A patient who is enrolled in the Neurodevelopmental Outcomes Study enjoying ice cream.
Greetings from Drs. Jennifer Puck, Chris Dvorak, and Elie Haddad, Multi-PIs

Hello PIDTC Members,

We are pleased to announce that the onboarding and site activation process is now in progress for the PIRD (6906), SCID (6907), and CGD (6908), protocols – read more details on page 12.

We have started the planning for our PIDTC Education Day – Scientific Workshop which will be hosted by Dr. Rebecca Marsh in Cincinnati. The Education Day will be held on April 17th to April 18th and the Scientific Workshop will be held on April 18th to April 20th, 2023.

We wish everyone a safe and fun-filled holiday spent with family and friends. Happy Holidays to all!

With appreciation,
Jennifer, Elie, and Chris

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ESID and IPOPI Meetings Gothenburg, Sweden

Heather Smith of SCID Angels for Life attended the European Society for Immunodeficiencies (ESID) 2022 as well as the International Patient Organisation for Primary Immunodeficiencies (IPOPI) meetings in Gothenburg, Sweden. While there she attended several exciting sessions involving newborn screening for SCID in other countries and she presented the SCID Compass Toolkit for competition at the IPOPI Global Patient's Meeting. Heather was delighted to meet with Nathalie Ljungback, a SCID mom from Sweden who had never had the opportunity to meet another SCID parent.

RARE Revolution Magazine

RARE Revolution Magazine highlighted Heather Smith and SCID Angels for life in its most recent edition. RARE Revolution aims to bring about a dramatic and wide-reaching change in conditions and attitudes for the rare disease community. The article on SCID Angels begins on page 37 with a look at what SCID Angels does and whom they serve. The theme continues on page 41 with an engaging article on Aidan Walsh, a 2021 recipient of the SCID Angels Aisha Chaudhary Educational Scholarship. The reader can gain insight into Aidan’s own feelings regarding his rare disease while tackling college amidst a pandemic. 


For more information about SCID Angels for Life click here: http://www.scidangelsforlife.com/
FDA (Food and Drug Administration) CBER (Center for Biologics Evaluation and Research) OTAT (Office of Tissues and Advanced Therapies) Patient Focused Drug Development Listening Meeting - Patient Perspectives on Gene Therapy Products

On November 15th both Heather Smith and Barb Ballard spoke during the public comment period for the FDA CBER OTAT Listening meeting regarding Patient Perspectives on Gene Therapy Products.

Heather spoke during the section on Patient and caregiver understanding and expectations of gene therapy risks and benefits highlighting her son’s own experience and personal concern regarding suspensions of clinical trials. There is a need to rapidly inform patient participants of the potential risks or concerns regarding such a suspension, before it’s made public and posted on clinicaltrials.gov.

Barb spoke during the section on Patient and caregiver involvement in clinical study design and execution highlighting a growing concern regarding the economic viability of bringing cellular therapies to market for rare disorders. She broached the question: when the therapy is unlikely to be transferable to a more lucrative market, what does the FDA propose? How would they prevent industry partners from abandoning those patients when the therapy proves to be too expensive to develop through the FDA approval process, to bring the successful treatment to market for those with a rare disease?

New Newsletter to be launched
SCID Angels will be starting up a new quarterly newsletter in 2023. Their goal will be to produce articles of interest not only to patients and their families, but also to all SCID stakeholders, including physicians, nurses, researchers, students, and industry partners. More information will be forthcoming on how to sign up.

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

Jeffrey Modell Foundation:

- Translational Research Program
  - The Jeffrey Modell Foundation awarded two grants for a total of $400,000 for Cycle 10 of the Translational Research Program.
  - Cycle 11 of the Translational Research Program will open in early 2023.
  - To learn more about the focus and topic of this grant, click on this link: https://info4pi.org/medical/

- Genetic Sequencing Program
  - The Jeffrey Modell Foundation presented at the RDCRN Fall Virtual Meeting regarding the latest publication from their Genetic Sequencing program.
  - Website link to publication: https://www.frontiersin.org/articles/10.3389/fimmu.2022.906540/full

For more information about JMF click here: https://www.info4pi.org/
Prioritizing Self-Care

Felicia Morton, founder of the CGD Association of America, is a huge advocate for CGD caregivers and other members of the CGD community to prioritize self-care. One way she is promoting self-care and health is by obtaining her yoga teacher training certification. We look forward to her teaching a yoga class to the attendees of the PIDTC Annual Scientific Workshop 2023.

