Since June, 2018, I have been trying to fill the shoes of our founding PI Mort Cowan, who is still very much involved in the PIDTC even after stepping down from this job. The biggest immediate task for all of us is the competitive renewal application for a 3rd cycle of funding from NIH. This renewal will be submitted by early October, 2018. It will be reviewed early in 2019 and we should hear about our score sometime next spring. Many of you have provided wonderful letters of support and commitment for this application—Thank you for your participation and enthusiasm!

The PIDTC has a lot of accomplishments to be proud of. For example, when we started in 2009, we had to generate the first definitions of severe combined immunodeficiency (SCID), leaky SCID and Omenn syndrome that did not rely on the clinical complications—failure to thrive, diarrhea, opportunistic infections – that were used before newborn
screening brought us healthy, but seriously at-risk infants in the newborn period. Now, 9 years later, we have enrolled over 1017 individuals with SCID, 372 with chronic granulomatous disease (CGD) and 306 with Wiskott-Aldrich syndrome (WAS). We have published well over 100 papers, with such important findings as recognizing early CD4 counts to be a good predictor of long-term immune reconstitution and proving that the inflammatory bowel disease associated with CGD resolves after allogeneic hematopoietic cell transplantation.

There are many more issues relating to PID that we can now tackle together. Here are just a few:

1) We will study an entire new group of diseases that we have termed Primary Immune Regulatory Disorders (PIRD);
2) We have generated our first prospective therapeutic trial and will soon start enrolling newborns with SCID to determine the lowest busulfan doses as conditioning for SCID transplants that will reliably result in B cell, as well as T cell reconstitution;
3) We will study the newly diagnosed SCID patients who do not have a known genetic etiology, currently about 7-10% of cases detected by newborn screening;
4) We will investigate ways to reduce the infection risk that remains in SCID babies despite diagnosis by newborn screening;
5) We will correlate intestinal microbiome composition with inflammatory bowel symptoms in CGD; and
6) We will incorporate quality of life assessments into all of our study protocols.

The new Research Funding Announcement, or RFA, for the Rare Disease Clinical Research Network, to which the Primary Immune Deficiency Treatment Consortium belongs, calls for strong relationships between the investigators and Patient Advocacy Groups (PAGs). In this area we are particularly fortunate to have thoughtful and energetic partners helping us understand primary immunodeficiency from the point of view of affected individuals and their families.

Thank you all,

Jennifer Puck, MD

“It is wonderful to have a career that bridges clinical medicine and discovery and I am most grateful to all the patients and families who have taught me by sharing their stories and becoming my partners.”

Check out the feature on Dr. Puck by the Clinical Immunology Society at:
https://clinimmsoc.org/CIS/About/Commitees/Women-in-Clinical-Immunology-Sciences/Jennifer-Puck-MD.htm
The 8th annual meeting was held May 9-11, 2018 in Philadelphia, PA. There were 128 attendees and 17 abstracts submitted to make this the largest of the PIDTC meetings thus far. This year represented the fourth Education Day component of the annual meeting. PIDTC meetings have a tradition of updating participants on the recent results generated by the consortium. This meeting represented a feast of results as many studies are now maturing.

During Education Day, 19 instructive cases were presented by trainees with the support of our fabulous mentors.

2019 WORKSHOP QUICK FACTS

Education Day: May 15 - 16, 2019
Workshop: May 16 –18, 2019
Hosted by: MSKCC
Location: The Warwick Hotel, New York, NY
Patient Advocacy Groups (PAGs)

PIDTC THANKS OUR PATIENT ADVOCACY GROUPS FOR THEIR CONTINUED SUPPORT AND COLLABORATION

Immune Deficiency Foundation (IDF) Receives Grant for Nationwide Screening and Education Program for Severe Combined Immunodeficiency (SCID): The Immune Deficiency Foundation (IDF), the national patient organization for people with primary immunodeficiency diseases (PI), recently announced they will be awarded a grant from the U.S. Health Resources and Services Administration (HRSA) to design and implement an advanced screening and education program for people with Severe Combined Immunodeficiency (SCID) in rural areas or underserved communities. The goal of the two-year program is to improve outcomes for infants with SCID detected through newborn screening by increasing awareness and knowledge about SCID, supporting state newborn screening programs, linking families, especially those living in medically underserved areas, to services and developing long-term follow-up strategies for infants identified through newborn screening.

