Carla J. Greenbaum, MD

Project: *Understanding immune and clinical causes of diabetes-related risk in COVID-19*

Institution: Benaroya Research Institute at Virginia Mason

Diabetes Type: Both type 1 and type 2 diabetes

Program Area: Immunology

"It is so gratifying to see decades of basic science research translating to improved health for people living with type 1 diabetes. With the knowledge that we can delay the onset of type 1 diabetes, the myriad of new therapies for type 2 diabetes, and the increasing use of technologies—research already impacts people with diabetes. While significant scientific, psychological, and health care delivery issues remain to be wrestled with, the commitment of the American Diabetes Association and researchers worldwide continue to move the needle to a better life for those with diabetes and their family members."

Project Description:

The aim of this project is to understand, as widely reported, **why people with type 2 diabetes appear to be particularly impacted by the COVID-19 pandemic**. People with type 2 diabetes who are infected with COVID-19 are more likely to suffer complications. They are more likely to be hospitalized, be placed in intensive care units (ICU), have to use a ventilator and are less likely to survive their infection than those without type 2 diabetes. We will study how the immune system's response to infection differs among individuals infected with COVID-19 who do and do not have type 2 diabetes. We will also try to understand if these differences are part of the type 2 disease process itself. A further goal is to understand why some, but not all, people with type 2 diabetes have a worse outcome than others.

Goal:

We hope that this understanding will help clinicians target specific risk factors for treatment or suggest the most effective therapies to combat the consequences of COVID-19 infection in people living with type 2 diabetes.

Senta K. Georgia, PhD

Project: *Investigating beta cell survival, function, and metabolism during the pathogenesis of COVID-19*

Institution: Childrens Hospital Los Angeles

Diabetes Type: Both type 1 and type 2 diabetes

Program Area: Islet Biology/Apoptosis

"I have been involved in diabetes research for my entire professional career. Research is about making incremental insights that can add up to monumental discoveries. Diabetes is a global health issue, and it is only getting worse. The fact that my research contributes fundamental insights that will lead to the monumental discovery, i.e. a cure for diabetes, keeps me motivated to work every day. I work for my grandmother, who has diabetes. I work for my students' families who have diabetes. I work for the children seen in our clinics at Children's Hospital Los Angeles who have diabetes. And I work for all of the people I don't know who have diabetes."

Project Description:

This project focuses on the **effects of COVID-19 on the function, survival and regeneration of insulin cells**.There is a direct relationship between the number of insulin-secreting cells a person has and their capacity to maintain healthy blood sugar levels. We are trying to understand if having COVID-19 acutely injures insulin cells and if these cells are able to recover from COVID-induced injury. This information is critical to understanding if a generation of people will develop diabetes as a result of the COVID-19 pandemic. We will use experimental methods to detect insulin cell injury during a period where someone has the COVID-19 disease.

Goal:

If we can detect active insulin cell injury and understand how COVID-19 is inflicting this injury, then we can devise strategies to protect insulin cells from injury or help them recover after patients have won their battle against COVID-19.

Zhi Q. Yao, MD, PhD

Project: *Characterize the host immune responses in subjects with or without COVID-19 and/or diabetes*

Institution: East Tennessee State University

Diabetes Type: Both type 1 and type 2 diabetes

Program Area: Immunology

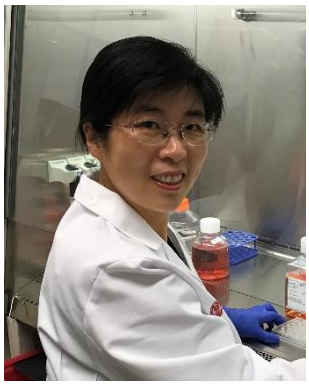
"The future of diabetes research will enable us to know more about prevention and treatment of both type 1 and type 2 diabetes, but this goal can only be achieved through scientific research supported by professional associations, physicians, scientists, and patients! We have to work together to fight diabetes and infectious diseases like COVID-19."

Project Description:

This study is meant to characterize the innate and adaptive immune responses in subjects with or without COVID-19 and/or diabetes to **have a better understanding of the impact of diabetes on COVID-19, and visa versa**.

Goal:

The purpose is to gain fundamental insights into their immunological profiles to guide future management of patients with COVID-19 and its complications with or without diabetes.



