Primary Immune Deficiency Treatment Consortium

NEWSLETTER

November | Fall 2024 | Issue 21

Dr. Elie Haddad with a celebratory bottle of champagne.

PIDTC Funding: R24 Grant

We are thrilled to announce that the PIDTC has received continued financial support from the National Institutes of Health in the form of the R24 grant. Thank you to our grant writers, steering committee, and PIDTC leadership for helping us secure funding, and thank you to the faculty and staff who contributed to the accomplishments and potential that earned our consortium this award.

We look forward to the continuation of our work together under our new funding source!

We would like to thank Linda Griffith for her support throughout the U54. We look forward to ensuring that the PIDTC continues to succeed under the new grant in whatever form it assumes.

Greetings from Drs. Rebecca Marsh, Chris Dvorak, Elie Haddad, and Troy Torgerson, Multi-PIs

Hello PIDTC Members,

The PIDTC Steering Committee is extremely pleased to announce successful 5-year funding (R24) of the PIDTC Resource by NIAID effective 9/3/24. The new PIs Christopher Dvorak, Elie Haddad, Rebecca Marsh, and Troy Torgerson wish to sincerely thank Jennifer Puck for her incredible leadership of the Consortium over the last grant (U54) cycle, as well as everyone who helped contribute work and ideas that led to our successful application. Over the coming months, we will be working hard to transform the Consortium from its prior iteration during the first 15 years of its existence into a sustainable resource for the future of investigations into inborn errors of immunity. More communications about this new format will come via emails, SPC calls, and talks at the planned 2025 PIDTC Workshop in St. Petersburg, FL, hosted by All Children's Hospital.

Cheers!

Rebecca, Chris, Elie, and Troy

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Protocol Leadership

6906

6907

6908

Under the R24, the protocols 6906 (PIRD), 6907 (SCID), and 6908 (CGD) will be led be Drs. Alice Chan, Jennifer Heimall, and Jennifer Leiding respectively. Additionally, Drs. Rosa Bacchetta and Geoffrey Cuvelier have joined Dr. Danielle Arnold as the vice-chairs for 6906, 6907, and 6908 respectively. As new leads for their protocols, Drs. Jennifer Heimall and Alice Chan have also joined the PIDTC Steering Committee.

All of these doctors bring a wealth of knowledge and expertise to their research teams and the PIDTC, and we eagerly anticipate working with them for the PIDTC's future!

New PIDTC Publication

High symptom burden in female X-linked chronic granulomatous disease carriers

Mary Ann Miranda, Athanasios Tsalatsanis, Jessica R. Trotter, Danielle E. Arnold, Jacqueline D. Squire, Sharon Kidd, Suhag Parikh, Rebecca A. Marsh, Linda M. Griffith, Kanwaldeep Mallhi, Deepak Chellapandian, Stephanie Si Lim, Eyal Grunebaum, Kathleen E. Sullivan, Peter E. Newburger, Mary C. Dinauer, Morton J. Cowan, Christopher C. Dvorak, Elie Haddad p, Donald B. Kohn, Luigi D. Notarangelo, Sung-Yun Pai, Jennifer M. Puck, Michael A. Pulsipher, Troy R. Torgerson, Harry L. Malech r, Elizabeth M. Kang, Felicia B. Morton, Jennifer W. Leiding. High symptom burden in female X-linked chronic granulomatous disease carriers. Clinical Immunology, Volume 268, 2024, 110364, ISSN 1521-6616, https://doi.org/10.1016/j.clim.2024.110364. PMID: 39278553. https://pubmed.ncbi.nlm.nih.gov/39278553/

CGD ASSOCIATION OF AMERICA

Lead Author: Mary Ann Miranda, MD

The CGDAA is extremely proud of our latest article, “High symptom burden in female X-linked chronic granulomatous disease carriers,” which will be published in *Clinical Immunology.* You can read the article here before its official publication on November 8, 2024.

This collaborative research project with the PIDTC represents three years of work to uncover the health issues and ailments that female carriers of X-linked CGD can face.