Read more on the IDF website: https://primaryimmune.org/news/immune-deficiency-foundation-idf-awarded-4-million-hrsa-grant-nationwide-screening-and. *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.

The Jeffrey Modell Foundation will be celebrating 50 years since the first Bone Marrow Transplant at the end of September. They will honor Dr. Good, whose work has been influential in getting nearly all 50 states on board with New Born Screening.

50 years since the first Bone Marrow Transplant!
A query was done of patients with Wiskott Aldrich Syndrome (WAS) and X linked Thrombocytopenia (XLP) to assess the patient’s quality of life. Patients in the bone marrow transplant cohort (regardless of stem cell source) reported a better QOL compared to those who did not receive a bone marrow transplant. This is presumably because the survival following a BMT is > 70% and most patients are cured of their disease. These patients had less long term complications, such as bleeding episodes or emergency room visits. The patients and their families did report more worry and difficulty with communication surrounding issues related to their child’s health. This study was small but highlights the importance of quality of life studies for patients with WAS. Thank you to Dr. Ami Shah, who is working on this paper, and a special thank you to the Wiskott-Aldrich Foundation.

Survey of 100 SCID Families, SCID Angels for Life Foundation

This past workshop, Heather Smith, Co-founder of SCID Angels for Life Foundation gave a presentation on survey data she gathered from 100 SCID families. The information was collected in just four short days. It amazed her to see the enthusiasm that was expressed by the SCID community and their willingness to help provide this valuable information in an extremely short period of time. The information came from patients seen at centers all over the world, which made the data extremely valuable. The oldest patient to complete the survey was 42 years old. Workshop attendees were so impressed with her findings that PIDTC is working with Heather to gain the needed IRB approval in order to publish this data. Stay tuned for further updates on this project!
**Severe Combined Immunodeficiency (SCID) - 6901/6902**

**Updates:** Our PI’s Chris Dvorak, Elie Haddad, and the SCID team are working towards finalizing their protocols for the U54 renewal. Congrats to Chris Dvorak, whose 6901 Genetic etiology of the first 250 paper was recently submitted to *JACI*. Reviewers have responded favorably! Additionally, congrats to the 6902 team, who’s Strata A and B manuscript was submitted to *Blood*.

**Enrollment: 1017**

**Goals:** Please continue to enroll patients in 6902 cross sectional (must be at least 2 years post-transplant). We are aiming for 250 patients and are currently at 208. As a reminder, these cross sectional visits can be done over the phone. We also wish to remind sites to continue enrolling in the T cell exhaustion, CD 24, and T Cell O’Reilly study.

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Above: **Jake** (9) and **Tyler** (6) are brothers with X-Linked SCID being followed at Duke Children’s Hospital. They had a great summer visiting summer flowers and a boat excursion in Cape Cod!

(Left and Right): **Charlie** is 5 years post-bone marrow transplant for X-Linked SCID at Children’s National in Washington DC. He is doing great and had a fun-filled summer. You can find him with Transformers at the zoo, as well as enjoying Disney World.

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From the front page: **Joy Littlesunday** (now 5 yrs old) with her parents at UCSF Benioff Children’s Hospital following a bone marrow transplant for treatment of Artemis-SCID. Navajo families like Joy’s are at a far higher risk of SCID than the rest of the population. Their tribe now screens newborns for SCID.

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**PIDTC wants to hear about your patients!** If you would like one of your patients featured in next quarter’s issue, Please send a photo and a brief blurb to Katie at: Catherine.Chang@ucsf.edu
**Updates**: The 6903 CGD team has been busy preparing for the grant renewal. Their Inflammatory Bowel Disease paper is in progress and nearing completion. The group plans to submit the manuscript in the next coming weeks. Additionally, Liana Falcone is sequencing samples for her microbiome research study and plans to submit a paper this fall. Thank you to our PIs Elizabeth Kang and Harry Malech!

**Enrollments**: 374

**Deadlines**: Please continue to finish your CRFS. Stay tuned for deadlines.

**Goals**: Please continue to enroll patients in the Cross sectional arm and stay up to date on CRFs.

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**Updates**: The 6904 WAS team has done a fantastic job cleaning up the retrospective data for patients. The manuscript will feature 129 patients transplanted 2005-2015. We have lots of data to share! Thank you to all sites that have responded to queries this past year. Special thanks to statisticians, Ruta Brazauskas, Joy Liu, and Brent Logan and our PI, Lauri Burroughs!

