Simmaron Research

Annual Report

2020 Review & 2021 Prospectus

Remaining committed to the study of ME/CFS & piloting critical work related to the COVID-19 global pandemic

A Message from the Executive Board

For much of society, a pandemic turned our world upside down in 2020 restricting life in a way most have never experienced. Yet for the ME/CFS community, it was very familiar: many people became suddenly ill, the medical community didn't know how to treat their disease, people had to severely reduce social interaction, and millions of patients called "long-haulers" are facing the potential of chronic, post-infectious disease. While there are differences too, there is now worldwide attention on the ME community's longstanding questions: Why do some people develop chronic disease from an acute infection, while others recover? And how do we develop treatments to restore people's health and return them to their lives?

Answering those questions has been Simmaron's mission since its inception.

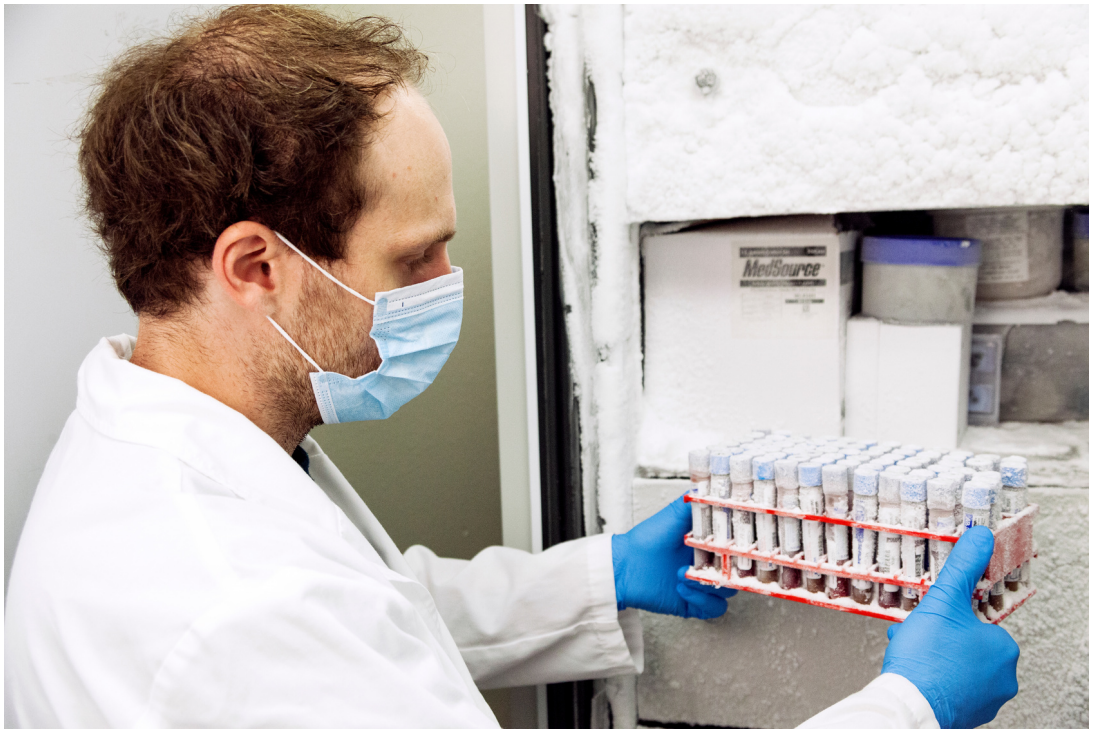
In 2020, Simmaron continued to propel our core research into ME/CFS subsets and treatments, with a new peer reviewed publication on subsets and progress on our unique ability to document responders to Ampligen and other IV treatments for ME. We also stepped up to serve in the COVID crisis. With our partners, we solved a shortage in COVID testing through practical innovation; we brought COVID testing to our home community in Northern Nevada and through a special donor we are funding free testing for essential workers; we are tracking cases and preparing to add long-haul COVID patients to treatments we have studied for ME. We also contributed to an advocacy milestone working with SolveME and Florida ME patients to get Florida's 27 Congresspeople to urge NIH to increase ME research. In this historic moment, Simmaron's core mission – to find treatments for ME/CFS – is poised to accelerate with a new attention on chronic, post-infectious patients. **Your support has helped us to drive patient-centered research and serve our community**, and we take your urgency for treatments and health into 2021 with a commitment to make the most of the opportunity ahead.

