

Primary Immune Deficiency Treatment Consortium

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Meet Dr. Matt Snyder, a WAS survivor, who now works as a resident physician in pediatrics and medical genetics.

Greetings from Jennifer Puck, Chris Dvorak and Elie Haddad, Co-Pls

We think it is fair to say that 2020 has been a difficult year for all of us. Many of us have had patients, co-workers, friends and family members infected with SARS-Cov-2, some of whom have not survived. Let us all take a moment to recognize the enormous burden of COVID-19 in our community, but also our resilience. We are beginning to believe the pandemic will end in 2021, as effective vaccines become widely available in record time.

As we move forward to initiate our NEW PIRD (6906), SCID (6907), and CGD (6908) protocols in the spring, we also take pride in the unprecedented data sets we have created through many years of successful PIDTC collaboration. With the new information at hand, we are addressing many of the pressing research questions in primary immune diseases. Our intensive efforts over the past months to finalize our data cleaning will make possible exciting data analyses with several manuscripts already planned. This has truly been a Herculean effort by the PIDTC site CRCs and investigators, with assistance from the PIDTC Protocol and Program Management Teams.

In addition to completing our legacy protocols, publishing our findings and opening the new protocols, the PIDTC will be undertaking major long-term planning initiatives for future growth and support for clinical trials in primary immune diseases. These will be made possible thanks to the strong natural history data sets we have established and our extensive connections with scientists and clinicians in the immunology and transplantation communities throughout the USA and Canada.

Thank you to everyone engaged with the PIDTC for your dedication and hard work. We have great days ahead of us in 2021 and beyond.

With appreciation, Jennífer, Chrís and Elíe



PIDTC continues important research work on primary immune deficiencies in challenging times

Greetings from Co-Pls Drs. Jennifer Puck, Chris Dvorak and Elie Haddad

- Dr. Snyder's WAS Journey
- Patient Updates
- Published! Multiplexed Functional Assessments
 of Genetic Variants of CARD 11
- Patient Advocacy Group Updates
- Published! Excellent Outcomes Following HCT for WAS
- SCID In the Media: Ending Disease (film)

IN THIS ISSUE

- Pilot Project Award: Sarah Henrickson
- Welcome! Jennifer Leiding, MD to the Steering Committee
- More Patient Updates!
- Protocol Updates
- Clinical Trials
- Upcoming Patient Surveys
- PIDTC Timeline
- Two Brothers with GCD Story

Dr. Matt Snyder's WAS Journey by Dr. Matthew Snyder



The earliest memory I have is inside of a hospital room. I still vividly remember the taste of the cherry toothpaste that would earn me stickers on a big wall chart when I brushed my teeth. The hospital staff was awesome at finding ways to keep a threeyear-old occupied through four months of a hospital stay. I didn't realize at the time that my childhood was different. My parents then explained to me as I got older that my early childhood was in fact very different because I was born with Wiskott-Aldrich Syndrome (WAS) and needed to have a bone marrow transplant to cure the immunodeficiency. Growing up I was so thankful for the care that I received and for the

advances in medicine that provided me the opportunity to live a full life.

My mother's brother passed away from a brain bleed in 1967 at the age of four shortly after he was formally diagnosed with WAS. My mother was only 11 months older than my uncle and they were inseparable. She doesn't have vivid memories of his ongoing illness, but she still remembers traveling to the NIH for him to be evaluated and diagnosed with WAS. She also remembers the night that her parents returned home from the

local hospital and told her that her brother had gone to meet Jesus.

When I was born, I seemed to be a very healthy baby, until about six weeks of age when I began to develop eczema, chronic diarrhea, and petechiae. These episodes continued to occur, and recurrent ear infections also developed. My pediatrician became suspicious enough for the diagnosis of WAS that he referred me to the Hershey Medical Center for genetic testing and then on to the NIH where the diagnosis was confirmed. Ironically enough, the same doctor that diagnosed me, also diagnosed my uncle in 1967. My parents



were informed that the only chance for a curative therapy for the disease would be a bone-marrow transplant, but unfortunately, I didn't have a perfect sibling match, so the treatment of choice was splenectomy to control my symptoms. It was 2 years later, as my condition deteriorated significantly, that an unrelated bone marrow transplant became the only option for my long-term survival.

