Primary Immune Deficiency Treatment Consortium

NEWSLETTER

Oct 2019 | Issue 10

Meet UCSF's Riley (Page 2)

IN THIS ISSUE

Greetings from Jennifer Puck and Don Kohn, PIDTC Co-PIs!

Five more years, three new protocols, two Co-PIs and one amazing consortium with the shared goal of improving the lives of people living with primary immunodeficiencies. We extend a huge thanks to everyone for helping secure funding for PIDTC!

This grant cycle, we introduce Primary Immune Regulatory Disorders (PIRD) to our list of diseases studied and look forward to collaborating with our partners at the newly funded Cincinnati DMCC.

With appreciation,
Jennifer and Don

PIDTC is refunded for another 5 years!

PIDTC patients!

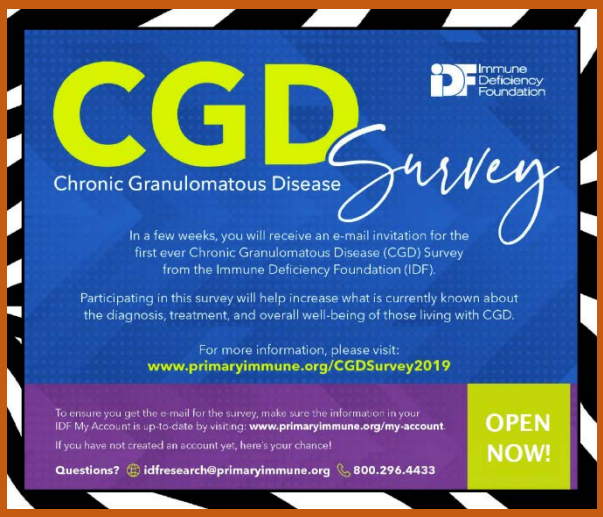
From cover and above: Riley Brown is UCSF's energetic and loveable 6 year who has been treated for SCID. Photo credit goes to her mother, Alissa, who photographs SCID families and other pediatric families at hospitals in the Bay Area. Her organization is The Mark Makers (www.themarkmakers.org).

X-SCID patient, Taylor Dahley, enjoyed a Dream Vacation cruise to Alaska last spring with his parents, Heather and John Smith, before receiving gene therapy at the NIH this past July.

Friends Michael Knott and Jason Wu connected with each other at the IDF Conference this past June!

The Immune Deficiency Foundation (IDF)

Attention Patients IDF's CGD Survey



The first-ever Chronic Granulomatous Disease (CGD) Survey from the Immune Deficiency Foundation (IDF) is now open! Developed with immunologists who are experts in primary immunodeficiency diseases, including CGD, this survey aims to learn more about how CGD affects individuals' lives, including diagnosis and treatment, along with overall well-being and quality of life. Participating will help increase what is currently known about CGD.

Left: Email announcement postcard to give to patient families.

Participate to Win!
You can be eligible to win an Amazon eGift Card. When you complete this survey, your household will be entered into a raffle to win either a $25, $50, or $100 Amazon.com eGift Card. Your survey must be completed no later than December 15, 2019 in order to be eligible. The winning households will be notified two weeks after the survey closes.

Although completing this survey is voluntary, it is extremely important to the CGD community. Be assured that all information is safe, confidential, and will be de-identified.

If you would like to participate or have any questions about this survey, please contact IDF at: idfresearch@primaryimmune.org or 800-296-4433.

IDF Seeks SCID Experts!

Immune Deficiency Foundation Seeks Healthcare Provider Experiences and Needs Related to SCID

The Immune Deficiency Foundation (IDF) requests your participation in the Severe Combined Immunodeficiency (SCID) Needs Assessment Survey for Healthcare Providers. IDF has partnered with the Association of Public Health Laboratories (APHL) and RTI International to develop a program called SCID Compass to address education, support, and long-term outcomes for children with SCID in rural and underserved populations. Whether you have treated a patient with SCID or not, this survey seeks your experiences or views about delivering care for a child with SCID. This information will be critical for the development of resources to support the needs for current and potential healthcare providers for SCID. The online survey can be found at **www.surveygizmo.com/s3/5243644/SCID-Provider-Survey-Experts.**

The survey should take approximately 10 minutes to complete. All information provided is confidential. If you have any questions about this survey, please contact the SCID Compass Program Manager at scidcompass@primaryimmune.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 $4 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.