**Enrollments**: 306

**Deadlines**: We closed enrollment for prospective and retrospective studies on September 1st, 2018. Please finish Retrospective CRFS by September 21st, 2018.

**Goals**: Please continue to register patients for 6904 Cross Sectional, through May 31, 2019!

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**RDCRN/DMCC Update**

It has been a busy year! In keeping with the NIH mandate that consortia start using a single IRB (sIRB), the DMCC’s OneIRB team has been acting as the coordinating center to assist PIDTC in transitioning all the sites to a sIRB, which is University of California – San Francisco. All four of PIDTC’s protocols have been approved by the sIRB. Additionally, 14 PIDTC sites have now joined the sIRB. All the PIDTC sites have now transitioned to using the new RDCRN electronic site delegation log. This log streamlines the onboarding process by allowing study staff to sign electronically and allowing site investigators to approve changes to the staff electronically also. This transition should decrease staff burden, while increasing efficiency and accuracy. The DMCC is proud to now be providing key variables flat files for 6901, 6902, and 6903. The flat file for 6901 also includes transplant data received from the CIBMTR. These flat files empower investigators to quickly assess the baseline data for the participants. For more information regarding the OneIRB, the electronic site delegation log or the key variables flat files, please contact Amoy Fraser. She is always happy to assist.
CAREER ENHANCEMENT OPPORTUNITY

2018 Conference on Clinical Research for Rare Diseases:
The RDCRN is hosting the 2018 Conference on Clinical Research for Rare Diseases (CCRRD) in Rockville, Maryland on November 19, 2018 for new investigators, trainees, junior faculty, and others interested in rare disease research methodology. Please refer to the attachments for more information. For full program details, registration material, and travel award application please visit: https://www.rarediseasesnetwork.org/researchers/ccrrd/2018.

ANNOUNCEMENTS:

Lentiviral gene transfer for SCID-X1 with low dose targeted busulfan conditioning
This trial is currently enrolling at Boston Children’s Hospital and Mattel Children’s Hospital UCLA, and will soon be enrolling at Great Ormond Street Hospital in London.
For eligibility or more information about the study, please contact: Sponsor: David A. Williams, MD (david.williams2@childrens.harvard.edu); Los Angeles PI: Donald Kohn, MD (dkohn1@mednet.ucla.edu); Boston PI: Sung-Yun Pai, MD (sungyun.pai@childrens.harvard.edu);

Gene Therapy Trial to Treat X-linked Severe Combined Immunodeficiency
This trial is currently enrolling at St. Jude’s, Seattle, and UCSF Benioff Children’s Hospital. In this research study, boys with SCID-X1 will receive a treatment called “lentiviral gene transfer,” also called “gene therapy.” This method inserts a normal copy of the SCID-X1 gene into blood-forming cells or “stem cells” from bone marrow that grow and develop into all blood cell types. The inserted gene will provide correct instructions to the defective stem cells in SCID-X1 so that functioning lymphocytes can develop.
For eligibility or more information about the study, please visit: stjude.org/LVXSCID-ND, or contact Ewelina Mamcarz, MD (ewelina.mamcarz@stjude.org), Aleksandra Petrovic, MD (Aleksandra.Petrovic@seattlechildrens.org), or Mort Cowan, MD (Mort.Cowan@ucsf.edu).

UCSF / 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)

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)

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

PIDTC extends a warm welcome to our new Project Manager, Katie Chang, this past May! She is new to the clinical research realm and brings experience in patient care coordination from her previous years working at UCSF. Her work thus far has included monitoring enrollment across protocols, managing CRF deadlines, all regulatory management, and maintaining close collaboration with our families and Patient Advocacy Groups! “I am inspired by PIDTC’s successes and commitment to serving the PID community.”

For questions or suggestions for our next newsletter, contact Katie at: Catherine.chang@ucsf.edu, 415-476-3837

Newsletter brought to you by Katie Chang and the PIDTC Management Team

2018 PIDTC Timeline

Sept 30th: Deadline to complete single IRB reliance Agreement. Please contact oneirb@epi.usf.edu with questions.

Oct 9th: U54 Grant Renewal Due! Thank you again to everyone working hard on this submission.

Sept 21st: 6904 Retrospective CRFs completed

Oct, 15th: All Year 9 Invoices are due! Please contact Kira.Burcknell@usf.edu or catherine.chang@ucsf.edu for questions

Nov 22nd: Enjoy your turkey!

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