Looking back, I know that I was incredibly fortunate with my transplant and post-transplant course as the only complication I had post-transplant was an infection shortly after discharge from the hospital. Now, the only complications I have to monitor are those related to my splenectomy. The majority of the first two decades of my life were spent focused on the sport of wrestling. This again can be largely attributed to the dedication of my parents: my father to travel across the country at all costs to help me improve my skills and compete, and

my mother to stay home and take care of my older sister while we traveled. I was incredibly fortunate to have their love and support, as well as be exposed to many brilliant minds in the sport who opened up doors for me



to compete in college at the University of Virginia (UVA). My experience at UVA was transformational, as I came to know the faith that I hold dear and developed deep friendships with mentors, coaches, and peers who continue to help me articulate my thoughts and hopes to this day.

In my third year of medical school, I had the opportunity to rotate on the Genetics service at Children's National Hospital in Washington D.C. There, while taking a family history of an infant with a new urea cycle disease (a condition that prevents the normal breakdown of protein waste products in the body), I realized that for the first time

I was on the "other side of the curtain." That the fear, pain, wonder, and hope that I could feel from this family during our encounter were the same emotions that my parents felt decades prior. This realization, and the understanding that I was now on the "other side of the curtain" was an important moment in the infancy of my training. If I could spend my career working to solve problems for families like this and have the opportunity to

sit with them through these incredibly vulnerable moments, then it would be worth every minute of my career.

Now as a third-year resident physician in pediatrics and medical genetics, I can attest that the journey continues to be worth it. I deeply enjoy building relationships with families that allows them to trust me with their worries surrounding the disease, personal concerns, and most importantly, their hope in medicine improving their outcomes. Finding the perfect balance of processing the emotional weight of such conversations with families, learning how to take care of many rare conditions, and loving my family well, is not easy. However, my own family's experience is a constant reminder that in medicine, it is not easy on either side of the curtain.

I don't know exactly what lies before me in my life or my career in medicine. However, I am able to look back in deep gratitude to many people who gave me the opportunity to pursue this journey, including



the physicians and researchers who studied WAS, the families who came before and after my transplant who lost their loved ones to WAS, my bone-marrow donor, my family, mentors and friends. I share this story as a story of hope: hope to the physicians and researchers who work tirelessly to take care of both their patients and their own families well, hope to those families who have children with rare diseases like WAS that don't know what the future holds, and as hope to families who have lost loved ones to rare diseases, to know your losses are not in vain. Baby Fitz showing off his Halloween spirit in not one but TWO costumes for Halloween this year!



Get ready for his magic trick! He will transform into a lion. "ABRACADABRA!"



Multiplexed Functional Assessment of Genetic Variants in CARD11



Iana Meitlis, Eric J Allenspach, Bradly M Bauman, Isabelle Q Phan, Gina Dabbah, Erica G Schmitt, Nathan D Camp, Troy R Torgerson, Deborah A Nickerson, Michael J Bamshad, David Hagin, Christopher R Luthers, Jeffrey R Stinson, Jessica Gray, Ingrid Lundgren, Joseph A Church, Manish J Butte, Mike B Jordan, Seema S Aceves, Daniella M Schwartz, Joshua D Milner, Susan Schuval, Suzanne Skoda-Smith, Megan A Cooper, Lea M Starita, David J Rawlings, Andrew L Snow, Richard G James