Welcome to PIDTC!

The Hyper IgM Foundation

PIDTC recently welcomed the Hyper IgM Foundation to collaborate with our Patient Advocacy Groups! The Hyper IgM Foundation was founded in 2015 by Akiva and Amanda Zablocki whose seven-year-old son Idan was born with X-Linked Hyper IgM Syndrome. The Hyper IgM Foundation aims to improve outcomes and quality of life for all Hyper IgM patients and their families through promoting and supporting research, creating and providing educational tools for the Hyper IgM patient and medical communities, and creating a community to support Hyper IgM patients and their families as they undergo treatment and cope with this disease. The Foundation runs an active global support group with over 230 Hyper IgM families. The Foundation also provides seed grant funding for researchers interested in the advancement of a cure for Hyper IgM. In 2019, the Foundation announced $25,000 in grant funding in support of several research projects, including for (i) an X-Linked Hyper IgM Quality of Life study by Seattle Children's Hospital, (ii) a carrier study, and (iii) cutting-edge gene editing research at UCLA. To learn more about the Hyper IgM Foundation check out www.hyperigm.org or email akiva@hyperigm.org.

Above & bottom right: Hyper IGM families gather at the IDF June conference
Top right: The Zablocki family

Akiva Zablocki was recently profiled by the *Global Genes Rare Daily* about his organization's strategy, where he noted that: *"Our primary objectives are to find a cure for Hyper IgM Syndrome, to develop and enhance the current understanding of Hyper IgM, and to provide education and support to our families. We focus much of our resources on connecting with researchers and working with doctors to better understand our disease and drive research into finding a cure. Importantly, we have cultivated an international network of experts that can connect with our patients (even in the remotest of areas) and a rich online support group for our families."*

Above: Dr. Iyengar, Executive Director of the WAS Foundation, and her family.

Wiskott Aldrich Foundation

Congrats to Ami Shah, Mort Cowan and Sumathi Iyengar, whose WAS Quality of Life paper was recently accepted for publication into the *Journal of Clinical Immunology*! Thank you to our patient families who completed the survey to make this manuscript possible.

Coming soon: The WAS Foundation is teaming up with the Hyper IgM Foundation to create a survey for X-Linked carriers. For more information about the WAS Foundation, visit www.wiskott.org

The CGD Association of America e-newsletter!

Spread the word! **The Chronic Granulomatous Association of America (CGDAA)**, recently launched its first e-newsletter. To sign up for the e-newsletter, go to: https://conta.cc/2nK8t0m and click the "Join e-mail list" button in the upper right hand corner. CGDAA is a nonprofit organization committed to advocating on behalf of patients, carriers, and families by providing clear, accurate, and independent news and information about CGD and advancing CGD research. For more information, please visit: https://cgdaa.org or send an email to felicia@cgdaa.org.

Coming soon: The CGDAA and the PIDTC's CGD protocol working team are collaborating on a survey for X-linked CGD carriers. Once IRB approval has been obtained, we will be sending the survey out to patient families.

Thank you to our Patient Advocacy Groups for their continued support and collaboration!

Jeffrey Modell Foundation

THINK ZEBRA! Immune Deficiency Foundation

SCID Angels For Life Foundation

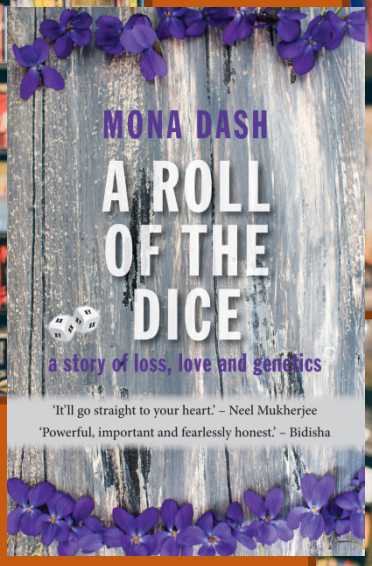
CGD

HyperIgM Foundation

SCID in the Press!

