, PhD

Tuesday May 3, 2022

2:00 – 4:00pm

Zoom Session

Assignment Presentation

Lina Shehadeh, PhD

Tuesday May 10, 2022

2:00 – 4:00pm

Zoom Session

Assignment Presentation

Lina Shehadeh, PhD

Tuesday May 17, 2022

2:00 – 4:00pm

Zoom Session

8 Mentors

<https://www.shehadelab.com/scholarly-research-md-students>

1) Chunming Dong, MD



Research Summary:

My research spans from genomics, epigenetics, to molecular and cellular biology, as it relates to cardiovascular disease (CVD). My major focuses are atherosclerosis and the dysfunction of endothelial progenitor cells (EPCs)—a form of stem cells derived from the bone marrow and circulating in the peripheral blood—in the contexts of biological aging, smoking, HIV infection and cocaine abuse. Indeed, I have had multiple Federal and State grants to study the in-depth molecular mechanisms, focusing on microRNAs, underlying EPC dysfunction in aging, smoking and HIV infection. Over the last 5 years, my research has expanded to study the molecular mechanisms that underlie cocaine-induced cardiovascular disease (CVD) using small RNA and RNA sequencing and functional genomics. We are also investigating the use of extracellular vesicles (EVs)/exosomes and EV RNA sequencing to identify EV-microRNA (EV-miR) candidates that predict CVD in people living with HIV (PLHIV) and use EV injections to reconstitute the effects of HIV infection in the cardiovascular system. Furthermore, we have generated tailored EVs that carry modified EV-miR cargo by genetically engineering mesenchymal stromal cells (MSCs) and have successfully used these tailored EVs to treat CVD.

Research Projects:

1. Study the role of plasma EVs in mediating the effects of HIV infection in the development of HIV-associated accelerated CVD and the use of tailored EVs to prevent/treat CVD.
2. Investigate the microRNA-mRNA pathways that regulate the cocaine effects in the cardiovascular system.
3. Use CRIPR-Cas9 technology to knockout MHC molecules to create universal organs for allograft transplantation

2) Dr. Derek Dykxhoorn, PhD



Research Summary:

Research in the Dykxhoorn laboratory focuses on understanding the molecular and cellular mechanisms that underlie a variety of neurological disorders including neurodevelopmental, neurodegeneration, and sensorineural disorders. To that end, we apply novel stem cell based models of neurons, glial cells, and organoids to study the role of specific genetic variants in disease development. The ultimate goal of these experiments is to identify therapeutic targets that will effectively restore/normalize cellular functional and abrogate the development of these diseases, including the application of high content screening approaches along with genome editing approaches.

Research Projects:

1. Study the role of genetic variants in Alzheimer-associated genetic variants play in disease development.
2. Understand the role of the excitation/inhibition balance in proper neuronal development in autism and epilepsy.
3. Genome engineering and cell-based therapeutic strategies in the treatment of sensorineural hearing loss.

3) Dr. Joshua Hare, MD



Research Summary:

Our goal is to develop better understanding and treatments for heart disease. Our lab utilizes multiple approaches, ranging from cell culture to animal models to clinical trials. We perform mechanistic studies focusing on the cellular and molecular effects of nitric oxide (NO), novel pharmaceutical agents and cell therapy. Our studies revealed that NO influences normal and pathologic cardiac physiology, and signals in a complex manner through interactions between NO and reactive oxygen species, a process termed nitroso-redox balance. We have determined that Growth Hormone Releasing Hormone Receptor agonists have beneficial effects in large and small animal models of myocardial infarction, and we expect to move them into clinical trials in the near future. We have a longstanding interest in the pathophysiology and clinical manifestations of dilated cardiomyopathy (DCM), particularly the role of immunological activation and the microarray/transcriptomic profile of patients as a cause/diagnosis of DCM. Our significant experience with adult stem cells, including induced pluripotent stem cells (iPSCs), spans the gamut from basic research to clinical trials.