If you want to read more about self-care and health in the CGD community, see the following links to articles Felicia wrote:


For more information about CGDAA click here: [https://cgdaa.org/](https://cgdaa.org/)

WAS Foundation Updates

- Sumathi Iyengar M.D., founder of the WAS Foundation, will be attending the FDA Meeting which is scheduled for February 3rd, 2023.
  - Dr. Don Kohn, UCLA, will also be speaking at this meeting, along with WAS patients.

- The Carrier Survey is closed, and the primary analysis is complete. The writing of the manuscript is in progress.

For more information about the WAS Foundation click here: [http://www.wiskott.org/](http://www.wiskott.org/)
IDF Grant Program Accepting Applications

The Immune Deficiency Foundation (IDF) is currently accepting applications for the IDF Research Grant Program. The program provides one-year ‘seed’ grants in the range of $25,000 to $50,000 to support well-defined research projects that have a specified benefit for improving the treatment, health, disease management, or diagnosis of people with primary immunodeficiencies (PID). Eligibility is limited to those currently residing in the U.S. The deadline to apply is February 28, 2023, and applicants will receive notification in April 2023. IDF is encouraging investigators who have an interest in pursuing a career in PID to apply. More information on the program and the application form are available at: https://primaryimmune.org/research-grant.

IDF’s new office boasts convenience, flexibility, savings

- The Immune Deficiency Foundation (IDF) has moved its headquarters to Hanover, Maryland. The new office location has improved cost savings and is conveniently located for the IDF employees and community.

- To learn more about the new office click on this link: https://primaryimmune.org/news/idf%E2%80%99s-new-office-boasts-convenience-flexibility-savings

For more information about IDF click here: https://primaryimmune.org/
Research Grants provided by the Hyper IgM Foundation in November 2022:

The Hyper IgM has awarded $40,000 in seed grant funding to two researchers working on Hyper IgM Syndrome in 2022. These grants are to accelerate work focused on improving the treatment, quality of life, and long-term outlook for patients with Hyper IgM. Awardees are Dr. Cheng Zhu from the Georgia Institute of Technology, studying Dysmechanoregulation of CD40-CD40L interaction, signaling, and function by Hyper IgM mutations, and Dr. Junghee Shin from Yale University School of Medicine, studying CD8 T-cell alteration in CD40 ligand deficiency.

2023 Grant Announcement:

The Hyper IgM Foundation is proud to announce the availability of $100,000 in grant funding for researchers interested in the advancement of a cure for Hyper IgM Syndrome. Special consideration will be given to well-defined projects focused on new approaches for curative treatment or significant improvement of existing treatments for Hyper IgM Syndrome aimed at reducing mortality and morbidity and improving quality of life. Grant applications for 2023 are due June 15th, 2023. For more information about grants, and submissions see our Research Grants page.

All inquiries should be submitted to the Hyper IgM Foundation by contacting research@hyperigm.org. Hyper IgM Foundation 215 W101st Street. Suite 7B New York, NY 10025 United States of America

For more information about Hyper IgM click here: https://hyperigm.org/

Thank you to all our PAGS!
Welcome to the newest member of the PIDTC Steering Committee, Dr. Rebecca Marsh! Dr. Marsh has been a longstanding member of the PIDTC community. She is currently the 6903 and 6908 CGD Protocol PI for the Cincinnati Children’s Hospital Medical Center. She was the first author of the PIDTC publication on improvement of CGD inflammatory bowel disease following allogeneic transplantation (J Clin Immunol, 2019; Oct;39(7):653-667). She will also be hosting the PIDTC Education Day – Annual Scientific Workshop in April 2023. Dr. Marsh is a wonderful addition to the Steering Committee, and everyone is looking forward to working with her further.
Breaking Barriers: Pioneering of Artemis-SCID Gene Therapy

This video relates the story of the first patient to undergo Artemis-SCID Gene therapy in the UCSF trial.

Link to YouTube video: https://www.youtube.com/watch?v=pL5U9pqNK2E

Infant Gene Therapy is a Breakthrough for Artemis-SCID Patients

Artemis SCID Gene Therapy publications in the New England Journal of Medicine, December, 2022:


Drs. Mort Cowan and Jennifer Puck led the UCSF gene therapy team.

To learn more about this study and the publication, click on this link: https://www.ucsf.edu/news/2022/12/424476/infant-gene-therapy-breakthrough-artemis-scid-patients
Other New Publications

We are pleased to announce four new PIDTC publications, including two primary PIDTC papers by Chris Dvorak et al. updating the diagnostic criteria for SCID, and two affiliated papers completed with PIDTC support. Congratulations to all the authors and everyone involved in creating these resources! Lay summaries and links to view these papers are below.