There has been a rapid increase in the availability and utilization of genetic testing in medicine, but the interpretation of these genetic results is often lagging. Patients often get reports labeling variants of "uncertain significance", which should not be used for medical decision making. This hinders precision medicine. There are many pieces of data that clinicians and geneticists use to interpret variants as either benign

or disease-causing including functional testing. Often this time-consuming process follows variant identification and delays treatment. In this study, we focused on a novel approach to simultaneously screen the functional effect of a large number of variants in the gene *CARD11*, an adaptor protein that expresses blocking or gain-offunction variants associated with distinct immunodeficiencies. We used genome editing to make a population of cells with all possible genetic changes at the same time to functionally screen them to provide a database to provide up front predictions. This information can now be utilized together with family history, clinical symptoms and other laboratory testing to aid in diagnosis. We generated functional scores for 2,542 coding and 38 noncoding variants of CARD11 and applied our predictions to new patients with novel mutations and compared to traditional methods.

The classification of reported clinical variants was sensitive (94.6%) and specific (88.9%), which rendered the data immediately useful for interpretation of seven coding and splicing variants implicated in immunodeficiency

found in our clinic. This approach is generalizable for variant interpretation in many other clinically actionable genes, in any relevant cell type.

Meet the Author: Eric Allenspach, MD, PHD



Dr. Allenspach is an attending physician and the medical director of Diagnostics for the Center for Immunity and Immunotherapies at Seattle Children's Hospital. His primary research interest lies in the development of autoimmunity in children and infection risks of immunosuppressed children. His lab uses genetic testing and immunophenotyping to help diagnose children.

Dr. Allenspach is also the recipient of our Pilot Project Award from 2017 which helped fund the research on CARD11 and the mechanisms of mutations in the pathogenesis of immune dysregulation.

PAG Updates:



Wiskott-Aldrich Syndrome Foundation

The WAS foundation has been working hard during COVID-19 to help support WAS families. Recently, they organized a Zoom call lead by Dr. Elie Haddad (CHU St. Justine) and Dr. Christina Mangurian (UCSF) to discuss navigating through COVID-19 for families with WAS.





The WAS Foundation also created a COVID-19 Guidebook for WAS Families and is available for download at: www.wiskott.org/resources.familyliterature

https://www.youtube.com/watch?v=S2QPKqiGmUE&feature=youtu.be

CGD Association of America





Felicia Morton, founder and executive director of the CGD Association of America, was honored to be nominated for a RARE Champion of Hope Award by Global Genes for her work advocating for patients and X-linked carriers with CGD. The Global Genes community nominated individuals and organizations who have made a significant impact in advocacy, industry, medical care and treatment, science and technology and young rising leaders. Global Genes is a 501(c)(3) nonprofit organization that provides hope for the more than 400 million people affected by rare disease around the globe.

SCID Angels

SCID Angels has kept in touch with its members this year by switching from in person, face to face **"CONNECT OVER COFFEE"** meetings at UCSF, to virtual, **"CONNECT IN THE CLOUD"** meetings for any SCID parent or adult patient that wants to join in. This switch in platform has given us the opportunity to grow and involve SCID families from all over the world, instead of just those who are at UCSF. SCID Angels is fortunate to have SCID Ambassadors; Sy Wu, Anne Klein, Lynette Westfall, along with occasional help from



Heather Smith lead these zoom sessions. We look forward to continuing this program in 2021, so please have any interested SCID family or SCID patient contact Heather Smith at Heather@SCIDAngelsforlife.com.





Immune Deficiency Foundation launches new plasma initiative



Increased global demand combined with a drop in donations during the COVID-19 pandemic has raised alarm bells for many who rely on plasma-derived therapies. In response, The Immune Deficiency Foundation has created Plasma Hero (www.plasmahero.org), an initiative designed to educate the general public on the critical need for plasma and to connect potential donors with resources to get started. The website consists of a donation center locator as well as practical information on what it's like to donate along with guidelines and tips for first-time donors.

The name 'Plasma Hero' was derived from the sense of overwhelming gratitude patients who rely on plasma-based therapies feel towards donors. Patients and

their families view donors as true lifesavers and heroes. The new campaign and website offer a platform for plasma donors to be recognized and share their motivations for donating and the emotions they associate with this heroic act. The site will also offer updated information and resources for people who rely on plasma-based therapies.