Research Projects:

1. Analysis of cardiac structure and function from small and large animal studies, e.g. magnetic resonance imaging, pressure volume loops, echocardiography, histology.
2. Manipulation of iPSCs and analysis of their differentiation into cardiomyocytes.

4) Dr. Robert Levy, PhD



Research Summary

Allogeneic hematopoietic stem cell transplantation (aHSCT) is a potentially curative therapy for a number of hematologic malignancies including acute myeloid leukemia (AML) and relapsed/refractory non-Hodgkin lymphoma (NHL). Unfortunately, graft vs host disease (GVHD) remains a serious clinical problem post-aHSCT which threatens anti-tumor (GVM) immune function and patient survival. As the number of aHSCTs rises, the need for better strategies to treat GVHD, while preserving the GVM response, remains paramount. The Levy lab is developing novel approaches to suppress GVHD while maintaining GVL. Our collaborative work with the Komanduri lab discovered that targeting the MEK pathway using a 3rd generation MEK inhibitor, trametinib specifically inhibits allo-reactive naïve and early memory T cells, while sparing pathogen- and cancer-specific donor T cells critical for GVM post-HSCT (Blood, 2013, PMC3674663; JCI Insight, 2016, PMC5033881). Building on these findings, we recently discovered a novel 2-pathway strategy for FoxP3+ Treg expansion in donors which spares GVM while suppressing GVHD (Biol Blood Marrow Transplant, 2017, PMC5625339 and 2018, PMID: 29751114). Recent work demonstrates their Treg strategy is superior to post-transplant cyclophosphamide (PTCy) for GVHD prophylaxis (JCI Insight, 2018 in revision). Based on the role of STING in modulating anti-tumor immunity, the Levy labs explored the role of STING in promoting the development of GVHD and discovered that GVHD following matched (“MUD”) HSCT is reduced in the absence of STING and worsened using STING agonists suggesting that inhibition of STING in recipient cells can be a novel strategy to reduce GVHD and maintain GVM (Sci Transl Med. 2020 Jul 15;12(552):eaay5006. doi: 10.1126/scitranslmed.aay5006.PMID: 32669421; <https://medicalxpress.com/news/2020-07-sylvester-protein-ease-graft-host.html>.)

Click [here](#) to see 2-slide summary and 7-minute video by Dr. Levy!

5) Dr. Asha Pillai, MD



There are 2 major areas within the Pillai Lab that are highly amenable to student involvement:

1. Graft-versus host disease (GVHD) is a common and often fatal complication of hematopoietic stem cell transplantation (HSCT), a curative treatment for cancers and non-cancerous diseases of the blood and immune system. The Pillai research group was first to discover that invariant natural killer T cells (iNKT cells, an arm of the innate immune system) allow tumor killing while preventing deleterious GVHD after BMT (Pillai et al, J Immunol 2007). The group further delineated an innate-adaptive immune regulatory pathway dependent upon iNKT cells and myeloid cells induced by them which augment graft-derived regulatory T cells through a PD-1/PD-ligand dependent process (Pillai et al, Blood 2009) van der Merwe et al, J Immunol Featured Article, 2013). Though this was first described in mouse models of HSCT, the findings have been successfully translated to advance the field of HSCT by allowing the development of reduced toxicity regimens of HSCT from mismatched donors, allowing >90% of patients without a matched donor to receive a transplant from a parent or child (Ped Transplant 2011, Blood 2017). The group recently published NIH-funded work in murine models of the hemoglobin disorders thalassemia (Shuyu E et al, Blood 2017) and (more recently) sickle cell disease/SCD, to demonstrate that the addition of alkylators to these regimens specifically promotes these immune axes in reduced-toxicity regimens to cure these disorders while protecting from development of GVHD. These findings are being translated to novel clinical trials to clear these disorders. Projects are available involving close collaboration with the PI and with senior molecular biologists and immunologists, allowing students to gain in-depth experience (with or without animal contact) with immune protocols such as advanced multi-parameter flow cytometry, 50+ immune marker analyses using mass cytometry/time-of-flight (CyTOF), and tissue-localizing mass cytometry as well as a variety of molecular immunology techniques. Additionally, advanced molecular immunology techniques and statistical methods will be emphasized.

