Primary Immune Deficiency Treatment Consortium

NEWSLETTER

Summer 2021 | Issue 13

Read about Melissa and Laila's Journey as CGD Carriers on Page 4

Greetings from PIDTC Co-PIs Drs. Jennifer Puck, Elie Haddad and Chris Dvorak!

We are finally getting close to opening our three new longitudinal protocols for this funding cycle. The SCID protocol (6907) is approved by the UCSF IRB, with other sites to follow; CGD (6908) will be submitted to the IRB shortly; PIRD (6906) investigators are reviewing comments from NIAID. All protocols should be up and running by the end of Fall 2021.

We are excited to announce the launch of our Neurodevelopment in SCID study in collaboration with the Immune Deficiency Foundation. As of now, UCSF will be seeing our first participant at the beginning of July. More centers will onboard to the study and enroll patients in the coming months. For more information about this study, please look at page six of this newsletter.

While we are pleased with progress fighting the virus, COVID-19 isn't gone yet. As we head into the summer, remember to take precautions as needed in your area and follow the advice of your physicians. Be sure to get fully vaccinated when you can. Enjoy to this summer to the fullest!

With appreciation,

Jennifer, Elie and Chris

IN THIS ISSUE

CONGRATULATIONS!

Donald Kohn, MD

Dr. Donald Kohn is the recipient of the 2021 Career Achievement Award from the International Society for Cell and Gene Therapy (ISCT). This award honors his contributions of scientific innovation and groundbreaking research in Gene Therapy that have advanced the field as well as his volunteer service and mentorship.

"Prof. Kohn developed the first successful hematopoietic stem cell gene therapy, for children with 'bubble baby disease'- ADA deficiency - and has now functionally cured over 50 children. He directs a large research program performing bench-to-bedside research on gene modification of blood forming stem cells and has brought this research to multiple clinical trials. He is an outstanding leader who is actively involved in training of undergraduate, graduate, medical students, as well as PhD and MD fellows," said Jan Nolta, PhD, UC Davis. "The entire field seeks to build upon his success in these trials and he is highly deserving of this award."

Catherine Bollard, MD

Dr. Catherine Bollard is the recipient of the 2021 ISCT Darwin J. Prockop Mentoring Award from the International Society for Cell and Gene Therapy (ISCT). This award honors her passion and commitment to the mentorship of aspiring professionals.

"I first met Dr. Bollard in the fall of 2006 as a graduate student in the Department of Immunology at Baylor College of Medicine (BCM)," said Patrick Hanley, PhD Director, GMP for Immunotherapy, Children's National Health System (CNH). "For the past 15 years, Cath has been a strong mentor, friend, advocate, and voice of reason for me and has been instrumental in my success, both at BCM and now at CNH. With her support and mentorship, I have published high impact papers, earned a number of awards, and received prestigious of grants. Cath's impact on the field of cellular therapy and the practice of medicine is no longer restricted to her own success, but is now emanating in seeds she has planted and nurtured in the over 93 individuals she has mentored, including 22 junior faculty, 27 post doctoral fellows, and 12 graduate students. Dr. Bollard acts as a mentor to other senior investigators at CNH as well, particularly those in the Bone Marrow Transplantation division. Cath is the most deserving mentor for this award."

Elie Haddad, MD, PhD

Dr. Elie Haddad is the new President Elect at the Clinical Immunology Society.

Dr. Haddad is a clinical scientist and full professor at the University of Montreal. He has been involved in Primary Immune Deficiency since 1993. He did a 4-year clinical fellowship in Alain Fischer's Unit, Paris, France, and a PhD in basic immunology. In 2005, he was recruited by CHU Sainte-Justine, a tertiary University Hospital in Montreal, Canada.

In his institution, he is Head of Immunology, Allergy and Rheumatology Division and Head of the Axis of research "Immune Diseases and Cancer".

Dr. Haddad is very involved in the teaching of clinical immunology and clinical research. He has created a specific program of pediatric clinical immunology in his institution and he is one of the Faculty of the CIS Primary Immune Deficiency Summer School.

Honoring CGD Moms and Carriers: Melissa and Laila

By Melissa L Fernandez, member of the CGDAA Executive Board

Ever since I was a young child, I always thought that I had something "wrong" with me.

My anxiety was always severe, and my parents would say I was just sensitive. I broke out in horrible rashes, and the doctors just said I had sensitive skin. I would get mouth ulcers that the doctors blamed on my braces. I had severe chronic fatigue, but I thought that everyone felt that way. These symptoms would come individually or sometimes a few together. It wasn't until I was pregnant with my first child that they all hit me at once and severely, sometimes I couldn't even lift my head off the pillow. My blood test even came back that I could possibly have lupus. As we know, lupus is hard to diagnose. They put me on baby aspirin just in case. Once I delivered my baby girl, Laila, it took some time, but my body finally got back to base line. We had our son, Rocco, when Laila was 5 years old. It wasn't long until he became very sick and was diagnosed with X-linked CGD. I remember when the doctor came into the hospital room to tell me his diagnosis. He then asked me if I had any lupus-like symptoms, because carriers of this disease presented with these symptoms. My heart dropped and at that moment, it all made sense. Both my son and I were diagnosed on the same day. I immediately thought of Laila and thought about symptoms she presented, and I knew she might be a carrier as well. The doctors would say "You're just a carrier." We are now finding out through the hard work of the **CGDAA** that we are not just carriers. We have real symptoms and can sometimes present as a CGD patient.