A Roll of the Dice: a story of loss, love and genetics
By Mona Dash

Check out this recently released book! Mona Dash is the mother of two X-SCID boys, one who died in India due to a lack of treatment, and another who is now 12 and was treated at Great Ormond Street Hospital in London. This book is published by Linen Press UK and the foreword is written by Professor Bobby Gaspar, a leader in SCID treatment and pioneer in gene therapy.



Above: Author Mona Dash

Dash's son, Krish (*middle right*) has been treated for SCID by Dr. Gaspar in London (*upper right*).

The Sky Is Pink feature film

This movie opened Friday, October 11th for a limited time in 25 countries. This film is a true story about a family who had two children born with SCID. It's told through the eyes of their daughter, Aisha, who was diagnosed with SCID early because of the death of her older sister, Tanya. Aisha was transplanted very young and thrived into adolescence. However, as a teenager she developed pulmonary fibrosis attributed to the conditioning chemotherapy received as an infant and that eventually took her life.

From Heather Smith of SCID Angels for Life *"The film portrays an accurate picture of what it's like to be the mother of a child with a life-threatening condition…you will go to the ends of the earth for your child. The struggle is real; uprooting your family, the isolation process for the family, the mother, who's usually the primary caregiver, and what it means to be alone and isolated from the outside world."*

CAREER ENHANCEMENT

Research Training Grant 2020

Deadline: March 2, 2020

Award Amount: $25,000 salary/consumables support.

The purpose of the award is to encourage **research in transplantation, gene therapy or outcomes of primary immune deficiency therapies**; however, applications may be on any aspect of primary immune deficiencies. Contact Catherine.chang@ucsf.edu for the application and send inquiries to Dr. Kate Sullivan sullivank@email.chop.edu or Dr. Elie Haddad elie.haddad@umontreal.ca.

Apply now & forward to anyone at your site, especially trainees!!

Previous Awardees:

Research Training Grant 2018-2019:
Kathryn Bradford (UCLA): TACI Gene Editing for CVID

Pilot Project 2018:
Don Kohn (UCLA): Gene Therapy for IPEX

PILOT PROJECT

Pilot Project 2020

Deadlines: December 2, 2019 (optional deadline: Nov. 15, 2019 for letter of intent)

Award Amount: $50,000 Direct Costs per year. Upon demonstration of sufficient progress during the first 8 months, recipients may compete for a second year.

Pilot Project Topic: Applications are now being solicited for Pilot Project proposals in the area of Primary Immune Regulatory Disorders (PIRD), a major component of the 2018 PIDTC competitive renewal application. The new PIDTC PIRD protocol will focus on defects in regulatory T cells (Treg) and impaired regulation of the immune effector cell axis. **The PIDTC is targeting this round of pilot funding for a PIRD-related project. Junior faculty are encouraged to apply and will receive special consideration!**

Contact: For guidelines, timeline, application submission and more information, contact Catherine.Chang@ucsf.edu

Selection Committee Chair: Dr. Pai at Sung-Yun.Pai@childrens.harvard.edu

Kathryn Bradford, UCLA Heme-Onc Fellow, received the 2018-2019 Research Training Grant to fund her project: TACI Gene Editing for Common Variable Immunodeficiency. The project aims to create models of TACI deficiency with subsequent site-specific gene insertion. Currently, she is optimizing the conditions in B cell cancer lines (Raji, Ramos) before exploring testing in hematopoietic stem cells (HSCs). "*Thank you PIDTC for making this award possible. I very much appreciate the opportunity to pursue this project through this funding!*"

ANNOUNCEMENTS

Got announcements? Contact Katie at Catherine.chang@ucsf.edu

2020 PIDTC Workshop- Save the Date!

Where: Asilomar Conference Grounds in Pacific Grove, CA
When: April 28-30, 2020 (Education Day April 27-28)
Hosted by: Dr. Ami Shah from Stanford University

