THE BENCH & BEYOND

Newsletter of San Diego Biomedical Research Institute

Giving Every Patient A Fighting Chance

Now that COVID-19 vaccines are being distributed and restrictions are lifting in the US, people are excited about the return to normal life. Many of our favorite businesses are once again open, in-person events are being scheduled for later this year, and people can meet their loved ones without the fear of becoming infected or infecting others. Despite still having to abide by current rules and guidelines, many are optimistic that the end of the pandemic is near. At SDBRI, we continue to be thankful for the first responders who got us through the pandemic, the scientific community who worked together to create the vaccines, and we are especially thankful for our dedicated staff and collaborators who persevered during the last year and a half to keep research at SDBRI active.

When COVID-19 began to spread, everyone was unsure of what the future would hold. However, our staff rose to the challenge and exceeded our expectations. They were able to adapt to a new working environment, continued to collaborate virtually with one another on their projects, and even expanded into new areas of interest such as SARS-CoV-2 and COVID-19. While the challenges have been incredible, our staff never forgot the goal that we are all working towards—giving every patient a fighting chance.

NEWEST INSIGHTS

While over 430 million people worldwide are now fully vaccinated, the fight against COVID-19 is still not over. With the release of multiple vaccines and the lowering case rate, it may seem as though we have defeated COVID-19. However, there is still much that scientists do not understand about the disease. Here at SDBRI, we have continued our SARS-CoV-2 and COVID-19 research with special attention to the long-term health impacts on patients who suffered from the disease.

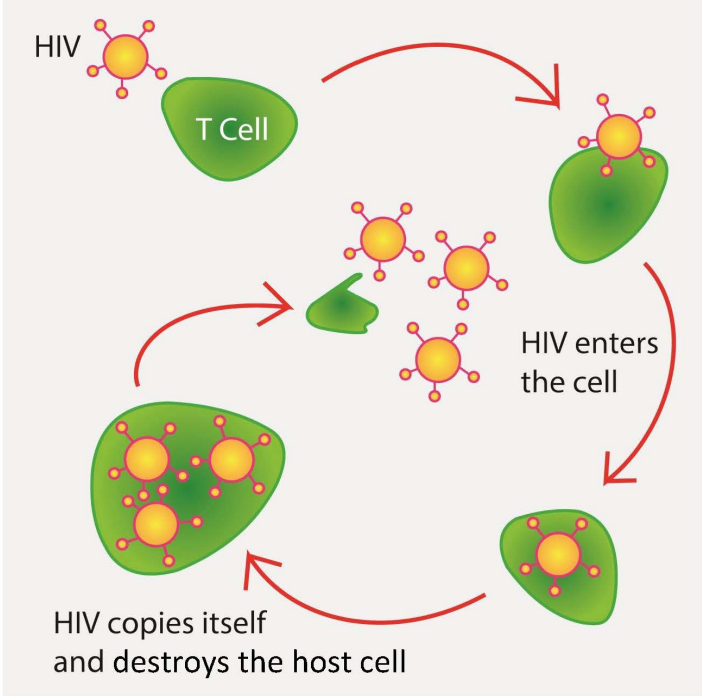
Researchers at SDBRI have been looking into post-acute COVID syndrome (PACS), also known as Long Hauler's Syndrome, or Long COVID. It has been reported that 30-50% of patients who survived COVID-19 have struggled with ongoing symptoms such as fatigue, shortness of breath, and memory retention for weeks or months after they are no longer contagious.

The SDBRI team, led by Dr. Cecilia Marcondes and her collaborator, Dr. Kimberly Shriner, the founder of the Long COVID Recovery Clinic at the Huntington Memorial Hospital, has initiated a new study that aims to understand the molecular and cellular underpinnings that drive PACS. They will screen blood samples of neuroimmune inflammatory markers and signatures and use statistical approaches to integrate molecular data, and social and health determinants. The goal is to understand the biological pathways that cause symptoms and predict disease progression. They also plan to establish a comparison with other chronic conditions that trigger similar symptoms including human immunodeficiency virus (HIV).

OTHER RESEARCH IN THE MARCONDES LAB

One disease that many SDBRI researchers have worked on extensively is HIV. HIV attacks and destroys the body's immune system, leaving the patient vulnerable to infections and illness. Many patients who have HIV also have other medical conditions such as cardiovascular problems, metabolic disorders, and kidney disease. Furthermore, drug addiction, a common problem associated with HIV infection, can play a critical role in modifying the patient's health and treatment.