1. Translating understandings of these immune parameters to human immunotherapy, the group has developed the first robust ex vivo expansion protocol for human iNKT cells, carefully optimizing means to expand these cells consistently as well as to optimally activate their anti-tumor killing capacity (Andrews et al, Cytotherapy 2020). We are currently focused on delineating specific pathways through which these activation signals regulate the anti-tumor capacity of human iNKT cells, with direct and major import for the development of novel iNKT immunotherapies of a variety of cancers, through the Sylvester Cancer Center. A number of focused projects exist in which human innate lymphoid subsets are being robustly expanded for immunotherapy and specific novel pathways that activate their therapeutic potential are being delineated and optimized. These studies involve collaboration with senior molecular biologists and immunologists in the group and will allow the student to rapidly gain proficiency in human T cell culture, management of cancer cell lines, transduction of cells with receptors targeting them for immunotherapy, and a variety of molecular immunology and data analysis techniques including advanced flow cytometry and CyTOF.

Students interested in the laboratory are encouraged to speak to one of our active medical students, Jamie Clarke, a Oncology Honors Pathway of the recently NCI-Designated Sylvester Comprehensive Cancer Center (SCCC). She can be reached at jamieclarke@med.miami.edu.

6) Dr. Lina A Shehadeh, PhD



Research Summary:

Click [here](#) to check out projects at the Shehadeh Lab.

Research Projects:

1. Screening of FDA-approved drugs to identify best candidates for reducing LDL cholesterol influx. The assay employs Alport patient-derived iPSCs differentiated into renal tubular epithelial cells, and live cell imaging.
2. Screening of FDA-approved drugs to identify best candidates for inducing cardiac regeneration (endogenous adult cardiomyocyte division). The assay employs mosaic analysis with double markers (MADM) mice in which cardiomyocyte division is evidenced by single colored red or green daughter cells.
3. Screening of FDA-approved drugs (and other reagents) to identify best candidates for reducing SARS-Co-V2-spike bearing pseudoviral infection. The assay employs inoculation with pseudovirus in various human cell lines, and live cell imaging.

7) Dr. Roberto I Vazquez-Padron, PhD



Research Summary:

My research focuses on the cellular and molecular mechanisms underlying obstructive vascular diseases like atherosclerosis, in-stent restenosis, transplant vasculopathy, and arteriovenous fistula failure. In particular, my laboratory aims at understanding the role of integrins, tyrosine kinases, and ECM modifying enzymes in the phenotypic switching and growth of constituent cells in arterial and venous walls in response to physiological and pathological cues. The work of my research group involves human studies and cellular and in vivo models. As a basic scientist with many clinical collaborators, my overall goal is to provide a better molecular understanding of these diseases so that improved vascular therapies can be designed.

Research Projects:

1. The role of microbiome in Inflammatory Bowel Disease related atherosclerosis.
2. Catheter infections and vascular diseases
3. The role of Lysyl Oxidase in vascular calcification

8) Dr. Karen Young, MD, MS



Research Summary:

Dr. Young's laboratory is housed in the Batchelor Children's Research Institute. Her lab's primary focus is understanding the molecular and cellular mechanisms that lead to endothelial dysfunction in preterm infants with bronchopulmonary dysplasia (BPD) and pulmonary hypertension (PH). Her **current projects** involve 1) defining the mechanisms by which mesenchymal stem cell cells and their exosomes reduce BPD/PH, 2) elucidating whether endothelial progenitor cell mitochondrial dysfunction is a common major cellular pathway that links neonatal intermittent hypoxia episodes to long-term endothelial dysfunctional states and impaired cardiopulmonary outcomes, 3) defining the role of aging pathways in BPD/PH pathogenesis and 4) understanding the molecular mechanisms that link placental dysfunction to BPD/PH. Over the past 2 decades, Dr. Young has mentored many undergraduates, medical students, residents, and fellows, many of whom have received research awards and themselves become leaders and mentors.