Shuibing Chen, PhD

Project: *Determine the impact of COVID-19 infection on human pancreatic endocrine cells*

Institution: Joan & Sanford I. Weill Medical College of Cornell University

Diabetes Type: Both type 1 and type 2 diabetes

Program Area: Islet Biology/Apoptosis

"Diabetes is a complicated polygenic disease. We study how genetic and environmental factors contribute to diabetes progression, and our research goal is to facilitate the development of personalized therapy. This grant will allow us to explore the impact of SARS-CoV-2 infection on human endocrine cells."

Project Description:

This study seeks to explore **what types of diabetes associated cells are infected and how those cells respond to COVID-19 infection**. Recent clinical studies show a strong association between COVID-19 and diabetes. In the Diabetes Program of Surgery at Weill Cornell Medicine, we focus on studying the impact of genetic factors and environmental factors on pancreatic β cell generation, function, and proliferation in type 1 and 2 diabetes. There is an urgent need for physiological models to study SARS-CoV-2 infection using diabetes-relevant human cells. We have created a platform comprised of human pluripotent stem cells (hPSC)-derived endocrine cells. We found that human pancreatic alpha and beta cells are highly permissive to SARS-CoV-2 infection, further validated using adult primary human islets. SARS-CoV-2 infection caused striking expression of chemokines, similar to primary human COVID-19 pulmonary autopsies.

Goal:

To validate the SARS-CoV-2 infection using autopsy pancreatic samples from COVID-19 patients and systematically evaluate the impact of SARS-CoV-2 infection on human endocrine cells.

Aaron S. Leong, MD, MSc

Project: *Using genetics to identify causal cardiometabolic risk factors of COVID-19 severity and diabetes-related complications in COVID-19*

Institution: Massachusetts General Hospital

Diabetes Type: Both type 1 and type 2 diabetes

Program Area: Epidemiology

"I have always wanted to do more for my patients and for people with diabetes around the world. My patients teach me about diabetes, which informs my research. Eventually, I hope to apply my research findings to the clinic. This award supports my overall research focus in the application of diabetes genetics to precision medicine and public health."

Project Description:

This project aims to examine the relationship between diabetes genetics and life-threatening complications of COVID-19 illness. We seek to **determine whether genetics can explain why some people with diabetes experience a more severe clinical course of COVID-19 than others.**

Goal:

We hope that this project will identify diabetes-related risk factors for COVID-19. By identifying genes and biological pathways related to COVID-19 severity and diabetes-related complications, we may target them therapeutically to reduce the risk of severe COVID-19 illness.

Michael David Maile, MD

Project: *Metabolic contributions to multiple organ failure in diabetic patients with COVID-19*

Institution: Regents of the University of Michigan

Diabetes Type: Type 2 diabetes

Program Area: Integrated Physiology/Fatty Acid Metabolism

"As a critical care physician, I routinely care for extremely sick patients, many of whom have diabetes. Critically ill patients are always at risk, and this risk is even greater for those with diabetes. Our lack of specialized treatments for patients with diabetes is frustrating as a clinician, and makes it particularly important for me to conduct diabetes research."

Project Description:

This project will investigate **why COVID-19 affects people with diabetes more severely than those without diabetes**. To better understand why this occurs, we will measure hundreds of metabolites and inflammatory proteins in serial samples collected over time from patients hospitalized with COVID-19. Differences between patients with and without a history of diabetes will be used to identify the pathways that produce this effect.

Goal:

Uncovering the underlying mechanisms will allow us to work on developing targeted therapies to improve the care of patients with diabetes suffering from COVID-19.

Tracey Lynn McLaughlin, MD

Project: *COVID-19: role of adipose tissue*

Institution: The Board of Trustees of the Leland Stanford Junior University

Research Type: Obesity

Program Area: Obesity/Clinical Treatment

"I study diabetes and obesity and feel compelled to address the obesity link since it has been identified as the strongest risk factor, besides age, for severe COVID-19. Indeed, obesity may represent the increased risk seen in individuals with type 2 diabetes. I study human fat cells/tissue and have access to cultivated virus and BSL3 where we can infect cells with SARS-CoV-2, making our group uniquely capable of addressing this question."

Project Description:

This project addresses the **link between severe COVID-19 disease and obesity/diabetes**. Specifically, ACE2, the receptor for the spike protein on COVID-19, is highly expressed in subcutaneous and visceral adipose tissue, which may allow for viral entry and replication. Particularly in peri-organ fat depots, inflammation, vasoconstriction and fibrosis as a consequence of viral infection and downregulation of ACE2 may contribute to organ damage including, the heart, gut, liver and kidneys.

Goal:

The goal of this project is to determine whether SARS-CoV-2 infects human adipocytes from subcutaneous (SAT), visceral (VAT) and epicardial adipose tissue (EAT), whether infection incites inflammation and whether pharmacologic compounds that target the renin-angiotensin system (RAS)/ACE2 alter infectivity and inflammation.