When it came to testing Laila, my husband and I decided that we would test at age 13. We did not take this decision lightly, as we had already been through the trauma of Rocco's transplant, and we had just lost a baby. When the test results came back, I was in shock. I thought that if she did come back as a carrier, then she would be like me with higher functioning neutrophils. This was not the case. At her last test, she tested at only 4 percent functioning and a repeat test with NIH at 11 percent. She also had all the symptoms that I had as a child.

When COVID-19 hit, we worried that she may not be able to fight a secondary infection to the virus if she were to contract it. She was put on Bactrim just in case. In July 2020, she was diagnosed with COVID. She got through the virus pretty well, but then a few weeks later, she was hospitalized with severe inflammation that was affecting her gut. Her doctors at Ochsner Hospital in New Orleans took her carrier status very seriously. They knew that the inflammation in her gut could be COVID or carrier related. This was the first time that I witnessed a physician take our carrier status seriously! Thankfully, it was Covid-related and not a long-term issue due to being a carrier.

I asked Laila if she was happy that she found out at the age of 13. She said, "Yes, because it made me understand previous issues that did not make sense."

Also, she said she was grateful that I had been able to explain to her family planning options and situations so that she could prepare earlier for the future. This is also helpful, she said, "Because I am not finding out when it is too late, and it gives me more time to become thoroughly educated about it. I know now, that everyone has different symptoms and some have none. What is important is that awareness is spread on the topic and CGD carriers are not forgotten. "I am very proud of my daughter, Laila. She has been through a lot at a young age, but it has made her the strong, mature, and educated young woman that I always knew she would be!”

CGD Carrier Survey Update:

In a joint effort between the CGDAA led by Felicia Morton and the PIDTC led by Dr. Jennifer Leiding, the CGD carrier survey received many responses from CGD carriers. This national survey supported by the PIDTC has completed assessing the symptoms and management of female X-linked CGD carriers. We want to thank everyone who helped advertise the survey and a big thank you to those who took this survey. We are excited to share the results with everyone in the near future.

Hematopoietic cell transplantation in patients with Primary Immune Regulatory Disorders (PIRD): A Primary Immune Deficiency Treatment Consortium (PIDTC) survey

Chan AY, Leiding JW, Liu X, Logan BR, Burroughs LM, Allenspach EJ, Skoda-Smith S, Uzel G, Notarangelo LD, Slatter M, Gennery AR, Smith AR, Pai SY, Jordan MB, Marsh RA, Cowan MJ, Dvorak CC, Craddock JA, Prockop SE, Chandrakasan S, Kapoor N, Buckley RH, Parikh S, Chellapandian D, Oshrine BR, Bednarski JJ, Cooper MA, Shenoy S, Davila Saldana BJ, Forbes LR, Martinez C, Haddad E, Shyr DC, Chen K, Sullivan KE, Heimall J, Wright N, Bhatia M, Cuvelier GDE, Goldman FD, Meyts I, Miller HK, Seidel MG, Vander Lugt MT, Bacchetta R, Weinacht KG, Andolina JR, Caywood E, Chong H, de la Morena MT, Aquino VM, Shereck E, Walter JE, Dorsey MJ, Seroogy CM, Griffith LM, Kohn DB, Puck JM, Pulsipher MA, Torgerson TR. Hematopoietic Cell Transplantation in Patients With Primary Immune Regulatory Disorders (PIRD): A Primary Immune Deficiency Treatment Consortium (PIDTC) Survey. Front Immunol. 2020 Feb 21;11:239. doi: 10.3389/fimmu.2020.00239. PMID: 32153572; PMCID: PMC7046837.

Primary Immune Regulatory Disorders (PIRD) are a new group of conditions where the immune system is not responding and regulating the immune response appropriately. These diseases can affect multiple organs and are often cared for by many different specialists. Thus, little is known about the natural history of this group of diseases and the ideal treatment for PIRD.

To help us better understand this group of disorders, we conducted a survey among 30 centers in the PIDTC and 3 centers in Europe to look at the outcome of patients that have been transplanted for PIRD. We collected data on 226 patients who had received a transplant for a PIRD condition. Roughly 75% of patients had a genetic diagnosis and a quarter did not. Most patients developed symptoms within a year of age. Almost all organ systems were affected, and many patients had multiple affected organs. The most common problems included gastrointestinal issues, blood count issues (autoimmune cytopenias), and rashes.

The main reason for transplant was autoimmune problems (41%), and the next most common reason was infections (26%). Roughly a quarter of the patients had multiple reasons for transplant. Nearly all of the patients were transplanted before 18 years of age, and approximately a quarter of the patients were transplanted before a year of age. More than half of patients had resolution of their symptoms, and the overall 5-year survival for transplanted PIRD patients was 67%.

This is the first study to look at transplant for PIRD and highlights a need to improve our understanding of this condition and what therapies are ideal for treating this group. This survey served as the basis for the development of the 6906 protocol which will focus on studying the natural history of PIRD to improve survival for patients with this condition.