Plasma Hero can also be found on Facebook and Instagram using @beaplasmahero. For more information, email hello@plasmahero.org.

Thank you to all of our Patient Advocacy Groups!



Excellent Outcomes Following Hematopoietic Cell Transplantation for Wiskott-Aldrich Syndrome: A PIDTC Report

Lauri M. Burroughs, Aleksandra Petrovic, Ruta Brazauskas, Xuerong Liu, Linda M. Griffith, Hans D. Ochs, Jack J. Bleesing, Stephanie Edwards,



Christopher C. Dvorak, Sonali Chaudhury, Susan E. Prockop, Ralph Quinones, Frederick D. Goldman, Troy C. Quigg, Shanmuganathan Chandrakasan, Angela R. Smith, Suhag Parikh, Blachy J. Dávila Saldaña, Monica S. Thakar, Rachel Phelan, Shalini Shenoy, Lisa R. Forbes, Caridad Martinez, Deepak Chellapandian, Evan Shereck, Holly K. Miller, Neena Kapoor, Jessie L. Barnum, Hey Chong, David C. Shyr, Karin Chen, Rolla Abu-Arja, Ami J. Shah, Katja G. Weinacht, Theodore B. Moore, Avni Joshi, Kenneth B. DeSantes, Alfred P. Gillio, Geoffrey D. E. Cuvelier, Michael D. Keller, Jacob Rozmus, Troy Torgerson, Michael A. Pulsipher, Elie Haddad, Kathleen E. Sullivan, Brent R. Logan, Donald B. Kohn, Jennifer M. Puck, Luigi D. Notarangelo, Sung-Yun Pai, David J. Rawlings, Morton J. Cowan

We are excited to share the results of our paper, "Excellent Outcomes Following Hematopoietic Cell Transplantation for Wiskott-Aldrich Syndrome: A PIDTC Report" that was recently published in the medical journal, Blood in June 2020.

PIDTC 6904 is a clinical research study of the outcomes of patients with Wiskott-Aldrich syndrome who have undergone transplant at PIDTC centers. The study was open at over 42 PIDTC centers and has enrolled over 300 patients across North America! Patients with Wiskott-Aldrich syndrome (WAS) are at increased risk for life-threatening infections, bleeding complications, and autoimmune problems due to their disease. Transplant is the primary curative approach, with the goal of correcting the underlying immune and platelet problems. In our first paper, we did a retrospective study of 129 patients with WAS who had undergone transplantation at PIDTC centers from 2005-2015. Importantly, we found excellent survival (>90%) following transplant regardless of what type of donor (sibling or unrelated donor) or hematopoietic cell source (bone marrow, peripheral blood, or cord blood) was used. Age at transplant remained a key factor with better survival in patients who were younger than age 5 years at the time of transplant versus those who were older.

This finding highlights the importance of performing the transplant early in the course of the disease before the patient develops complications which can make it more difficult to do the transplant safely. We also looked at how the type of conditioning the patient received (full intensity versus reduced intensity) affects transplant outcomes. We did not find a difference in survival; however, we did find a difference in engraftment (how well the transplant took) with higher donor cell percentage in patients who received Busulfan-based conditioning regimens versus other reduced intensity regimens. Higher donor cell percentage in turn was needed to correct the platelet count. Which conditioning regimen is best remains an unanswered question that we are hoping to study further in our next paper, which includes more retrospective cases and data from patients who enrolled in our prospective natural history study. Additional studies are also needed that look at the long-term outcomes of patients who have undergone transplant.

This study highlights the importance of centers working together to advance patient care, particularly for patients with rare diseases. The PIDTC is a consortium of 43 centers in North America whose shared goal is to improve the outcomes of patients with rare, life threatening, inherited disorders of the immune system

including WAS, severe combined immunodeficiency (SCID), chronic granulomatous disease (CGD), and primary immune regulatory disorders. We would like to thank all the patients and families who made this work possible!