In this largest analysis of XL-CGD female carriers reported to date, frequent self-reported symptoms affecting nearly every organ system are apparent. Our cohort of XL-CGD female carriers reported high degree of susceptibility to autoimmune and inflammatory diseases, similar to patients affected with CGD who are susceptible to systemic autoimmunity and autoinflammation that can be difficult to treat.

We look forward to continuing to work with the PIDTC to establish guidelines to ensure these women receive better medical care for the high symptom burden they can experience as an X-linked carriers.

We urge members of the PIDTC to encourage X-linked carriers of CGD to reach out to the CGDAA to learn how to advocate for their health needs as they care for their families.

PAG Updates

Jeffrey Modell Foundation

C.H.I.L.D.R.E.N. and Specific Defect Research Programs

The JMF has opened two new research programs to fund primary immune disorders research and provide resources to interested researchers.

The goal of the Specific Defect program is to support research that studies the mechanisms and presentation of specific defects of the immune system to gain a better understanding of the defects and their impact on overall health outcomes. The JMF patient database includes high numbers of various genotypes around the world, which provides an excellent platform for international collaboration.

The purpose of the of c.h.i.l.d.r.e.n! grant is to support research focused on children living with PI throughout the world, while addressing healthcare disparities, especially in developing countries, through education, testing, diagnosis, and treatment.

For more information about both grant programs and how to apply, visit this link.

Jeffrey's Insights

Jeffrey's Insights is JMF's no-cost genetic sequencing program for patients within the JMCN living with an underlying PI but no genetic diagnosis. Proper genetic sequencing helps to identify specific defects, enhances clinical management, and enables physicians to establish earlier and more effective treatment for their patients. Please reach out if you have patients who are unable to get sequencing due to financial and/or insurance issues.

jmGENIE

The Global Education and Information Exchange (G.E.N.I.E.) funds programs with a focus on Primary Immunodeficiency (PI) to encourage global collaboration, meaningful dialogue, and ongoing education about PI to improve the quality of life of patients worldwide.
More information here:
https://info4pi.org/medical/genie/

For more information about JMF click here: https://www.info4pi.org/

SCID Angels for Life Foundation

SCID Angels Scholarships

SCID Angels for Life Foundation is happy to offer SCID Family Scholarships to affected US families with a child currently undergoing treatment for Severe Combined Immune Deficiency. Scholarships of up to $1,000 are available to approved families. The application can be found on our website at: https://www.scidangelsforlife.com/2019/12/scid-angels-family-scholarship-application/

For the 2024-45 academic year, SCID Angels awarded 3 educational scholarships to students attending postsecondary education. Read more about the 3 scholars at https://www.scidangelsforlife.com/scholarship-info/

SCID Families with Second Babies

The SCID Angels for Life Foundation urges families of children with SCID to test any subsequently-born children immediately for SCID and not to wait for newborn screening results. There are more immediate and decisive testing methods than newborn screening that can be used if the newborn's sibling has SCID.

Connect in the Cloud

Connect In The Cloud is monthly Zoom call hosted by SCID Angels. This is an excellent opportunity for SCID parents and/or adult patients to connect and learn more about one another or ask questions. Our next Connect In the Cloud will be on October 23rd at 7:00 pm EDT. Click to register at https://www.scidangelsforlife.com/scid-angels-presents-connect-in-the-cloud/. Registration is FREE but required.

For more information about SCID Angels for Life click here:
http://www.scidangelsforlife.com/

Immune Deficiency Foundation

Educational Webinars

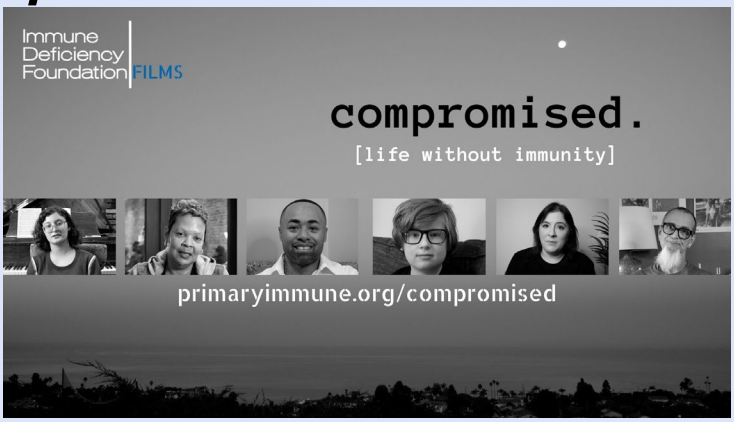
The IDF is hosting educational webinars once a month until December. The next one is titled *Decoding PI: Antibody deficiencies*, and will be held on October 24th and feature Dr. Luke Wall, MD, from the Children's Hospital of New Orleans. We invite you to join and learn with us!