Franck Mauvais-Jarvis, MD, PhD

Project: *Role of sex, metabolic disease and inflammation in COVID-19 severity*

Institution: Tulane University

Research Type: Obesity

Program Area: Obesity/Pathogenesis

"I have spent my research career trying to understand the mechanism of type 2 diabetes and find new therapeutic approaches. I feel it is my duty to use my knowledge of diabetes to help better understand and find novel therapeutic approaches to combat COVID-19. This award will open a new avenue of research in my effort to better understand the effect of diabetes and obesity on COVID-19 severity."

Project Description:

This project is conducted to gain a better understanding of **the role of type 2 diabetes, obesity and metabolic syndrome, as well as male biological sex and race, particularly in non-Hispanic Black men**, in increasing COVID-19 severity and mortality.

Goal:

Understanding why non-Hispanic Black men with type 2 diabetes, who are obese and have metabolic syndrome are at a greater risk of COVID-19 mortality is important. It will provide novel approaches for the development of personalized diagnosis tests, as well as health monitoring and preventive precision medicine strategies.

Joshua L. Denson, MD

Project: *Prognostic biomarkers for severity of disease in COVID-19 and metabolic syndrome*

Institution: Tulane University

Research Type: Obesity

Program Area: Obesity/Pathogenesis

"Diabetes is a disease that has personally affected many of my immediate family members and continues to be an ongoing issue in my life. As a physician-scientist working in the ICU, I have seen firsthand the effects of COVID-19 and who this disease affects the most. Unfortunately, it is my hypothesis that diabetes predisposes patients to greater severity of illness, particularly patients who also have obesity, hypertension, or hyperlipidemia. This area of research has become a priority for me as I want to help prevent severe disease for patients with diabetes, not only within my family, but also around the world. This award will be a launching point for my research efforts into COVID-19 and metabolic disease with the hope to continue to learn and help those suffering from these disease processes."

Project Description:

The study focuses on the relationship between **metabolic syndrome, diabetes, obesity, and COVID-19**. Emerging data suggest high risk groups may exist such as those with obesity and diabetes, yet clinical trials have not begun targeting these at-risk patients due to the need for further research. Obesity, diabetes, hypertension and hyperlipidemia make up the essential components of metabolic syndrome, and are extremely prevalent in the American population, particularly in Louisiana. One out of every three (36.8%) residents are considered obese, ranking Louisiana among the top 10 states for adult obesity. Similar numbers are seen for diabetes, with almost 12% (more than 500,000) of Louisiana residents aware that they have diabetes and another 5% with prediabetes.

A subset of COVID-19 patients are at risk for developing severe disease, often resulting in lung inflammation. Obesity, diabetes and metabolic syndrome are associated with a

chronic low-grade inflammation predominantly manifested in elevated serum biomarker levels. Additionally, we know that acute respiratory distress syndrome (ARDS), the most common manifestation of severe COVID-19, is associated with a similar inflammatory biomarker profile. Thus, there is a critical need to determine the prognostic value of these biomarkers in COVID-19 patients presenting with ARDS and metabolic syndrome.

Goal:

To have identified metabolic syndrome as a risk factor for severe disease in COVID-19, as well as the nature of the inflammatory profile predisposing these patients to worse outcomes. These results are expected to have an important, positive impact on precision treatment strategies by identifying a group of patients who may benefit from early intervention, particularly those with metabolic syndrome and diabetes.

Alexandra Lansky, MD

Project: *Colchicine/statins for the prevention of COVID-19 complications in diabetic patients (colstat-dm) trial*

Institution: Yale University School of Medicine

Diabetes Type: Type 2 diabetes

Program Area: Clinical Therapeutics/New Technology

"As the COVID-19 pandemic is taking a high death toll, it is our overarching goal to find the best treatment of care for people with diabetes and contribute to the global effort of preventing COVID-19 complications and death. Our study has the potential to provide insights in the disease progression and treatment of COVID-19 patients with diabetes, and to contribute to new avenues for diabetes research."

Project Description:

This project aims to determine whether **COVID-19 complications in hospitalized patients with diabetes could be prevented with a combination of colchicine and statins** in addition to standard of care.

Goal:

We believe that a combined treatment of colchicine and statins has a synergetic effect to antagonize COVID-19 infection and modulate the inflammatory response, ultimately reducing the morbidity and mortality associated with acute respiratory distress syndrome (ARDS) and myocardial injury in COVID-19 patients.