Quarterly Update from Dr. Cowan

As we welcome the next quarter I just want to thank everyone for their continued hard work. In preparation for the U54 grant renewal we have some exciting changes and progress occurring within the PIDTC! I am pleased to announce two new members to the PIDTC Steering Committee team: Dr. Sung-Yun Pai from Boston Children's Hospital, and Dr. Elie Haddad from Ste. Justine's Children's Hospital in Montreal. Both Dr. Pai and Dr. Haddad have had very long-standing active roles in the PIDTC with Dr. Haddad serving as the PI for our 6902 protocol, and Dr. Pai leading the implementation of the new 6905 protocol. We are very excited to have them as a part of the leadership team!

In addition, I am pleased about the progress being made towards adding a number of new protocols to the PIDTC in preparation for the U54 grant renewal. In addition to Dr. Sung-Yun Pai and Dr. Mike Pulsipher's 6905 protocol, we also have a team in place led by Dr. Troy Torgerson to put together an Immune Dysregulation Disorder protocol. These studies will be shortly followed by the implementation of 6907, which will combine 6901 and 6902 and be led by Dr. Chris Dvorak. Please let us know if you are interested in joining any of these new protocol teams, we would be happy to have you!

Also, significant progress is being made on our current studies. Dr. Elie Haddad just received the best abstract award for the 6902 abstract that he presented at the ASBMT meeting in February. This is quite an achievement for Dr. Haddad and the 6902 team! Our 6903 and 6904 retrospective studies are also progressing nicely. We are approaching our final deadline for these studies, June 30th, and have begun to clean up and analyze these data sets. Thanks to all of the center PIs, CRAs, and protocol teams that have made this possible. I ask that you continue your hard work to meet the final deadline!

Finally, I wish to remind you of the upcoming PIDTC Scientific Workshop and Education Day. This year we will be travelling to Bethesda, MD where the meeting will be hosted by Linda Griffith at the NIH. I look forward to seeing you at Education Day on May 23, 2017 and/or at the Workshop on May 24-26, 2017! —Mort
### PAG Update

Many of you are aware that we have a contact registry available on our website that allows patients to sign up and ask more about participating on our studies. We have made a lot of progress in connecting PID patients across the country with our studies thanks to the incredible help of our Patient Advocacy Groups with special thanks to Barb Ballard with the IDF and Heather Smith with SCID Angels! The annual IDF conference will be held June 15-17th 2017 in Anaheim, CA this year where the PIDTC will have an exhibition presence and both Dr. Cowan and project manager Megan Murnane will be speaking at the SCID symposium! Be sure to check out the PIDTC booth if you are at the conference! Information was sent out regarding special symposiums for SCID, CGD, and WAS. Please contact Megan Murnane at megan.murnane@ucsf.edu if you need this information.

We would also like to invite all PIDTC centers to help in our collaborative efforts with the IDF to provide educational materials to SCID families. The IDF has provided all PIDTC centers with IDF Packets that include a number of brochures and materials for SCID families. You should either have received these already or will be shortly and we ask that CRAs, social workers, nurses, and physicians at each center make a mindful effort to provide their SCID patients with these much needed resources!

For any inquiries regarding PIDTC patient accrual or DMCC related inquiries please contact the DMCC project managers, Rosalie Holland at Rosalie.Holland@epi.usf.edu or Amoy Fraser at Amoy.fraser@epi.usf.edu

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### CURRENT ENROLLMENTS AND GOALS:

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<tr>
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For any inquiries regarding PIDTC patient accrual or DMCC related inquiries please contact the DMCC project managers, Rosalie Holland at Rosalie.Holland@epi.usf.edu or Amoy Fraser at Amoy.fraser@epi.usf.edu

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### 6901 Prospective SCID Update

Our First 100 patient’s manuscript is currently being reviewed by the publications committee and we are hoping to submit to Blood shortly. We would like to thank Dr. Chris Dvorak of UCSF, Dr. Jennifer Heimall of CHOP, and our fabulous statistician, Dr. Brent Logan of the Medical College of Wisconsin for all of their hard work on the manuscript and to all the centers, including the physicians and CRA’s who contributed patients and completed the CRFs for the first 100!

The 6901 V4.0 protocol revisions were recently released! Significant changes to the 6901 protocol include following patients beyond 4 years post-transplant to capture late effects, the inclusion of T cell exhaustion studies, and updates to the eligibility criteria!

Please contact Tara Bani at Tara.Bani@ucsf.edu for 6901 inquiries.