UCSF physicians, families, patients and zebra participating in a Walk for PI at the San Francisco Zoo.

In-Person Walks for PI

The IDF has been hosting fundraising walks for primary immune disorders at zoos across the country. Learn more about upcoming walks, including the virtual Coast to Coast walk, here:

Compromised: Life Without Immunity



The Immune Deficiency Foundation's feature-length documentary film, *Compromised: Life Without Immunity* is now availab le to stream. The film debuted asspecial screening at the 2024 PI Conference in June in Chicago.Since then, it has been selected for the Social Impact Film Festival and is now available for home-based and community screenings. Visit www.primaryimmune.org/compromised for more information.

For more information about the Immune Deficiency Foundation:
https://primaryimmune.org/

Wiskott-Aldrich Foundation

Wiskott-Aldrich Syndrome Research Symposium: November 18th

The fourth international symposium for researchers and clinicians on Wiskott-Aldrich Syndrome is being held in Milan, Italy and offers access to the latest research and analysis related to this rare disease.

The conference will feature the following keynote speakers:

Luigi Notarangelo, MD

Alessandro Aiuti, MD, PhD

Alessia Cavazza, PhD

WAS Foundation at the IDF Conference

Over 45 patients and family members of the WAS foundation attended the IDF conference this summer in Chicago!

CGD Association of America

CGDAA at the IDF Conference

The CGDAA provided scholarships that enabled 30 patients and their families to attend the recent IDF Conference in Chicago, Illinois!

Wellness Retreat Planned for Caregivers of X-Linked CGD Patients

CGDAA is planning a wellness retreat for the first quarter of 2025 with funding assistance from Amgen. Please contact Felicia Morton if you are interested in helping to organize this event.

Hyper IgM

Hyper IgM Patient Voices Podcast

Hyper IgM Foundation has launched an innovative podcast, where children affected by X-Linked Hyper IgM Syndrome share their own stories. Led by Ezra Fineman,15-year-old high school freshman and two-time recipient of a hematopoietic stem cell transplant due to Hyper IgM Syndrome, young patients interview one another, providing intimate and informative conversations about their experiences with Hyper IgM Syndrome and life with a rare disease.

Hyper IgM Fundraisers

Over the summer we had two large fundraisers, the first for the Foundation's founders' son, Idan Zablocki's 8th Transplantversary which raised over $16,000, and the second in the UK for the family of a child, Alfie, who passed away a few years ago, organized their annual Alfie McGurn Lego Cup Golf Day Fundraiser raising over $11,000 in Alfie's memory for the Foundation.

Hyper IgM Swag Store

Hyper IgM has launched a branded swag store on Bonfire:

Hyper IgM Social Media

Our social media channels have recently been revamped with weekly content on Instagram and Facebook, including Tuesday posts breaking down information about Hyper IgM and PI into bite-size content easy to digest and Faces of Hyper IgM Fridays, showcasing members of our community. Follow us on Instagram @hyperigm or Facebook www.FB.com/HyperIgMFoundation/

Ongoing Clinical Studies

C-SIDE

The purpose of this trial is to test the efficacy of regimens containing busulfan targeted to 30 mg*h/L vs 60 mg*h/L in patients with X-linked SCID, JAK3 SCID, RAG1/RAG2 SCID. To date 13 IL2RG/JAK3 and 10 RAG1/RAG2 patients have been enrolled. The vast majority of patients have done very well with reconstitution of T cells and varying degrees of humoral immune reconstitution. We encourage all sites to be sure to offer enrollment on CSIDE to every eligible patient. If you have any questions, please email:

Sung-Yun Pai, MD (sung-yun.pai@nih.gov), **Mike Pulsipher** (mpulsipher@chla.usc.edu), and **Janelle Olson** (jolson@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).