- Courtney Miller, SRI Executive Board President

Remaining Committed to Mission

For nearly a decade, the Simmaron Research foundation has been dedicated to the study of ME/CFS. Drawing on the clinical expertise of Dr. Daniel Peterson, strategic **collaborations with distinguished partners**, and a data bank unlike any other in the world, the foundation has made great strides to advance understanding of the disease. The Simmaron Research team has published over **20 peer-reviewed articles** on ME/CFS subsets, immunology, and treatments. To date, the foundation has raised over **3 million dollars** to conduct pilot projects all pursued with intent to bring hope to the ME/CFS community through practical insight and the **informed transformation of clinical care.**

The Simmaron Research team has several projects in progress and is only gaining momentum in our goal to publish findings in our field. While the advent of the COVID-19 pandemic this year presented an unforeseen set of needs to which our team has proven uniquely equipped to respond, our mission has not changed. Read on for progress updates.



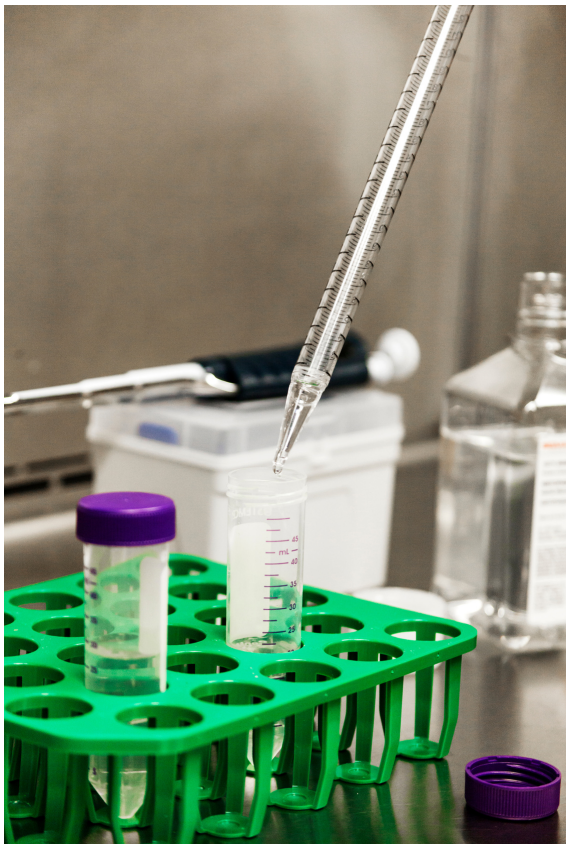
A Year Unexpected

Simmaron's Response to the COVID-19 Pandemic

SRI began its response to the Global Pandemic in as early as January 2020, as emerging reports of a flu-like novel corona virus began to surface in Wuhan, China. SRI completed its first clinical diagnostic for SARS-CoV-2 on January 21st, 2020 and in only weeks later, obtained FDA Emergency Use Authorization (EUA) Status for both the molecular diagnostic PCR as well as the serological test to detect the S1-glycoprotein of SARS-CoV-2.

In June of 2020, SRI was awarded a significant grant from an anonymous foundation allowing us to provide no-cost testing to individuals in our local community. This support allowed us to test thousands of individuals in North Lake Tahoe throughout the summer, even while effective testing was (and remains) largely unavailable.

Our primary testing population included many of the essential front-line workers in the area who were desperate to get back to work. We are extremely proud of the heroic efforts from the clinical research team comprised of Marco Maynard and Jane Green, RN who tested these individuals in our outdoor testing center at the SRI clinical center. This past October, SRI was able to test the entire faculty, staff, and student body of Sierra Nevada University, allowing in-person classes to occur on campus safely.