Meet the Author: Alice Chan, MD, PhD

Dr. Alice Chan is the Director of the Immune Dysregulation Clinic at the University of California, San Francisco. She is a pediatric immunologist and rheumatologist dedicated to diagnosing and managing patients with complex immunological disorders and researching genes regulating the immune system.

Dr. Chan is also the co-chair of the 6906 PIRD Protocol and have greatly helped the development of our new case report forms for our new protocols.

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Immune Deficiency Foundation launches collaborative study with PIDTC to assess long-term neurodevelopmental outcomes in SCID Patients

By Tammy Black

SCID Compass is an educational program launched by the Immune Deficiency Foundation in 2018. It was designed to guide parents of infants diagnosed with severe combined immunodeficiency (SCID), people living with SCID, and the medical community through the journey of learning about this rare, life-threatening medical disorder and finding support to navigate the lifelong health challenges. In 2020, SCID Compass partnered with the Primary Immune Deficiency Treatment Consortium (PIDTC) on a collaborative study to assess long-term neurodevelopmental outcomes in SCID Patients.

It has long been recognized that some patients with SCID can have increased frequencies of neurodevelopmental problems, including overall cognitive delays and slower acquisition of motor and verbal skills that can affect school performance. These deficiencies may be due to severe infections (including meningitis and pneumonia) and prolonged malnutrition and hospitalization during diagnosis and treatment. Many of these are complications from undiagnosed immune deficiency.

The primary hypothesis is that adverse neurodevelopmental outcomes in SCID patients will be reduced with newborn screening. To test this, the study will perform formal neurodevelopmental assessments on patients with SCID diagnosed by newborn screening - versus those diagnosed by clinical manifestations.

Neurodevelopmental outcomes also may be compromised by exposure to high dose alkylator chemotherapy used to condition patients prior to definitive therapy with hematopoietic stem cell transplantation (HSCT). However, conditioning regimens have been shown to enhance immune reconstitution and may be associated with better neurodevelopmental outcomes. It is essential to determine whether such treatments improve or worsen outcomes. Answering this question is critical for guiding clinicians to determine the best treatment strategy for babies diagnosed by newborn screening.

There may be specific risks for neurodevelopmental deficiency in patients with certain SCID genotypes. ADA-SCID is associated with an elevated risk for neurocognitive and hearing problems. Radiation-sensitive SCID (e.g., *DCLRE1C, PRKDC, LIG4*) is associated with DNA repair defects and increased sensitivity to alkylating agents used for HSCT.

The prospective study of SCID (Protocol 6901) was initiated in 2010, after the introduction of newborn screening. Of the 317 patients enrolled to date, 161 are at an age (6-16 years old) when neurodevelopmental testing can reliably be done for the purposes of this study. An additional 90 patients from the cross-sectional portion of the SCID Protocol 6902 are also eligible. Neurodevelopmental testing will be offered to all living subjects who are at least five years post-treatment (those treated between 2010-2015). The PIDTC, together with the Immune Deficiency Foundation, can provide important information about the neurodevelopmental outcomes for patients with SCID and determine whether diagnosis by newborn screening improves outcomes.

The test battery will be determined according to the age of the subject. Outcomes will be determined with measures of:

- neuropsychological functioning in the areas of overall intellectual development (IQ),
- executive function,
- memory,
- behavioral adjustment.

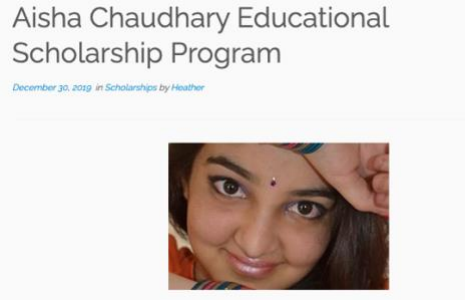
Patients will have testing done at their treatment center by a qualified neuropsychologist using a validated standardized set of tests. Local testing will provide the greatest access for families to this opportunity. The Project Neuropsychologist will coordinate the testing at sites, which may include a combination of in-person and online testing. The results of testing will be made available to families via the site PIs and could be used as part of an Individualized Educational Program (IEP) for the child if needed. The project aims to test at least 80% of eligible patients, who will be given a stipend to compensate for their time and a travel allowance.

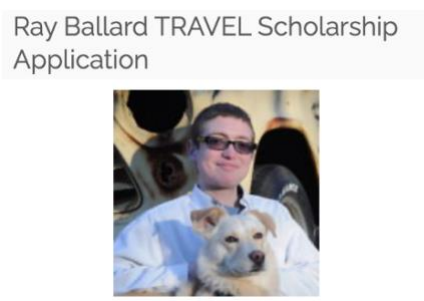
For more information about SCID Compass, visit scidcompass.org.

HRSA Acknowledgement/Disclaimer: *This project is supported by the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services (HHS) as part of an award totaling $2.97 million with 0% financed with nongovernmental sources. The contents are those of the author(s) and do not necessarily represent the official views of, nor an endorsement, by HRSA, HHS, or the U.S. Government.*

PAG Updates:

Scholarship Opportunities from SCID Angels





SCID Angels For Life awarded in 2020 it's first two recipients of the Aisha Chaudhary Educational Scholarship fund for undergraduate students, graduate students or those attending a trade school in the US who have been diagnosed with Severe Combined Immune Deficiency (SCID). The Educational Scholarship is available for any patient diagnosed with SCID who is age 17 or older and has a US residency. This scholarship is not degree specific and can be applied towards a four-year or two-year degree program or trade school. Students must be enrolled or planning to enroll in an accredited course(s) for Fall 2021 Semester.