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### PIDTC Patient Highlight

**UCSF’S JA’CEON**

Earlier this year, Ja’ Ceon became the first SCID baby at UCSF Benioff Children’s Hospital to undergo Gene Therapy. He is currently still at UCSF and is thriving!

The 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 Megan.Murnane@ucsf.edu
6902 Retrospective and Cross-sectional SCID Update

We have been undergoing an extensive clean-up of the 6902 retrospective data sets. The near completion of this massive feat is largely thanks to Brent Logan, Elie Haddad, and Tara Bani, and the rest of the 6902 protocol team.

URGENT REMINDER: Sites should be recruiting for the 6902 Cross Sectional Study!

We cannot emphasize enough the importance of recruiting 6902 patients in for a cross sectional visit and that all centers make a large push in the next coming months to do so. Our goal is to bring in an additional 100 patients for a cross-sectional visit by August. Sites will receive a reimbursement of $750 per patient enrolled for a cross-sectional visit and CRF completed! We would like to extend a special thank you to the Jeffrey Modell Foundation for providing the funding that allows us to make these reimbursements!

It is now possible for centers to do a cross sectional visit over the phone for patients that have moved away using a revised consent and interview script. Project manager, Megan Murnane, will be contacting you in the next coming weeks to discuss a plan to meet the August cross sectional goal and bring in each of the remaining 6902 patients at your center for a cross sectional visit.

In addition, we would like to remind centers to be sending the optional study samples for the cross sectional visits, especially retrospectively for the CRDs and WAS retrospective patients for your center. Please contact Tara at Tara.Bani@ucsf.edu for any questions regarding the expected numbers of CGD and WAS retro patients for your center.

The 6902 V4.0 protocol revisions have been released! Some changes to the 6902 protocol include the phone consent and interview to complete cross-sectional visits over the phone, and the ability to conduct subsequent follow-up visits!

61% of goal

153 6902 Cross-sectional visits to reach our goal of 250 total visits by June 30, 2017

6903 Chronic Granulomatous Disease & 6904 Wiskott - Aldrich syndrome Update

With the conclusion of our February 28th retrospective deadline, we have completed 177 CGD retrospective patients and 159 WAS retrospective patients. Please see the details below on our goals for the remaining two deadlines this year towards completion of the 6903 and 6904 retrospective studies. We cannot emphasize the importance of meeting these deadlines, as we are currently undergoing a preliminary analysis and hope to start a full analysis of all completed patients by July 2017. Specifically, we want centers to focus on patients for both 6903 and 6904 that were transplanted since 2010 first so we can analyze and publish papers on these WAS and CGD cohorts. Our protocol teams have already begun this initial analysis focused on select questions from the data sets and are currently putting together teams for drafting the manuscripts!

Our project manager, Megan Murnane, has sent notices to each site regarding what is expected for the FINAL 6903/6904 Retrospective Deadline, June 30th. A number of centers are behind on these deadlines and we ask that all centers dedicate time to these enrollments and CRFs as soon as possible. Please contact Megan Murnane at Megan.Murnane@ucsf.edu for any questions regarding the expected numbers of CGD and WAS retro patients for your center.

Again, the FINAL Retrospective Deadline is June 30th, 2017

35% of goal

177 6903 CGD retrospective patients enrolled and completed of 503 total patients by June 30, 2017

53% of goal

159 6904 WAS retrospective patients enrolled and completed of 297 total patients by June 30, 2017

Please contact Tara Bani at Tara.Bani@ucsf.edu for any 6902 inquiries and Megan Murnane at Megan.Murnane@ucsf.edu for 6903 and 6904 inquiries.

RDCRN/DMCC Update

BY ROSALIE HOLLAND

As all of you are aware we are in the process of implementing a central IRB for the PIDTC. Thank you to Kaleena Dezsi from the DMCC and Tara Bani with the PIDTC, who have been hard at work to implement a central IRB with UCS F as the lead center. Also, thank you to all of the coordinators and PIs working with their local IRBs to get this approved. We currently have 16 centers signed, with 7 centers reviewing. We are excited for the potential simplification that the central IRB will bring in the future!

I am also excited to announce the DMCC is currently working on implementing an electronic site delegation log. This should be available to the PIDTC Summer 2017!

Lastly, I would like to welcome Amoy Fraser, PhDc, PMP! As of April 21, 2017, Amoy will be the Project Manager at the DMCC for the PIDTC. Amoy has 8 years of experience as a Project Manager and Clinical Research Coordinator with the VA. We are excited to have Amoy join our team at the DMCC and know she will take great care of PIDTC.

You can contact Amoy at Amoy.Fraser@epi.usf.edu
Announcements

Soon to say goodbye to two of our project managers: Rosalie Holland and Megan Murnane!