The foundation now aims to raise funds in support of our effort to bring testing on-site using a newly developed rapid molecular diagnostic platform. This testing platform will allow us to test hundreds, if not thousands of samples per day and provide accurate diagnostic results to individuals in less than 12 hours. As the only rapid molecular instrument in the Lake Tahoe Basin we could assist our local healthcare partners at Incline Village Community Hospital and others to address their testing needs. Most importantly, this platform would also significantly reduce the cost of testing by cutting out expensive shipping and courier services.

SRI is not only looking to continue our testing efforts. In collaboration with the CDC and the NV Department of Public Health, SRI has been placed on a short list of institutions selected to store and distribute the vaccine in our local area.

SRI is uniquely positioned to lead local efforts to distribute vaccines that require ultra-low storage at -80°C not only because we have the required freezers, but furthermore, because of our long history of executing FDA drug approval studies.

Simmaron is equipped to study the progression of COVID-19 patients who develop long term effects. The CDC estimates that nearly 10% of individuals who suffer from SARS-CoV-2 infection never return to their pre-illness state. These individuals, formally recognized as "long-haul" COVID patients present with unexplained fatigue, weakness, cognitive dysfunction and dysautonomia. The symptoms of long-haul COVID eerily overlap with SRI's internationally recognized research on post viral infectious myalgic encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS). Our study of Ampligen, long a trial-based treatment for ME/CFS, has the potential to include long-haul COVID patients, as Dr. Peterson and AIMimmunotech have obtained approval to expand the protocol to include COVID patients whose symptoms persist 3 months after acute infection. Information on this trial can be found here:

https://clinicaltrials.gov/ct2/show/NCT00215813.

Keep reading for more on our core work studying treatments in ME/CFS.

Project Updates

Project: Red AMP

Collaboration: Centers for Disease Control

In this retrospective, longitudinal study we are analyzing both unstructured patient medical records from our clinical partner and structured case report folders derived from the Ampligen® 511 Phase III clinical trial. With the help of partners at CDC, we aim to 1) validate our responder cohort and 2) to identify surrogate clinical makers of response to Ampligen® therapy.

Update: *Our team is nearing the competition of the REDamp project with the CDC. With the help of interns, we have scanned and uploaded 80 case folders and 60 sets of progress notes for each patient. The CDC will now begin analyzing these documents.*

Project: AMP-Nano

Collaboration: Cornell University

In this prospective, longitudinal study we aim to identify why some ME/CFS patients respond to specific intravenous therapies provided by our clinical partner. Our primary goal is to identify phenotypic responders to therapies and develop a treatment algorithm that can be shared with other clinicians in the field of ME/CFS patient care.

Update: *Work on this project is ongoing. The research team enrolled 7 more patients from last year, bringing the total number enrolled to 31. Enrollment efforts continue with focus on securing more healthy controls.*

Project: Whole exome sequencing of families suffering from ME/CFS

Collaboration: Open Medicine Foundation, Stanford University

This project involves collecting DNA samples from families that have multiple lineages of ME/CFS. We aim to compare individuals within families that are both affected and non-affected, potentially enabling identification of novel genetic aberrations.

Update: *Our research team has completed its initial work. Samples are currently being analyzed by our collaborator.*

Project Updates

Project: Ampligen Trial

We have investigations derived from the ongoing Phase III Ampligen trial in order to study the response of individuals before, during, and after treatment in collaboration with Cornell University, Dr. Maureen Hanson and AIM Immunotech.