Meet the Author: Lauri Burroughs, M.D



Dr. Lauri Burroughs is the Director of the Non-Malignant Transplant Program at Fred Hutchinson Cancer Center in Seattle as well as an Associate Professor of Pediatrics at University of Washington. Her research includes developing safer and more effective BMT procedures for children with childhood cancers and nonmalignant disorders focusing on gentler regimens in pre-transplant conditioning.

Dr. Burroughs is also the Protocol lead for 6904, which follows WAS patients over time, and she also works to support the WAS group in the writing of our planned publications.

SCID in the Media: Ending Disease (Film)



SCID Angels has partnered with the theater and director of the film "Ending Disease: The Stem Cell, Anti-Cancer T-Cell, & Antibody Revolution In Medicine", in an effort to promote the film and to educate people about stem-cell research. As a partner, SCID Angels will receive 50% of the revenue from ticket sales using this link, so please purchase your \$10 tickets <u>here</u> (https://watch.eventive.org/endingdisease/play/5fcaaf26501f7000cb04628c). This link will be good through the end of December. After purchasing your ticket, you'll have 14 days to start watching the film. Once you've started the film, you'll have 7 days to finish. It's approximately 3 hours in length (4episodes, 45 minutes each episode) but well worth every minute, not to mention, PIDTC's own Dr. Chris Dvorak is also featured in the film as one of the treating physicians that follows the patient with ART-SCID.

ENDING DISEASE



Ending Disease is about the first generation of clinical trials using stem cell and regenerative medicine to cure or successfully treat many of the most devastating diseases. This film is about how scientists are able to cure, or put into remission, certain types of blindness, a broken spinal cord, HIV/AIDS, different types of cancer, and SCID. The director had unprecedented access to 10 clinical trials in progress, for brain cancer, breast cancer, leukemia and lymphoma, HIV, repairing a broken spinal cord, eve disease and Severe Combined Immunodeficiency disease, and the results are truly inspiring.

More Patient Updates!



Just a few of the families who are sharing their experiences with the SCID Compass initiative, an educational program, funded by HRSA. PIDTC and IDF are working jointly as part of the project. Learn more at <u>www.scidcompass.org</u>.



Meet the Hargroves! Kai was diagnosed with Xlinked SCID and has gone through 2 HSCTs and gene therapy.

https://primaryimmune.org/scid-compass/navigatehospital-stay-q



Say hi to the Wus! Jason was born as a triplet and diagnosed with X-linked SCID. He was treated with an HSCT.

https://primaryimmune.org/scid-compass/planfuture-q



Say hi to the Billy-Georges! Ava was diagnosed with ART-SCID and has undergone 2 HSCTs.

https://primaryimmune.org/scidcompass/understand-scid-q



Meet the Duggans! Dean was diagnosed with X-linked SCID has undergone one HSCT.

https://primaryimmune.org/scid-compass/cope-withpost-treatment-q-duggan-family

Pilot Project Recipient: Sarah Henrickson, MD, PHD



Dr. Sarah Henrickson is an attending physician at Children's Hospital of Philadelphia in the division of Allergy and Immunology. She is also a newly promoted Assistant Professor at CHOP's Department of Pediatrics, Division of Allergy Immunology. She is passionate in presenting complex research and clinical topics to make them clear and pertinent to practicing medicine.

The Henrickson lab develops hypotheses using multimodal immunometabolic research studies and systems immunology research. These hypotheses are tested using human cells *in vitro* and mouse models.

Dr. Henrickson's pilot project will focus on the STAT1 and STAT3 transcription pathways to deepen our understanding of shared dysfunction mechanisms in patients with PIRD. In this project, Dr. Henrickson seeks to move towards new precision diagnostics and targeted therapeutics by quantifying molecular mechanisms underlying immunometabolic dysfunction in altered STAT1 and STAT3 pathways.

Welcome Dr. Jennifer Leiding to the PIDTC Steering Committee!