The Marcondes lab is focused on how HIV infection leads to central nervous system dysfunction and the impact of substance abuse disorders. In her most recent publication, Dr. Marcondes and her team have developed new methodologies to study rare post-mortem brain specimens from HIV+ subjects that were Methamphetamine abusers.



Dr. Cecilia Marcondes

Most studies interrogating molecular changes are done by analyzing RNA, which are little pieces of messages copied from DNA and sent out to build specific proteins in cells. By doing this, scientists can gather information on molecular pathways and biological processes and learn how brain cells can be damaged by drug use. However, there is a limited availability of high-quality RNA specimens for this type of analysis which can lead to a delay of important research. One of the reasons for this delay is the time taken for post-mortem samples to be collected and properly preserved.

To overcome this problem, Dr. Marcondes and SDBRI scientist Dr. Liana Basova, designed new strategies to extract information from specimens damaged by long post-mortem intervals. Their solution was to examine epigenetic mechanisms that preserve information encoded by DNA and control the RNA message.

OTHER RESEARCH IN THE MARCONDES LAB CONT.

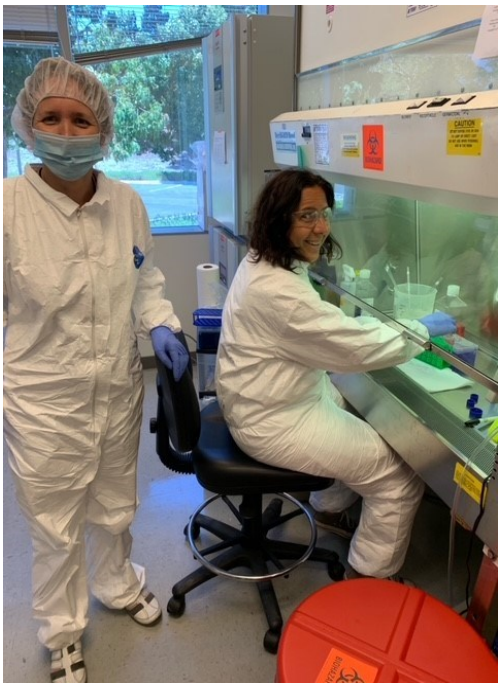
They found that by analyzing these more stable mechanisms that precede RNA production, they could collect the necessary information about neurological and inflammatory processes associated with HIV and Methamphetamine use. These new methods can be used to increase the number of specimens analyzed from which we can learn about other neurological conditions and chronic disorders, including COVID-19, in tissues damaged by long post-mortem intervals.

In a separate study focused on substance abuse, a manuscript by the Marcondes lab was awarded the Editor's Award for Best Manuscript in the category of Biology by the International Journal of Hyperthermia. In this paper, published in 2020, Dr. Marcondes, with fellow SDBRI investigator, Dr. Fahumiya Samad, investigated the mechanisms that cause a dramatic increase in the body's core temperature known as hyperthermia, following Methamphetamine use. This life-threatening condition is commonly observed in clubs and streets after stimulant drug use, but there are no pharmacological treatments to rescue those impacted by drug-induced hyperthermia.

The body's core temperature is controlled by the coordinated actions of several areas of the brain, muscles, and a special type of body fat known as brown adipose tissue (BAT). The Marcondes/ Samad team has shown that drug-induced hyperthermia involves the activation of brown adipocytes (BA), which are cells in BAT that can produce large amounts of energy to keep the body warm. When Methamphetamine is released into the body, BA are activated causing the body's core temperature to rise to dangerous levels. Immune cells called macrophages are also activated during this process.

In this award-winning paper, Marcondes and Samad describe how Methamphetamine interacts with the neurotransmitter norepinephrine and with free radicals to modify the function of BA and macrophage cells in the BAT forming a "communication loop" which leads to hyperthermia. It is hoped that by identifying and understanding these cellular and molecular changes, pharmacological treatments for Methamphetamine-induced hyperthermia can be developed to save lives and give drug users a second chance.

These studies are just a few examples of the extraordinary research done by the scientists here at SDBRI. Between identifying targets for potential treatments to creating new methodologies to conduct important, life-saving research, these SDBRI scientists are working hard to give every patient the chance that they deserve.



The Marcondes lab hard at work!