The Israeli Wiskott Aldrich Syndrome Association

Call for Proposals! The Israeli Wiskott Aldrich Syndrome association (IWASA) announces its 1st public international call for the submission of research proposals to be granted in 2020. IWASA will grant seed money funding for a maximum of two projects, for up to amount of maximum ***$100,000 per project***, with a special emphasis on basic science research, especially in regard to platelets and WAS Protein. Contact Amir Kedar, President of the Israeli WASA Association, for more information and the letter of intent at akedar@kedmor.co.il. **Due November 15th.**

Patient with novel severe (auto) inflammatory skin condition: compound heterozygous mutations in the gene CTNNA3

Dear Colleagues,

I am writing to inquire if any of you might have a patient similar to mine. The patient is a 10-year-old boy with a lifelong history of severe skin disease with large plaque-like lesions, some resembling psoriasis and others more sclerodermatous. He also has chronic inflammation of the eyelids and oral cavity/tongue. He does not have recurrent fevers. He has had genetic testing that revealed compound heterozygous mutations in the gene CTNNA3, which encodes alpha-T-catenin. Mutations in this gene have previously been associated with a cardiac arrhythmia, but he does not have that phenotype.

We are trying to determine in the laboratory if the identified mutations are disease-causative. I am interested in collaborating with anyone who has a patient with a similar chronic inflammatory skin phenotype with mutations in CTNNA3 or other catenin-encoding genes. If you do, I will be happy to provide more detailed information.

Bryce A. Binstadt, M.D., Ph.D., University of Minnesota Medical School
E-mail: binstadt@umn.edu

Attention CRCs/CRAs!

- ☐ For non single-IRB centers, reminder to modify your ICFs for 6901, 6902, 6903 to reflect the change in the database location; refer to memo released to sites on 10/9/19
- ☐ Eligibility determinations for all protocols will be done over email using paper CRFs during the DMCC transition period. **We especially do not want to miss any prospective** patients!

Protocol Updates-6901, 6902, 6903, 6904

Severe Combined Immunodeficiency (SCID) - 6901/6902

Updates: Congrats to Monica Thakar for submitting PIDTC's first 6901/6902 combination abstract to the 2020 TCT meeting! Thank you to our PIs **Chris Dvorak**, **Elie Haddad** and **Jen Heimall** for leading the SCID team on cleaning up the 6901 and 6902 datasets, finalizing the new 6907 protocol and overseeing the numerous manuscripts that are in the works. We thank our outstanding statistician team, led by **Brent Logan,** for their efforts pulling together this data. Lastly, be on the lookout for data cleanup queries from **Katie Chang**.

Goals: Do not miss enrolling your 6901 Prospective SCID patients during the DMCC transition period! Email Elizabeth Dunn and Katie Chang at Elizabeth.dunn@ucsf.edu, Catherine.chang@ucsf.edu to finalize patient eligibility via email. For 6902, October 31st is the last day to enroll 6902 Cross Sectional patients for manuscript inclusion. As a reminder, these cross sectional visits can be done over the phone.

Chronic Granulomatous Disease (CGD)-6903

Updates: The CGD is thrilled to begin finalizing the 6908 protocol which will be led by Co-PIs **Jen Leiding**, **Harry Malech**, and **Elizabeth Kang.** The entire 6903 team, especially **Dani Arnold, Kanwal Malhi, Rebecca Marsh and Suhag Parikh** have been busy cleaning the 6903 dataset in preparation for an overall manuscript. Thank you to our statisticians **Rachel Wu** and **Brent Logan** for all their efforts!

Enrollment. The 6903 CGD Prospective and Cross Sectional Arms are still open to patient enrollment. **We especially do not want to miss prospective patient enrollment during the DMCC transition period!

Wiskott-Aldrich Syndrome (WAS)-6904

Updates. Thank you to our fantastic 6904 PI, **Lauri Burroughs** who has been a PIDTC champion leading the WAS team the last five years. Although the protocol closed to enrollment and data collection on 8/31/2019, the WAS team is working on data clean-up, data analysis and manuscript writing for the 6904 overall paper. We especially want to thank investigators **David Shyr**, **Blachy Davila, Jessie Barnum**, and **Ami Shah** and our talented statisticians **Ruta Brazauskas**, and **Joy Liu**. In the new grant cycle, WAS patients with dysregulated immunity will be incorporated into PIDTC 6906.