Update: *Our team currently has two patients on the trial with another that will restart within the month. We recently enrolled a new patient that is eager to determine if Ampligen is an effective treatment for their ME/CFS. AIMImmunotech has recently begun to accept post-COVID chronic fatigue patients in the Ampligen 511 trial. Our team is working with AIMImmunotech to initiate recruitment and enrollment of these patients. This is a unique opportunity that will open up doors to develop research projects that investigate the early stages of chronic fatigue.*

Project: Small Fiber Neuropathy & Auto-antibodies

Evidence of autonomic dysfunction are commonly reported symptoms in patients with ME/CFS. Many of these symptoms are routinely reported in cases of autoimmune associated small fiber poly neuropathy (aaSFPN). ME/CFS and aaSFPN have been suggested to share a common autoimmune etiology and present with nearly identical clinical symptoms of dysautonomia. Identifying ME/CFS patients who also meet the clinical criteria for aaSFPN may present a novel pool of patients who are likely to respond favorably to IVIG therapy.

Update: *Our research team has analyzed the data on autoantibody presence and correlated this data with the presence or absence of ME/CFS and small fiber neuropathy. Based on this data, our team put together a presentation that our Gap-Year Intern presented at the IAMECFS conference. MedScape featured the presentation in September of this year. A research manuscript is currently bring completed to submit for publication.*

Project Updates

Project: Assessment of 25 bone marrow biopsies from ME/CFS patients and healthy controls harboring B-cell clonal rearrangements

Collaboration: Stanford University

In this project, We aim to analyze bone marrow tissue at the molecular level to identify the driving force behind a dangerous immune perturbation related to b-cell clonal rearrangement found in some ME/CFS patients.

Update: *Our research team is currently sending samples from our biobank to the University where they will be analyzed.*

Project: HLA typing in ME/CFS families

Collaboration: University of Montreal

Using Human Leukocyte Antigen (HLA) typing, we aim to better understand the potential genetic predisposition for the immune dysfunction observed in ME/CFS patients. ME/CFS patients' HLA types cluster into groups that are different than unaffected individuals, making this a particularly significant inquiry.

Update: *The collection of family pedigrees is currently underway.*

Project Updates

The Development of Patient Derived Induced Pluripotent Stem Cells (IPSCs) from Skin Fibroblasts and Peripheral Blood Mononuclear Cells—Modeling Drug Response

Collaboration: Avik Roy Ph.D., C. Gunnar Gottschalk Ph.D.

Induced pluripotent stem cells (IPSCs) are cells that have been genetically reprogrammed to an embryonic stem cell–like state by being forced to express genes and factors important for maintaining the defining properties of embryonic stem cells. IPSCs can be further cultured to express the phenotype of any cell residing in either the periphery or central nervous system. Recently, we have developed a protocol to isolate IPSCs from easily accessible whole blood and skin fibroblasts samples taken in the clinic. Following isolation, IPSCs can be immortalized prior to further differentiation. The downstream differentiation of IPSCs into the cells relevant to a disease phenotype provides a non-invasive mechanism for personalized drug screening investigations, and complementary studies aimed to understand the role of functional genomics, proteomics and metabolomics within that individual. Using this tool, we recently described for the first time the functional role of a homozygous BPOZ-2-point mutation as it relates to the development Parkinson's Disease in a severely affected pediatric patient. IPSC technology is slated to be the future of personalized medicine, and its implementation in the field of ME/CFS is both novel and critical. Funding goal: $100,000

Update: *Dr. Gottschalk, in collaboration with Dr. Avik Roy and Dr. Heng Wang of the DDC clinic for Special Needs, in Middlefield Ohio have begun collecting patient samples in order to study a rare genetic form of juvenile Parkinson's disease using IPSC modeling techniques. At present, the team is working on a series of case reports outlining their findings. The DDC clinic in Middlefield Ohio, is run by Dr. Wang and specializes in rare genetic forms of illnesses that occur in the Amish Community that the clinic serves. Dr. Roy and Dr. Gottschalk believe that the IPSC techniques they are developing with Dr. Wang may translate into a model for drug discovery in ME/CFS.*

Simmaron Team Accomplishments

Conference Presentations:

SRI Gap-Year Intern Ryan Whelan

“Autoantibodies and Small Fiber Neuropathy in Patients with ME/CFS: A Pilot Study”

International Association for CFS/ ME Annual Conference, August 21,2020

Featured in MedScape: "Small-fiber polyneuropathy may underlie dysautonomia in ME/CFS", September 02,2020