Details and applications for all THREE of our scholarship programs; the Aisha Chaudhary EDUCATIONAL Program, the Ray Ballard TRAVEL Program and the SCID Angels FAMILY Scholarship Program can be found on the SCID Angels website at http://www.scidangelsforlife.com/category/scholarships/ or by clicking on the pictures above.

Update: Gene Therapy Clinical Trial for ADA SCID

With the support of SCID Angels for Life, parents of children with SCID encouraged Orchard Therapeutics to return the successful lentiviral gene therapy treatment for ADA SCID back to the university setting after the company de-funded the program due to financial and technical issues. Dr. Bobby Gaspar, Orchard CEO, wrote on May 28, 2021, that Orchard is turning the ADA-SCID gene therapy program back to the University of California Los Angeles (UCLA) and the University College, London.

Although Orchard Therapeutics will no longer supervise the clinical trials, the company is dedicated to help gain access to this treatment. "Despite our decision to return the license, we will continue to stand by the commitment we made to our academic partners to support them with financial and material resources to seek to treat ADA-SCID patients under a separate compassionate use program that would be led and administered by their institutions," wrote Dr. Gaspar. Under such a program, ADA gene therapy could potentially be given outside of a clinical trial. Dr. Don Kohn at UCLA has begun the process of applying to the FDA for an expanded use of this life saving treatment as soon as possible. For more, see https://www.latimes.com/business/story/2021-05-28/californias-biotech-partner-permanently-kills-the-project.

Jeffrey's Insights: Jeffrey Modell Foundation's Global Genetic Sequencing Program

Jeffrey Modell Centers Network

The Jeffrey Modell Centers Network (JMCN) was created over the past decade by the Jeffrey Modell Foundation (JMF) to meet the rising need for specialized centers to accommodate the increasing number of patients identified with Primary Immunodeficiency (PI), and provide the necessary infrastructure for referral, earliest possible diagnosis, appropriate treatments, and cutting-edge research. The JMCN serves as the infrastructure for referrals and treatment. Currently, the JMCN consists of 904 expert physicians at 395 institutions, in 313 cities, and 86 countries spanning six continents.

Importance of Genetic Sequencing

The Jeffrey Modell Foundation offers the unique advantage of utilizing existing sequencing technologies but applying an unprecedented level of pre-test probability by leveraging the vast JMCN. The Network provides organized and direct access to expert immunologists, a majority of whom harbor numerous clinically diagnosed patients in need of genetic diagnostics. Certain diagnoses are definitive, but many go undiagnosed.

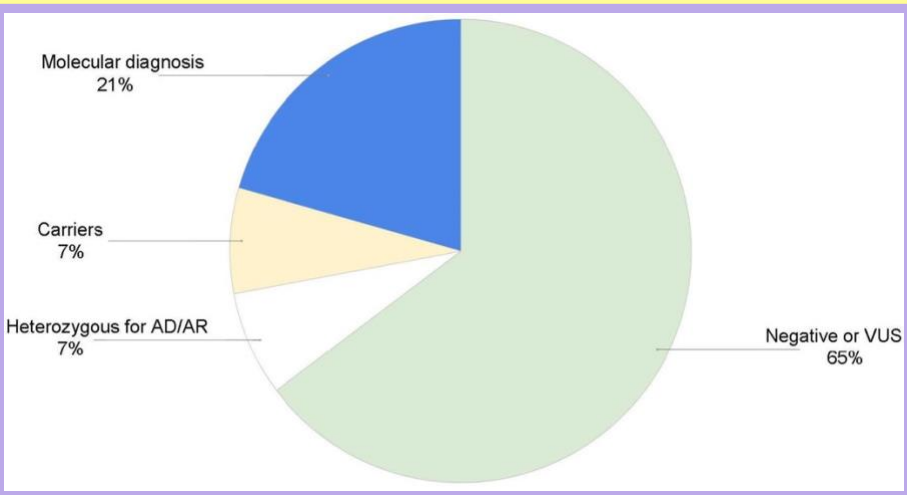
Patients with PI frequently endure a diagnostic odyssey including numerous specialty referrals and an exhaustive number of expensive and often unhelpful tests. Delays in reaching a clear diagnosis, management and treatment contribute to continuing suffering by the patient with chronic, recurring infections and in some cases, organ or tissue damage. Rapid technological developments in next generation DNA sequencing (NGS) has provided knowledge, hope, and relief from such a diagnostic odyssey. Outcomes from NGS have significantly influenced patient diagnosis and management.

These valuable resources are frequently unavailable owing to cost and insurance constraints around access to broad-based genetic diagnostics, or access to these methodologies in particular regions of the world. As a result, there are patients in the JMCN that have genetically definable PI who have not been evaluated. Through the utilization of the JMCN, we link those patients most likely to have a genetic diagnosis to genetic diagnostics, and as such, offer an unprecedented high pre-test probability.