“The diagnosis of severe combined immunodeficiency: Implementation of the PIDTC 2022 Definitions”
- Link to paper: https://www.jacionline.org/article/S0091-6749(22)01478-6/fulltext
- Lead Author: Christopher Dvorak, MD

In 2014, the Primary Immune Deficiency Treatment Consortium (PIDTC) published the criteria developed for diagnosis and classification of severe combined immunodeficiency (SCID) patients enrolling in their protocols. Since then, newborn screening for SCID has become increasingly common, as well as more rapid and less costly genetic sequencing. In light of these advances, the PIDTC updated their definitions in 2022. In this study, researchers compared the performance of the original vs. updated definitions. The team analyzed 379 patients who had been proposed for enrollment in a PIDTC prospective protocol that follows SCID patients longitudinally, focusing on the ability to distinguish patients with various subtypes of SCID. Results showed that the 2022 definitions described SCID and its subtypes more precisely than the 2014 definitions. Authors state that these updates can facilitate improved analyses of SCID characteristics and outcomes.

The diagnosis of severe combined immunodeficiency (SCID): The Primary Immune Deficiency Treatment Consortium (PIDTC) 2022 Definitions”
- Link to paper: https://www.jacionline.org/article/S0091-6749(22)01479-8/fulltext
- Lead Author: Christopher Dvorak, MD

Severe combined immunodeficiency (SCID) is a severe form of primary immune deficiency characterized by extreme weakness or absence of immune system function, manifesting at birth. SCID results from abnormalities in responses of both T cells and B cells, which are types of white blood cells needed for immune system function.

In 2014, the Primary Immune Deficiency Treatment Consortium (PIDTC) published criteria used to qualify patients for enrollment in their prospective and retrospective studies of SCID. In this article, researchers have updated the criteria, incorporating contemporary diagnostic approaches, including increased availability of gene sequencing as well as widespread population-based newborn screening for SCID. This article proposes that these criteria be used to establish a diagnosis of SCID in 2022. Authors state that the new definitions allow for more precise categorization of patients with SCID and atypical or leaky SCID. However, the definitions do not imply a preferred treatment strategy.
“HSCT using carrier donors for CD40L deficiency results in excellent immune function and higher CD40L expression in cTfh”
- Lead Author: Shanmuganathan Chandrakasan, MD

CD40 ligand (CD40L) deficiency is a rare X-linked immunodeficiency disorder that leads to recurrent bacterial infections. Not much is known about the immune status of CD40L-deficient carriers, or possible outcomes of hematopoietic stem cell transplantation (HSCT) using these carriers as donors for CD40L-deficient patients.

In this study, researchers evaluated the immune profiles of 7 carriers—including 4 who acted as HSCT donors for family members with CD40L deficiency—and characterized their HSCT outcomes. Results show that most carriers with CD40L deficiency have a normal immune profile with differential high CD40L expression in circulating T follicular helper (cTfh) cells, which are critical for immune response. The team also reported excellent long-term immune reconstitution in CD40L-deficient patients after HSCT using carrier donors.

Authors state that HSCT using X-linked carriers seems to be safe and results in excellent outcomes. Authors also note that this decision should be individualized and driven by the biology of the disease.

Note: First author Shanmuganathan Chandrakasan, MD, received the 2017 PIDTC Fellowship Award.

“A Spot of Good News: Israeli Experience With SCID Newborn Screening”
- Author: Jennifer Puck, MD
Protocol Updates

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

Updates:
Congratulations to SCID Working Group who recently published two publications! Further details about these publications can be viewed on page 10. Thank you to our Protocol PIs, Drs. Chris Dvorak, Elie Haddad and Jen Heimall for leading the SCID team, finalizing the new 6907 protocol and overseeing the numerous manuscripts that are in the works.

The consents are UCSF IRB–approved and we began the process of onboarding many of our PIDTC sites in January of 2022. We currently have thirteen activated sites.

Goals: Do not miss enrolling your Prospective SCID patients into 6901 (while awaiting onboarding into 6907) during the DMCC transition period! Enter your eligibility data into the CRFs in the South Florida database and then email Elizabeth Dunn at Elizabeth.dunn@ucsf.edu, to finalize patient eligibility.

Chronic Granulomatous Disease (CGD) – 6903/6908

Updates: The 6908 Protocol has been approved by the UCSF IRB. The CGD Working Group plans to submit the Overall Paper before the end of the year. The most recent publication from the 6903 data set is the “Granulocyte Transfusions in Patients with Chronic Granulomatous Disease Undergoing Hematopoietic Cell Transplantation or Gene Therapy” with Dr. Dani Arnold as the first author. (Link to paper: https://pubmed.ncbi.nlm.nih.gov/35445907/)

Enrollment: Do not miss enrolling your Prospective CGD patients into 6903 (while awaiting onboarding into 6908). 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 analysis and manuscript writing for the second 6904 paper with a larger “N” of patients. We want to welcome Sravya Dammalapati as one of the new statisticians for the 6904 WAS Protocol. She will be assisting Dr. Ruta Brazauskas with the data analysis.