Biobank Update:

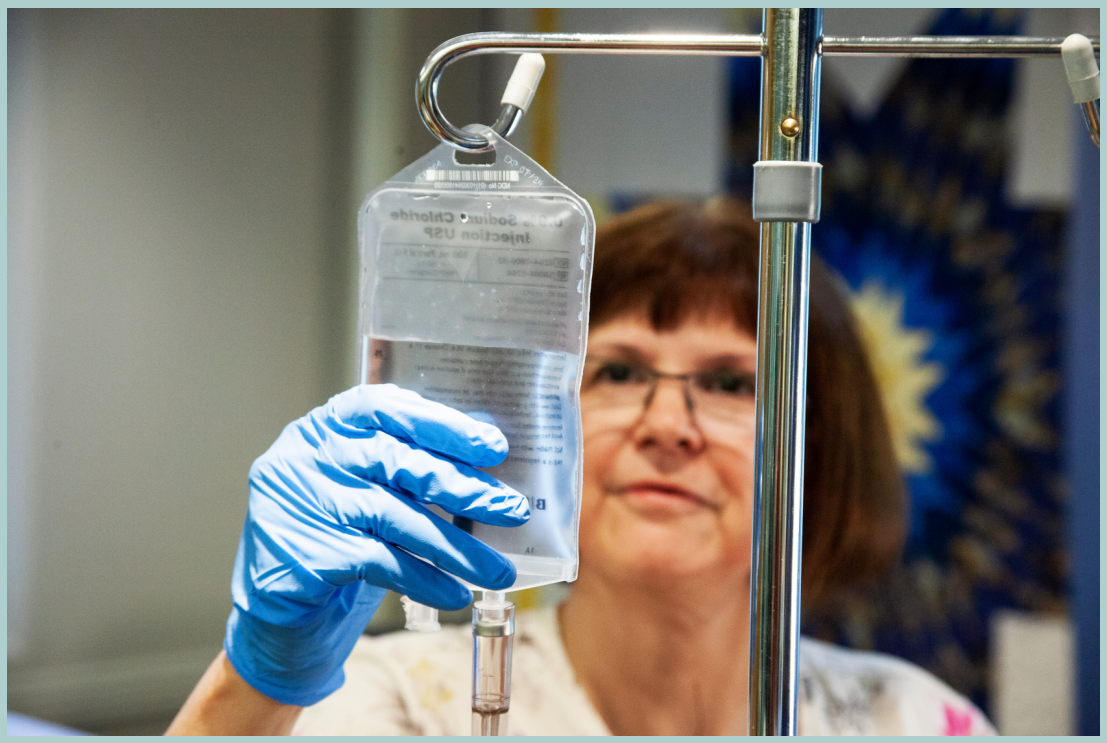
One of Simmaron's distinguishing attributes is a 30-year, deeply characterized biobank of samples from ME/CFS and other neuro-immune patients. Simmaron seeks to hire an experienced biobank manager to integrate the biobank and patient data to make the most of research opportunities presented by this rare bioset.

New Website Launch:

Our team spent much of 2020 working diligently to launch a a new website for the Foundation (**simmaronresearch.com**). Our aim for this project was threefold: 1. Update the site to be a more accurate representation of Simmaron's work and team, 2. Create more space for the presentation of information that is important to our community of patients/supporters, and 3. Streamline processes for receiving donations and managing donor information.

Gratitude

This past year has been a challenging one for our community and our team. In these difficult times, our team has chosen to focus on the diligent application of our skills and resources in faithfulness to our supporters.Your generosity has always been appreciated. This year however, its power to move ME/CFS research and COVID-19 response is felt even more deeply by our team. It is with the utmost sincerity that, as 2020 comes to a close, we thank each of our donors for their charitable contributions and investment in our mission.



You're Invited to Partner with Simmaron Research

Ready to join our community of philanthropists and donors?
Want to continue supporting Simmaron's work?

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& online atsimmaronresearch.com

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