Pilot Program

In 2019, JMF launched a gene sequencing pilot program for patients diagnosed with an underlying PI disease. The aim of this initiative was to help identify a specific defect and provide medical professionals precise diagnosis for appropriate management and treatment. The purpose of this pilot program was to demonstrate the value and clinical utility of PI NGS through JMF's unique and established network, which provides an unprecedented high level of pre-test probability.

A total of 21 sites were invited to participate. Approximately 50% of participating sites were located in the US. JMF utilized the Invitae PI panel for this pilot program, which included 207 genes associated with PI. This program also provided Family Variant Testing (FVT) at no charge for any relative of the patient that was tested and had a pathogenic or likely pathogenic variant. This program was offered to the community as a free service and no hospitals, patients, physicians, or agencies were charged for the sequencing. One hundred fifty-eight patients and 29 family members were tested in this pilot study. The clinical results are shown in the Figure below.



After genetic sequencing: What do we know about these patients?

- Expert Physicians reported to JMF that many of these patients saw a healthcare provider an average of 5.28 times in the past year.
- 42% had been admitted to the hospital at least once
- 34% to the emergency room at least once
- 13% to the ICU at least once
- Most had multiple admissions

After genetic sequencing:

- 45% of responding physicians altered their suspected clinical diagnosis.
- 40% of the patients had a change in disease management.
- 36% of the patients had a change in treatment.
- 45% of the patients had a change in outcomes.
- 80% of the patients could access an approved therapy.

The entire patient cohort, US and outside the US, faced barriers to obtaining genetic testing such as onerous pre-approval processes, burdensome co-payments, and access to only a limited array of genetic tests and not the ones needed. This pilot study highlights the cost-efficiency and importance of genetic testing, the mandate for broad scale sequence-based diagnostics for PI and justifies greater access to NGS sequencing in the right context. **Results of the Pilot Program were Published in a Immunologic Research in May 2020, and can be accessed here.**

The Global Rollout

In early 2020, JMF rolled this program out globally, offering all 395 Jeffrey Modell Centers an opportunity to participate. The gene panel was expanded from 207 to 407 genes representing 95% of the Primary Immunodeficiency Genes recognized by the IUIS. To date, 218 Centers have joined the Program, with a total of 764 patients sequenced, and 3,752 variants identified. Of the 407 genes on the PI panel, variants in 386 genes (95%) have been identified in these patients. The program is ongoing and we are collecting data to further evaluate barriers to access, and changes in disease management and treatment. We plan to publish regarding our experience with this program in 2021, and showcase the impact, importance, and necessity of genetic sequencing for patients with a suspected Primary Immunodeficiency.

The Hyper IgM Foundation is committed to supporting our families and patients and this includes our carrier moms, sisters, and daughters. Many of our carriers face a lot of unknowns regarding their own health and our families face many obstacles to getting carriers tested, especially when the girls are young. The Foundation is hoping to change the way the medical community approaches and thinks about X-Linked Hyper IgM Carriers. To this end, the Foundation is working on two exciting projects this year.

Dr. Shanmuganathan Chandrakasan, PIDTC Site PI, at Emory University School of

Dr. Suhag Parikh at Emory University School of Medicine

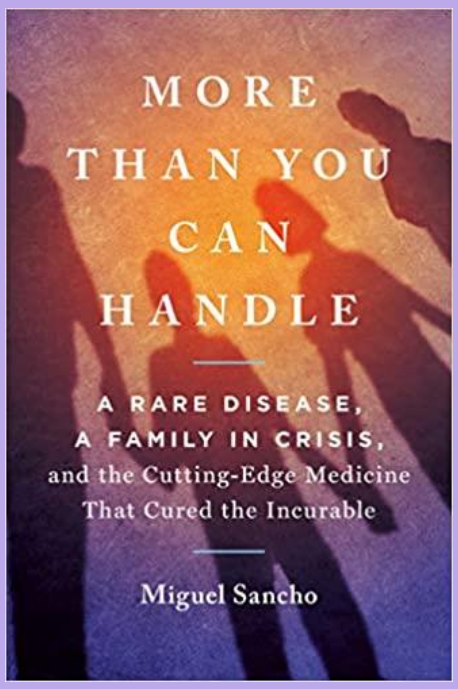
The first, a $30,000 grant given at the end of 2020 to Dr. **Shanmuganathan Chandrakasan** and the Emory University School of Medicine towards research into comprehensive immune evaluation of carriers with CD40L deficiency HIGM.

And the second is a carrier survey created together with the WAS Foundation and the PIDTC which will hopefully give insight into our carriers' health and quality of life challenges. The survey has been approved by IRB at Emory University School of Medicine with Dr. Chandrakasan and Dr. Parikh as the Principal Investigators.

Lastly, the Hyper IgM Foundation is proud to be participating in the upcoming National Organization for Rare Disorders (NORD) 2021 Living Rare, Living Stronger NORD Patient and Family Forum. Hyper IgM Foundation President, Akiva Zablocki (right), will speak on a panel titled *Shared Decision-Making with Your Team on the subject of* Cultivating a strong and healthy collaboration with care providers and medical experts for people affected by rare diseases.