PIDTC Protocols

New protocols!

Rare Disease	2014-2019 (current)	2019-2024
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"

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 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@childrens.harvard.edu); Los Angeles PI: **Donald Kohn, MD** (dkohn1@mednet.ucla.edu); Sponsor: **David A. Williams, MD** (david.williams2@childrens.harvard.edu).

UCSF Artemis SCID Gene Therapy

In this research study, children with ART-SCID receive a treatment called "lentiviral gene transfer," also called "gene therapy." This method inserts a normal copy of the DCLRE1C 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 ART-SCID so that functioning T and B lymphocytes can develop.

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).

CSIDE

CSIDE is open to enrollment 12 sites and 6 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@childrens.harvard.edu), **Mike Pulsipher** (mpulsipher@chla.usc.edu), and **Jenny Vogel** (jvogel@nmdp.org).

UCSF / Stanford Transplant Anti-c-KIT Transplant Protocol

This Phase I study is a single arm, open label, dose escalation trial being conducted at 2 centers: UCSF Benioff Children's Hospital and Lucile Packard Children's Hospital at Stanford. 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 **Julie Shizuru, MD** jshizuru@stanford.edu), or **Christopher Dvorak** (Christopher.dvorak@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 Mamcarz, MD** (ewelina.mamcarz@stjude.org), **Aleksandra Petrovic, MD** (Aleksandra.Petrovic@seattlechildrens.org), or **Mort Cowan, MD** (Mort.Cowan@ucsf.edu).

Single IRB update

The goal of utilizing UCSF's sIRB for multi-site studies is to streamline the IRB review process, reduce duplication of effort and increase consistency of IRB determinations and approved study procedures. Additionally, the use of a central IRB for multisite studies has been addressed in the Common Rule Notice of Proposed Rulemaking (NPRM) and was mandated by the NIH on June 21, 2016, with an effective date of January 25, 2018.

Once our new protocols are finalized and approved at UCSF, we will use the IRB Exchange (IREX) platform by Vanderbilt to file all agreements and IRB-related documents. Sites will work directly with UCSF's IRB contact and PIDTC project management team to finalize onboarding and any IRB-related procedures. IREX offers training modules that we will distribute when we begin the process as well. www.irbexchange.org.

IREx IRB Reliance Exchange
YOUR SYSTEM SOLUTION FOR SINGLE IRB REVIEW

PIDTC: Fall Timeline 2019

Nov. 28: Happy Turkey Day!

Nov. 15: Pilot Project Letter of Intent due

Nov. 18: RDCRN Steering Committee in- person meeting

Dec 2nd: Pilot Project application due

Oct. 31: Last day to enroll 6902 cross sectional patients for manuscript inclusion

Nov. 15: Israeli WAS Foundation grant application due

Nov. 19: RDCRN Coalition of Patient Advocacy Groups (CPAG) in-person meeting

Dec or Jan: DMCC E-Reg binder will go live

Oct. 31: Trick or Treat!

Attention Families!

If you are a PID patient and would like to participate in a PIDTC study…

….join the **RDCRN PIDTC Contact Registry**!

The Contact Registry is a way for patients with primary immune deficiency and their family members to learn about PIDTC research studies and find out if they may be eligible to participate in one of our studies. Registration is voluntary and you may choose to withdraw at any time. There is no cost to join the Contact Registry. Visit the link to join today: *https://www.rarediseasesnetwork.org/cms/pidtc/Get-Involved/ContactRegistry*

PIDTC

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

Got announcements? Email: Catherine.chang@ucsf.edu

Farewell Tara!

We bid a bittersweet farewell to Tara Bani, who has been with the PIDTC for five years. Starting as a Clinical Research Coordinator, she loved working with the consortium so much that she pursued a masters in healthcare management and went on to oversee PIDTC operations as Senior Project Manager. During her time with the PIDTC, Tara was instrumental in implementing PIDTC's singleIRB, establishing SOPs and strengthening consortium communications. She is moving on to work in health-tech, but is excited to watch the continued success of the PIDTC! Congratulations Tara, we will surely miss you!