We are sad to announce that Rosalie Holland will be leaving us this May. Rosalie has been with the DMCC for over 3 years as a DMCC project manager working with the PIDTC. Her last day will be April 21st, so be sure to let her know by then how much you have appreciated her help! Though we are sad to see her go, we are thrilled for her as she will be entering a new stage of her life to pursue a career as a Physician Assistant at PA school! What an incredible achievement! Congratulations Rosalie!

During her time working with the DMCC and PIDTC she has been instrumental in many projects such as implementing the E Regulatory binder, initiating the use of the RDCRN Data Explorer, reconstructing the PIDTC public website, maintaining protocol compliance across PIDTC studies, and many other contributions!

Before she begins her busy life in the classroom, Rosalie has a few words for the PIDTC:

“I am most proud to see the progress of the PIDTC. When I first started working with the consortium in 2013, PIDTC6903 and PIDTC6904 had not yet been activated. It has been exciting to see the progress made to all of the protocols through the years! It has been a pleasure to work with you all and I am confident in the continued success of the PIDTC!

We wish you all the best, Rosalie, at PA school and everyone at the PIDTC thanks you for all of your hard work!

Though she will still be around for another few months, Megan Murnane will also be leaving us this coming fall after serving over two years as the PIDTC project manager at UCSF. Her last day is still undetermined, so we will be sure to make the transition as smooth as possible for everyone. Though we are sad to see Megan go, we are excited to announce that she will be pursuing a career in medicine starting with medical school in the fall! Congratulations Megan!

During her time with the PIDTC, Megan has been instrumental in keeping steady progress in the 6903 and 6904 retrospective studies, establishing a strong collaboration with our Patient Advocacy Groups, implementing the PIDTC Newsletter on a regular basis, facilitating a connection with our patients through the RDCRN contact registry, and many other contributions!

A quick message from Megan:

“It’s been a privilege to work with everyone at the PIDTC and I want to extend a huge thank you to the investigators, the CRAs, the patients, the PAGs, and especially to Mort and my fellow project managers: Tara, Liz, and Rosalie! I feel honored that I have been part of the PIDTC and that I have been able to give my contribution. I am incredibly proud of the progress we have made and hope to embody the same fortitude and collaboration in my future career that the PIDTC does. I look forward to my next few months with the PIDTC and hopefully continuing to contribute to the field of PID in the future!”

We wish you all the best, Megan, during medical school and we thank you for your dedication to the PIDTC!
Congratulations to our new Steering Committee Members!

Sung-Yun Pai
of Boston Children's Hospital
Dr. Pai's contributions to the PIDTC include participation in all workshops, helping write the original 6901/6902 protocols and CRFs, co-hosting the 2nd Scientific Workshop in Boston in 2012, serving on the 6901/02 team, serving on Review Panels for 6901, 6902 and 6904, conducting studies of B cell reconstitution for 6901/02 and contributing those data to the U54 renewal, serving as PI at BCH for all studies, writing the 2000-2009 6902 paper (NEJM 2014) as lead author, and leading the planned 6905 prospective SCID trial, and more. We look forward to Sung-Yun's future contributions on the leadership team!

Elie Haddad
of CHU Sainte-Justine University Hospital
Dr. Haddad's contributions to the PIDTC date back to the beginning of the PIDTC and include helping write the original 6902/6902 protocols and CRFs, serving as the site PI for Ste. Justine on all the studies, serving on Review Panels for all four studies, hosting the 5th PIDTC Scientific Workshop in 2015 in Montreal, and serving as the 6902 Protocol PI and leading the analysis and authoring the current 6902 manuscript underway, and more! We look forward to Elie's future contributions and enthusiasm for the continuation of PIDTC on the leadership team!

Congratulations to Dr. Pai and Dr. Haddad!

Make sure you register for the 2017 PIDTC Annual Workshop!

The 2017 Annual PIDTC Scientific Workshop will take place:
May 24-26th, 2017
at the NIH in Bethesda, MD

Education Day will be held on:
May 23rd, 2017

!!! Attention PIs: Please complete the Immune Dysregulation Disorder Survey if you have not yet done so!!

In order to help establish a future protocol on patients with immune dysregulation who have been transplanted and not transplanted, we are conducting a survey to take a closer look at this patient population. We have sent each center an excel file for data entry with the questions and list of diseases considered. If you have not already done so, please email the completed file to Alice Chan at alice.chan1@ucsf.edu as soon as possible!