Please visit the newly redesigned Hyper IgM website for more updates! https://hyperigm.org/

CGD in the Media: *More Than You Can Handle*



Miguel Sancho, the husband of Felicia Morton, president and CEO of The CGD Association of America, just wrote a book, published by Penguin Books/Avery, which follows their journey through the deepest valleys and highest peaks of living with a rare primary immunodeficiency. When their two-month-old baby falls ill, his apparently ordinary symptoms turn out to signal Chronic Granulomatous Disease (CGD). The discovery that their son, Sebastian, has CGD upends their lives and leaves the family with few options, all of them terrifying. With Sebastian at constant risk of deadly infection, they spend the next six years in some degree of self-quarantine, with all its attendant anxieties and stressors, as they struggle to keep their son alive, their marriage intact, and themselves sane.

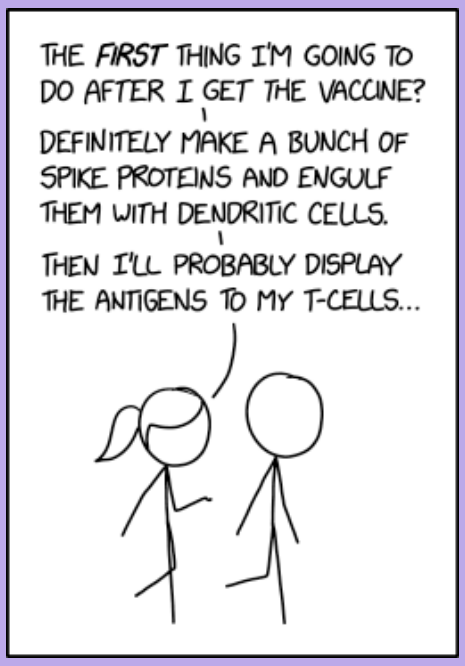
The quest for a cure leads them into the alternate universe of the rare-disease community, and to the cutting edge of modern medicine, as their personal crises send them fumbling through various modalities of self-help, including faith, therapy, and meditation. With brutal honesty, Miguel Sancho describes how his struggles affected his career, his marriage, and his family.

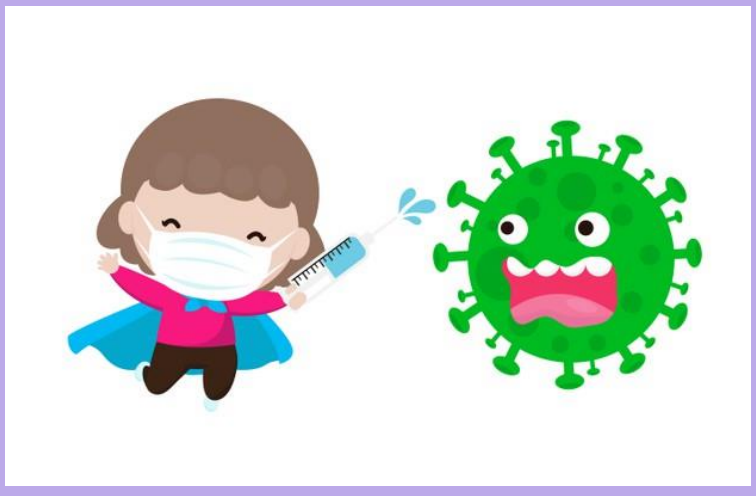
This riveting tale of the diagnosis and treatment of their son's illness takes us deep inside the workings of the immune system, and into the radically innovative treatment used to repair it. Ultimately Sebastian is saved with a stem cell transplant using discarded umbilical cord blood, a groundbreaking technique pioneered and practiced by the medical wizards at Duke University Hospital.
Deeply researched and darkly humorous, this is a wrenching tale with a triumphant ending.

About the Author

Miguel Sancho is an Emmy Award-winning television producer currently show-running and developing series and specials for A&E. For seven years he helped run the ABC primetime news magazine 20/20. Prior to that, he was an investigative producer at 20/20 and CBS News' 48 Hours. He lives in New York with his wife, Felicia, and their two children, Lydia and Sebastian.

Vaccine Humor





Protocol Updates:

Severe Combined Immune Deficiency (SCID) - 6901/6902/6907

Updates:
Thank you to our PIs, **Drs. Chris Dvorak**, **Elie Haddad** and **Jen Heimall** for leading the SCID team on cleaning up (correcting inaccurate data) the 6901 and 6902 datasets, finalizing the new 6907 protocol, and overseeing the numerous manuscripts that are in the works. We thank our outstanding statistics team, led by **Dr. Brent Logan,** for its efforts pulling together this data.

The 6907 protocol is IRB approved at UCSF. We will be activating sites for this protocol beginning in August.

Goals: Do not miss enrolling your 6901 Prospective SCID patients during the DMCC transition period! Enter your data into the CRFs in the South Florida database and then email Elizabeth Dunn at Elizabeth.dunn@ucsf.edu, to finalize patient eligibility via email.

Chronic Granulomatous Disease (CGD)-6903/6908

Updates: The 6903 Team is hard at work finalizing the 6908 protocol for UCSF IRB review which will be led by PIs **Drs. Jen Leiding**, **Harry Malech**, and **Dani Arnold.** The entire 6903 team, especially **Drs. Elizabeth Kang, Suhag Parikh, Stephanie Si, Kanwal Malhi, Deepak Chellapandian and Rebecca Marsh,** have been busy cleaning the 6903 datasets in preparation for an overall manuscript. Thank you to our statisticians, **Rachel Wu** and **Dr. Brent Logan,** for all their efforts!