We are proud to welcome Dr. Jennifer Leiding to the PIDTC Steering Committee. Dr. Leiding is an immunologist and allergy specialist at Johns Hopkins All Children's Hospital in St. Petersburg, Florida.

Dr. Leiding's research focuses on understanding the causes of auto-inflammation in Chronic Granulomatous Disease (CGD) and Primary Immune Regulatory Disorders (PIRD).

At the PIDTC, Dr. Leiding is the current protocol lead for 6903, as well as our new protocol, 6908. She leads our protocol calls with great enthusiasm and is very active in developing our new modules and case report forms.

Protocol Updates: 6901, 6902, 6903, 6904

Severe Combined Immune Deficiency (SCID) - 6901/6902

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 their efforts pulling together this data.

<u>Goals</u>: 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 <u>Elizabeth.dunn@ucsf.edu</u>, to finalize patient eligibility via email.

Chronic Granulomatous Disease (CGD)-6903

<u>Updates:</u> The 6903 Team is hard at work finalizing the 6908 protocol for NIH 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, 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 <u>Elizabeth.dunn@ucsf.edu</u> to finalize patient eligibility.

Wiskott-Aldrich Syndrome (WAS)-6904

<u>Updates</u>. The WAS team is now working on data cleanup, 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.

Lookout: WAS queries will be sent by our WAS investigator from December 2020 to January 2021.

			New protocols
	Rare Disease	2014-2019 (current)	2019-2024 (
PIDTC Protocols	Severe Combined Immune Deficiency (SCID)	6901 – Prospective 6902 – Retrospective and Cross-sectional	Merged to continue as 6907 , "Severe Combined Immune Deficiency: Prospective and Longitudinal Study of Genotypes, Management and Outcomes"
	Chronic Granulomatous Disease (CGD)	6903 – Prospective, Retrospective and Cross-sectional	6908 , "Chronic Granulomatous Disease: Determinants of Auto-Inflammation and Complications following Hematopoietic Cell Transplantation"
	Wiskott-Aldrich Syndrome (WAS)	6904 - Prospective, Retrospective and Cross-sectional	Completed (WAS patients with dysregulated immunity will be studied in PIRD)
	Primary Immune Regulatory Disorders (PIRD)	N/A	New – 6906 , "Primary Immune Regulatory Disorders: Clinical Presentations, Treatments and Outcomes"

Ongoing Clinical Studies

**The PIDTC does not endorse these studies but provides this information to our readers as a courtesy.

Lentiviral gene transfer for SCID-X1 with low dose targeted

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** (<u>sung-yun.pai@nih.gov</u>); Los Angeles PI: **Donald Kohn, MD** (<u>dkohn1@mednet.ucla.</u> <u>edu</u>); Sponsor: **David A. Williams, MD** (<u>david.williams2@childrens.harvard.edu</u>).

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 (sungyun.pai@nih.gov), Mike Pulsipher (mpulsipher@chla.usc.edu), and Jenny Vogel (jvogel@nmdp.org).

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).

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.



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/NCT03812 263?term=NCT03812263&rank=1 or https://www.rocketpharma.com/lad-i-

UCSF / Stanford Transplant Anti-c-KIT Transplant Protocol

This Phase I study is a single arm, open label, dose escalation trial being conducted at 3 centers: 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 tandemly purified allogeneic CD34+CD90+ human stem cells (HSC) in patients with Severe Combined Immune Deficiencies (SCID) conditioned for transplantation with AMG 191, a monoclonal antibody that targets human CD117.

"For questions regarding the trial please contact Rajni Agarwal, MD (<u>rajnia@stanford.edu</u>), or Christopher Dvorak, MD (<u>Christopher.dvorak@ucsf.edu</u>)."

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: <u>stjude.org/LVXSCID-ND</u>, or contact **Ewelina Mamcarz**, MD(<u>ewelina.mamcarz@stjude.org</u>), Aleksandra Petrovic, MD (<u>Aleksandra.Petrovic@seattlechildrens.org</u>), or Mort Cowan, MD (<u>Mort.Cowan@ucsf.edu</u>).