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 visit:

https://clinicaltrials.gov/study/NCT03812263

Ongoing Clinical Studies

Clinical Trial at Mayo for LADII Deficiency

A Phase 3 Randomized, Double-blind Crossover Study to Assess the Efficacy and Safety of AVTX-803 in Subjects with Leukocyte Adhesion Deficiency Type II (LAD II; also called SLC35C1-CDG) enrolled the first patient at Clinical Genomics, Mayo Clinic Rochester.

The study enrolls LAD II patients older than 6 months receiving dietary supplements containing L-Fucose and randomizes patients into a two-period study with a withdrawal phase (placebo) and treatment phase (L-Fucose) with crossover. Patients with abnormal sialyl-Lewis antigen and a history of recurrent infections are eligible for the study. Please see the link for more information.

For more information, visit https://clinicaltrials.gov/study/NCT05462587

A Study of Mavorixafor in Participants With Severe Congenital Neutropenia and Chronic Neutropenia Disorders

This Phase 1b study will determine the safety and tolerability of mavorixafor in participants with severe chronic idiopathic neutropenia (CIN) and selected congenital neutropenia disorders.

Website: https://www.x4pharma.com/patients/chronic-neutropenia/

Anti-c-KIT (JSP191) Transplant Protocol

This Phase I study is 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, monoclonal antibody that targets human CD117.

For more information, visit https://clinicaltrials.gov/study/NCT02963064.

Protocol Updates

Severe Combined Immunodeficiency (SCID) – 6901/6902/6907

Protocols 6901 and 6902 are closed to new enrollments and are in the process of final data collection and cleaning. Several papers incorporating data from these legacy protocols are nearing completion, including manuscripts describing outcomes of unrelated cord blood HCTs, matched sibling HCT, racial/ethnic disparities in outcomes, neurodevelopmental outcomes, and differential outcomes by the trigger for diagnosis. Other manuscripts in the works include genotype specific papers (on Artemis, IL2RG/JAK3, and CD3D), outcomes of 2nd transplants and boosts, and the entire 6901 dataset, as well as several other ideas. The SCID working group is always happy to hear new proposals for potential analyses to be performed on this rich dataset.

Protocol 6907 is now open at most centers and is actively accruing all available SCID patients, both newly diagnosed and previously treated, using its carefully-designed case report forms to assemble the premier database on outcomes of patients with SCID. Please continue to enroll patients!

Chronic Granulomatous Disease (CGD) – 6903/6908

The CGD team is actively working on several manuscripts, including umbilical cord blood and HLA-mismatched donor HCT, second HCT, and several microbiome papers.

Protocol 6903 has closed to enrollment, and the dataset is actively being cleaned. Thank you everyone for responding to queries and completing data entry for patients enrolled to 6903. Protocol 6908 has been activated or is near activation at the majority of PIDTC centers. Reach out to the CGD program managers (lisa.lim@ucsf.edu and jessica.ni@ucsf.edu) with any questions related to 6903 data completion or 6908 enrollment.

Wiskott–Aldrich Syndrome (WAS) – 6904

6904 WAS patients can be rolled over onto the 6906 PIRD Protocol. Look out for an email containing a list of eligible rollovers!

Primary Immune Regulatory Disorders (PIRD) – 6906

The PIRD Protocol currently has 31 activated sites and anticipates that the REDCap database will open in the next few weeks. We enrolled 36 patients over the past fiscal year and have confirmed their eligibility for reimbursement.

PIDTC: Fall/Winter 2024

Planned opening of 6906 REDCap Database

March 10-13th: PIDTC Annual Workshop 2025

February 12th-16th: TCT Meeting

February 28th to March 3rd: AAAAI Annual Meeting

Nov. **Dec.** **Jan.** **Feb.** **Mar.**

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

Got announcements?
Email: rafael.ricon@ucsf.edu