Primary Immune Regulatory Disorders – 6906

Updates: The 6906 Protocol has been approved by the UCSF IRB. The PIRD team is led by Protocol PIs Drs. Troy Torgerson, Alice Chan and Rosa Bachetta. Plans for networking with Adult Immunology providers are underway to capture many adults with PIRD that might otherwise be missed.

Neurodevelopmental Outcomes Study - 6909

The 6909 Protocol has enrolled 49 patients from 14 sites as of mid-December. With an approval from the funding agency (HRSA), the study has been extended to a final enrollment date of July 31, 2023.
Ongoing Clinical Studies

PIDTC/IEWP
STAT1 GOF HSCT STUDY - Now open!

On behalf of the PIDTC 6906 Project Working Team and in collaboration with the IEWP, we are collecting data to assess the outcomes of patients with STAT1 Gain of Function of any age who have undergone hematopoietic cell transplantation since 2010 including survivors and non-survivors with any length of follow-up. Data collection will be performed via an electronic CRF (Castor software).

This project serves to update the report written by Jen Leiding and Troy Torgerson in 2018. Given that these patients will also likely be eligible for PIDTC Protocol 6906, we encourage you to save the data gathered for this sub-project so as to not duplicate efforts for entry of the patient onto 6906 if eligible.

Inclusion criteria are STAT1 GOF patients of any age post HSCT (survivors and non-survivors alike). STAT1 mutations should be previously described as GOF or confer GOF in an in vitro model.

Data will be collected via eCRF. The CRF can be completed on a rolling basis (information is saved as completed) and will be open until February 28, 2023.

For further information and access to the eCRF, please contact Jennifer Leiding at jleidin1@jhmi.edu, Emmeline Buddingh E.P.Buddingh@lumc.nl, or Catharina Schuetz Catharina.Schuetz@ukdd.de
CSIDE is open to enrollment at 48 sites and 24 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 Janelle Olson (jolson@nmdp.org).

As you remember, 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. You can also feel free to contact Sung-Yun or Mike with any questions on potentially eligible patients, and/or bring cases for discussion to the monthly PI meetings.

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).

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 Mancarz, MD (ewelina.mancarz@stjude.org), Aleksandra Petrovic, MD (Aleksandra.Petrovic@seattlechildrens.org), or Mort Cowan, MD (Mort.Cowan@ucsf.edu).
Lentiviral gene transfer for SCID-X1 with low dose targeted Busulfan conditioning

This trial is open and enrolling at Boston Children’s Hospital, Mattel Children’s Hospital UCLA, Cincinnati Children’s, Children’s Hospital of Atlanta, 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 (sungyun.pai@nih.gov); Boston PI: Susan Prockop (susan.prockop@childrens.harvard.edu)
Los Angeles PI: Donald Kohn, MD (dkohn1@mednet.ucla.edu); Atlanta PI: Shanmuganathan Chandrakasan (shanmuganathan.chandrakasan@emory.edu)
Cincinnati PI: Sharat Chandra (sharat.chandra@cchmc.org); Sponsor: David A. Williams, MD (david.williams2@childrens.harvard.edu).

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).

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 UCLGOSH (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-clinical-trial-for-health-care-providers/
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. The anticipated enrollment is up to 25 participants.

For questions regarding the trial, please email clinicaltrialinfo@x4pharma.com or call 857-529-5779.

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

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 enrols LAD II patients older than 6 months receiving a dietary supplement containing L-Fucose, and randomizes patients in to a two-period study with a withdrawal phase (placebo) and treatment phase (L-Fucose) with crossover. Patients with abnormal sialyl-Lewis antigen and history of recurrent infections are eligible for the study. Please see the attached study design summary and link for more information.

Website: https://clinicaltrials.gov/ct2/show/NCT05462587?term=NCT05462587&draw=2&rank=1

For questions regarding the trial please contact Senior Program Coordinator, Kaitlin Schwartz (email: Schwartz.Kaitlin@mayo.edu) or call 507-293-9114.
PIDTC: Winter 2022 / Spring 2023

January

Ed Day Application Deadline: January 15th

February

ASTCT & CIBMTR (Tandem) Meeting: February 15th – 19th

AAAAl Meeting February 24th – 27th

Protocol 6907 version 2.0 to be implemented

March

April

Education Day: April 17th & 18th

Annual PIDTC Scientific Workshop: April 18th – April 20th

January February March April

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

Got announcements?
Email: kiana.soriano@ucsf.edu