Enrollment: Do not miss enrolling your 6903 Prospective CGD patients. Enter in your Eligibility data into the South Florida database and then email Elizabeth Dunn at Elizabeth.dunn@ucsf.edu to finalize patient eligibility.

Wiskott-Aldrich Syndrome (WAS)-6904

Updates. The WAS team is now working on data clean-up, data analysis and manuscript writing for the second 6904 paper with a larger "N" of patients. We especially want to thank investigators **Drs. David Shyr**, **Blachy Davila, Jessie Barnum**, and **Ami Shah** and our talented statisticians **Dr. Ruta Brazauskas**, and **Joy Liu**. We would also like to thank **Dr. Sumathi Iyengar** for her advice and active participation in our protocol calls.

Primary Immune Dysregulation Disorder (PIRD)-6906

Updates: The PIRD team led by Drs. Troy Torgerson, Alice Chan and Rosa Bachetta, are reviewing comments from their NIAID submission.

Ongoing Clinical Studies

Lentiviral gene transfer for SCID-X1 with low dose targeted Busulfan conditioning

This trial is open and enrolling at Boston Children's Hospital and Mattel Children's Hospital UCLA, as well as at Great Ormond Street Hospital in London. For eligibility or more information about the study, please contact: Overall PI: **Sung-Yun Pai, MD** (sung-yun.pai@nih.gov); Los Angeles PI: **Donald Kohn, MD** (dkohn1@mednet.ucla.edu); Sponsor: **David A. Williams, MD** (david.williams2@childrens.harvard.edu).

Gene Therapy Trial to Treat X-linked Severe Combined Immunodeficiency

This trial is currently enrolling at St. Jude's, Seattle, and UCSF Benioff Children's Hospital. In this research study, boys with SCID-X1 will receive a treatment called "lentiviral gene transfer," also called "gene therapy." This method inserts a normal copy of the SCID-X1 gene into blood-forming cells or "stem cells" from bone marrow that grow and develop into all blood cell types. The inserted gene will provide correct instructions to the defective stem cells in SCID-X1 so that functioning lymphocytes can develop.

For eligibility or more information about the study, please visit: stjude.org/LVXSCID-ND, or contact **Ewelina Mamcarz, MD**(ewelina.mamcarz@stjude.org), **Aleksandra Petrovic, MD** (Aleksandra.Petrovic@seattlechildrens.org), or **Mort Cowan, MD (**Mort.Cowan@ucsf.edu) .

UCSF Artemis SCID Gene Therapy

In this trial, newly diagnosed or previously treated patients with insufficient immunity due to ART-SCID receive "lentiviral gene transfer," also called "gene therapy." A normal copy of the DCLRE1C gene is inserted into blood-forming stem cells that grow and develop into all blood lineages. The inserted gene provides correct instructions to the defective stem cells so that functioning T and B lymphocytes can develop. So far 10 patients have been treated.

For eligibility or more information about the study, please contact: **Mort Cowan, MD** (Mort.Cowan@ucsf.edu) or **Jennifer Puck, MD** (Jennifer.Puck@ucsf.edu).

LAD-I gene therapy trial

This Leukocyte Adhesion Deficiency Type I (LAD-I) gene therapy trial is currently enrolling patients at UCLA (US). Additional treatment centers will include UCL/GOSH (UK) and Hospital Infantil Universitario Niño de Jesús (Spain). The trial is sponsored by Rocket Pharmaceuticals, Inc., and funded by the California Institute of Regenerative Medicine (CIRM). For more information, please contact LADclinicaltrial@rocketpharma.com or visit https://clinicaltrials.gov/ct2/show/NCT03812263?term=NCT03812263&rank=1 or https://www.rocketpharma.com/lad-i-clinical-trial-for-health-care-providers/

Anti-c-KIT (JSP191) Transplant Protocol

This Phase I study is a single arm, open label, dose escalation trial being conducted at multiple PIDTC centers, including: UCSF Benioff Children's Hospital, Lucile Packard Children's Hospital at Stanford and Memorial Sloan Kettering Cancer Center in New York. The study objective is to evaluate the safety and tolerability of allogeneic CD34+ human stem cells (HSC) in patients with Severe Combined Immune Deficiencies (SCID) conditioned for transplantation with JSP191, a monoclonal antibody that targets human CD117. The trial is open for both patients in need of repeat HCT as well as newly-diagnosed patients undergoing first HCT.

For questions regarding the trial please contact Wendy Pang (wpang@Jaspertherapeutics.com).

CSIDE

CSIDE is open to enrollment 34 sites and 13 patients have been enrolled to date. More centers are currently being activated! If you have any questions about getting your site on board, please email **Sung-Yun Pai, MD** (sung-yun.pai@nih.gov), **Mike Pulsipher** (mpulsipher@chla.usc.edu), and **Jenny Vogel** (jvogel@nmdp.org).