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 antiviral therapy. If you and your institution are interested in participating in this clinical trial, please contact **Dr. Mitchell S. Cairo** (Mitchell cairo@nymc.edu).

Got announcements? Contact Sharon at sharon.kidd@ucsf.edu and Alison at alison.yip@ucsf.edu

Research Survey for CGD Carriers

In keeping with the mission of the CGD Association of America (CGDAA) to advance important CGD research, we hope that you will fill out this important survey about X-linked CGD carriers. The survey was designed by the Principal Investigator, Dr. Jennifer Leiding, who is a clinical immunologist at the University of South Florida (IRB#001208) in collaboration with the Primary Immune Deficiency Treatment Consortium, and Felicia Morton from the CGDAA, and will focus on X-linked female CGD carriers. Funding for this project was provided by a grant from Horizon Pharma.

The purpose of this confidential study is to find out the symptoms and diseases that X-linked carriers experience. The results from this survey will help physicians and researchers learn more about how being an X-linked CGD carrier affects women's lives, including diagnosis and treatment experiences, along with overall well-being and quality of life.

For many years, female X-Linked CGD carriers were thought to be asymptomatic. Yet, a growing amount of research shows that they can have serious health issues relating to being an X-linked CGD carrier. This study aims to understand the medical problems carriers face and whether they have access to the appropriate health care.

Completing this online survey is an opportunity to make sure your experiences are heard and will help support our mission to raise awareness for the health problems and ailments that X-linked CGD carriers have and improve their access to the medical care and treatments they may need. The survey takes approximately 30 minutes to complete.

Please pass this on to your daughters, mothers, sisters, aunts, and grandmothers who have been diagnosed as X-linked CGD carriers. Together, we will make a difference for our women and girls!

https://redcap.health.usf.edu/surveys/?s=M7LAWAPNAM



Brothers with Life-Threatening Genetic Disease Now Thriving by Ashley Roberts



Dr. Chellapandian and Dr. Leiding with brothers, Jerrick and Evian

Brothers Jerrick and Evian are three years apart—Jerrick is 5 years old and also the twin of their sister, Jelena. Evian is the baby of the family, a bubbly and energetic 2-year-old. Although years apart, they share a very special bond: Both were diagnosed with and treated for rare, lifethreatening genetic disease called Xlinked chronic granulomatous disease (CGD).

"After a family barbeque one day, I was about to give Jerrick a bath and I noticed a huge bump on his chest," explains the boys' mom, Jessica. "I assumed a ball hit him because he was

playing soccer and basketball that day, but all he told me was that 'it hurt'. Automatically I thought the worst, so I ended up taking him straight to the Emergency Room."

It was a massive abscess caused by a common fungus, Aspergillus, that formed in his lungs and spread to his chest. After a surgery and treatment from a few local hospitals, the Daytona Beach family was referred to see Jennifer Leiding, M.D., an immunologist and allergy specialist for the University of South Florida at the Pediatric Allergy/Immunology Program at Johns Hopkins All Children's Hospital and USF Morsani College of Medicine. Jerrick underwent another, more extensive surgery where two ribs and a large portion of his right lung were removed, and he received a skin graft.

"After the surgery, I think that was my lowest point when I just saw him lying there lifeless, but I felt like it was so amazing because within a couple of hours he was sitting up, willing to sit on a chair," Jessica says. "Dr. Leiding ultimately told us it was CGD. She pretty much knew right away with all the symptoms in the pass with pneumonia because Jerrick actually got a couple pneumonias every year."

While a child with GCD may go without symptoms for a while inevitably they will become very sick. Repeat cases of pneumonia are a key indicator of the disease. CGD can cause blood-borne infections, so common places for infection include the lymph nodes, lungs, liver and central nervous system.