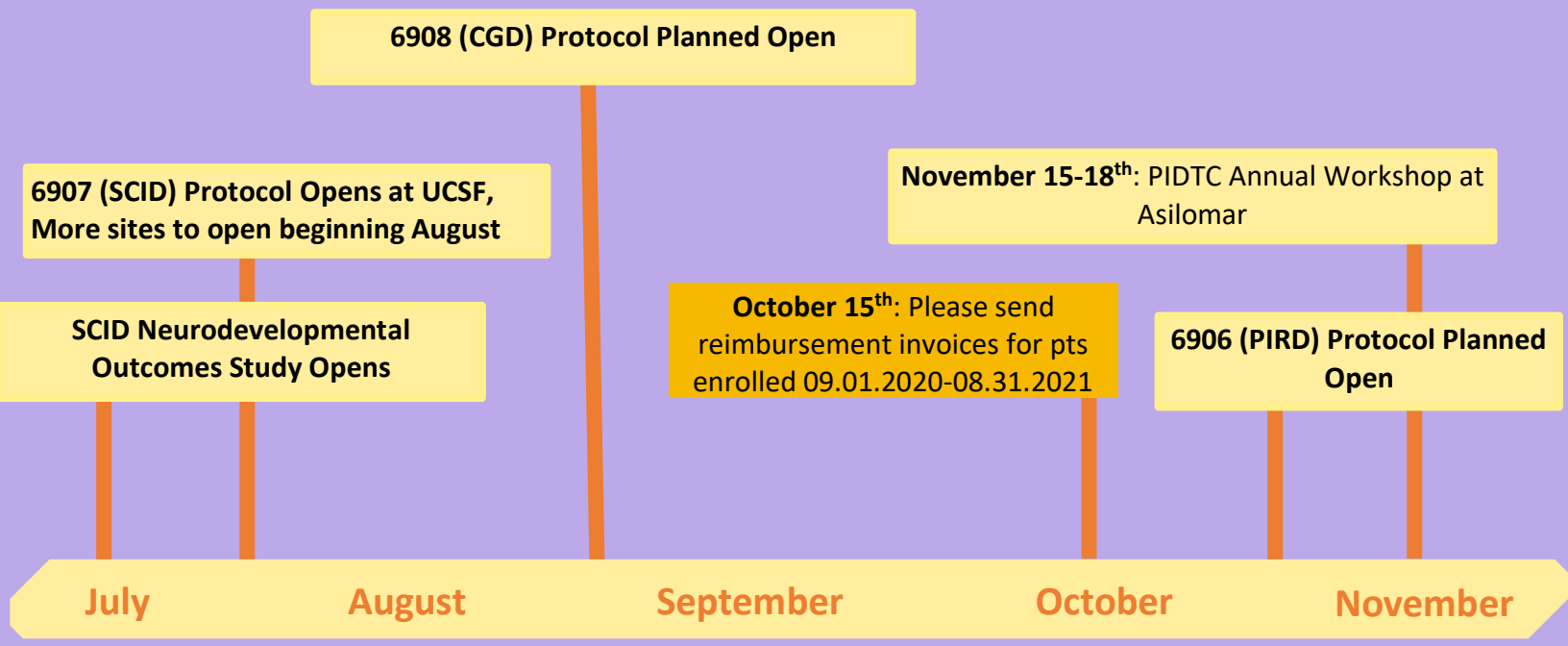
Viral CTL Consortium (VIRCTLC)

Principal Investigator Mitchell S. Cairo, MD and Study Chairs Julie Talano, MD and Nancy Bunin, MD, are studying (funding by the FDA) the safety, efficacy and biology of viral CTLS derived from related donors by the Cytokine Capture System using the Prodigy device in patients with immunodeficiencies either secondary to HSCT or primary immunodeficiencies with refractory CMV, ADV and/or EBV or intolerant to anti-viral therapy. If you and your institution are interested in participating in this clinical trial, please contact **Dr. Mitchell S. Cairo** (Mitchell_cairo@nymc.edu).

UPMC clinical trial: BOLT-BMT

The University of Pittsburgh, sponsored by NIAID, is conducting a study for patients with primary immunodeficiency (PID) and end-stage lung disease. In this study, patients receive a lung and bone marrow transplant (BMT) from the same donor. Lung transplant prior to BMT would allow for restoration of pulmonary function prior to BMT, allowing PID patients to proceed to BMT, which would be curative for the patient's underlying immunodeficiency. For more information, please contact Dr. Paul Szabolcs at paul.szabolcs@chp.edu or Shawna McIntyre at mcintyresm@upmc.edu or 412-692-5552.

PIDTC: Summer/Fall Timeline 2021



PIDTC Ed Day – Scientific Annual Workshop 2021

PIDTC will be holding its 11th PIDTC Annual Scientific Workshop for investigators, trainees, and PIDTC patient advocates. Prior to the PIDTC Annual Scientific Workshop we will also be holding for the 6th year the PIDTC Education Day.

- Education Day: 12:00 PM, November 15 - 12:45 PM, November 16, 2021. (PST)
- Scientific Workshop: 12:00 PM, November 16 - 12:00 PM, November 18, 2021. (PST)

This will be held at the Asilomar Conference Center in Pacific Grove, CA. We will also have a virtual option for those who cannot attend in person.

Reminder!
Please respond to the invitation from Kiana Soriano (Kiana.Soriano@ucsf.edu) to confirm if your attendance will be in person or virtual and who will be representing your institution by July 23rd!

PIDTC

Newsletter brought to you by the PIDTC Program Management Team. Thank you to our partners at the RDCRN/DMCC!

Got announcements?
Email: alison.yip@ucsf.edu