"X-linked CGD is one of the most common, but most severe forms of CGD," Leiding says. "Kids typically present within the first five years of life with either a life-threatening infection or some auto immune complication from the disease."

CGD Explained

CGD is a disorder that affects certain types of immune cells, which makes a person more susceptible to bacterial and fungal infections. X-linked means one of the genes in the X-chromosome is mutated. Females have two X-chromosome is mutated. Females have two X chromosomes and males have both an X and a Y. In Jessica's case, she has one healthy X chromosome that does the job of the mutated X, which is why she doesn't have the disease, but instead is a carrier. Carriers have a 50 percent chance of passing it along to their children—for sons, that means a 50 percent of actually getting the disease, and for daughters, becoming a carrier—in very rare cases does a female get this particular disease. About one in every 200,000 live births result in CGD.

"It was definitely a huge shock," Jessica says. "It's a condition I had never heard of throughout my entire life. My first thought is, "Is my son going to die from this? What are our options? Treatments?"

Treatment for CGD

Johns Hopkins All Children's Hospital has a Conjoint Immunology/Bone Marrow Transplant Clinic to treat specific transplantable immunodeficiencies like CGD. The only way to cure CGD is by a bone marrow transplant (BMT). Leiding works closely with Deepak Chellapandian, M.D., in treating CDG patients referred from all over Florida. Chellapandian is an assistant professor in the Johns Hopkins University School of Medicine and a Blood and Marrow Transplant Specialist at Johns Hopkins All Children's Hospital who specializes in transplantation for nonmalignant blood disorders.

"The cure is, we need to get rid of this defective bone marrow producing those abnormal immune cells and need to replace them with healthy stem cells from the donor," Chellapandian says. "The best match for any transplants is finding a sibling donor without the same disease."

For Jerrick, his twin sibling Jelena turned out to be his perfect match. While testing Evian, Jerrick's younger sibling, the team found that he, too has CGD. "He did not have any symptoms at all. We just incidentally found out through routine screening that he had the same genetic mutation," Chellapandian says.

But it would have only been a matter of time before Evian would get sick, too and he would also need a BMT. Fortunately, a non-family member donor match was identified for Evian, and both brothers had transplants within a few months of each other.

"Finding a donor for rare populations is always difficult," Chellapandian says. "Anyone can register to be a donor, so I strongly encourage every adult, especially of rare ethnicity, to join the Be the Match Registry."

It was nearly two years of treatment, hospital stays, appointments, tests and traveling to and from Daytona Beach for Jessica and her boys.

"My mind was always racing when it came to do the doctor appointments, I had to be strong for them," Jessica says. "The doctors were my support system."

The BMTs were successful and now Jerrick and Evian are healthy, energetic, and most important, clear of CGD. They continue to have follow up appointments, which decrease with time.

"They are cured," Jessica says." Now is a time where I can actually allow them to be free, allow them to be the kids that they deserve to be."

Deeper Studies into CGD and Immune Deficiency at Johns Hopkins All Children's Hospital

Leiding and Chellapandian serve in a national group called the Primary Immune Deficiency Treatment Consortium (PIDTC). It is a National Institute of Health funded consortium that studies treatment outcomes of patients with immune deficiency, and Johns Hopkins All Children's is the only center in the state of Florida involved in the PIDTC.

Leiding specifically leads PIDTC protocols #6903 and upcoming protocol #6908 that investigates disease manifestations and treatment outcomes of CGD, while Chellapandian is developing a clinical trial to treat children with CGD and other rare immune deficiency disorders using a novel transplantation technique where he uses a half-matched (haploidentical) family member as donor.

https://www.hopkinsallchildrens.org/ACH-News/General-News/Brothers-with-Life-Threatening-Genetic-Disease-now

HAVE A SAFE AND WONDERFUL HOLIDAY!



Baby Fitz is enjoying the holidays and posing for his mama Christina's camera. We hope you're also getting into the holiday spirit with family, food and fun!





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



Got announcements? Email: <u>alison.yip@ucsf.edu</u>