We greatly appreciate your participation. If you have any questions or issues with the survey, feel free to email Alice Chan at alice.chans@ucsf.edu
Anti C-Kit Clinical Trial for SCID patients who never gained B cells

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. It will enroll SCID patients sequentially in three groups based on age: Groups A and B will enroll patients ≥ 12 and from > 2 to ≤ 12 years of age respectively, who have previously undergone an allogeneic human stem cell transplants (HCT) but have low-level donor engraftment and inadequate T and/or B cell function. Group C will enroll patients > 3 months of age with newly diagnosed SCID. Group B will start enrollment after the first dose cohort of Group A has been completed. Group C will start enrollment after the first dose cohort of Group B has been completed.

For questions regarding the trial please contact Dr. Mort Cowan (Mort.Cowan@ucsf.edu, 415-476-2659) or Dr. Chris Dvorak (Chris.Dvorak@ucsf.edu, 415-476-2188) at UCSF, and Dr. Rajni Agarwal (rajin@stanford.edu, 650-724-7173) at Stanford.

Gene Transfer for SCID-X1 using a self-inactivating (SIN) gammaretroviral vector

The trial is currently open and enrolling and performed as a collaboration among U.S. sites at Children’s Hospital Boston, Cincinnati Children’s, and Mattel Children’s Hospital (UCLA), and the Great Ormond Street Hospital in London.

For eligibility or more information about the study, please contact:

Sponsor - David A. Williams, M.D. (david.williams2@childrens.harvard.edu)
Boston – Sung-Yun Pai, M.D. (Sung-Yun.Pai@childrens.harvard.edu)
Cincinnati – Rebecca Marsh, M.D. (Rebecca.Marsh@cchmc.org)
Los Angeles – Donald Kohn, M.D. (dkohn1@mednet.ucla.edu)

Clinical Trial for X-Linked Combined Immunodeficiency in Newly Diagnosed Infants

A Pilot Feasibility Study of Gene Transfer for X-Linked Severe Combined Immunodeficiency in Newly Diagnosed Infants Using a Self-Inactivating Lentiviral Vector to Transduce Autologous CD34+ Hematopoietic Cells. This trial is currently enrolling at St. Jude Children’s Research Hospital in Memphis Tennessee and future enrolling sites include Seattle Children’s Hospital/Fred Hutchinson Cancer Research Institute and University of California, San Francisco.

For eligibility or more information about the study, please contact Dr. Brian Sorrentino at ((901) 595-2727, Brian.Sorrentino@stjude.org) or Dr. Ewelina Mamcarz ((901) 595-3434, Ewelina.Mamcarz@stjude.org)

A Phase I/II Open Label Study of Gene Transfer (Lentiviral vector transduced CD34+ cells) in Patients with CGD

Gene therapy for patients with the Chronic Granulomatous Disease (CGD) is now available at University of California, Los Angeles, Boston Children’s Hospital, and the National Institutes of Health. This is a trial of gene transfer using a safety-improved, third generation self-inactivating lentiviral vector to transduce CD34+ selected hematopoietic stem cells. Genetically modified cells are infused after busulfan preparative conditioning. This trial will be conducted under an FDA Investigative New Drug Application and will be overseen by the NHLBI-appointed Data Safety Monitoring Board. The costs of research aspects of the protocol will be provided for patients treated on the trial by the California Institute of Regenerative Medicine (CIRM) and the Gene Therapy Resource Program, NHLBI and NIH.

Contact Information:
University of California, Los Angeles: Donald B. Kohn, M.D (dkohn@mednet.ucla.edu) or Caroline Kuo M.D. (ckuo@mednet.ucla.edu)
Boston Children’s Hospital: David A. Williams, M.D. (David.Williams2@childrens.harvard.edu) or Sung Yun Pai, M.D. (Sung-Yun.Pai@childrens.harvard.edu)
National Institutes of Health: Elizabeth Kang, M.D. (ekang@niaid.nih.gov) or Harry Malech, M.D. (hmalech@nih.gov)

**The PIDTC does not necessarily endorse these studies, but provides this information to our members as a courtesy.**
If you are a PID patient and would like to participate on 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 on one of our studies. Registration is completely voluntary and you may choose to withdraw at any time. There is no cost to join the Contact Registry. Follow the link to join today:

https://www.rarediseasesnetwork.org/cms/pidtc/Get-Involved/ContactRegistry

Deadlines

Next 6903/6904 Retro Deadline: June 30th, 2017

Retrospective 6903/6904 data entry completed for 1/3 of remaining patients in yr 8

Feb 28, 2017

6902 Cross-Sectional visit completion for all retrospective patients

June 30, 2017

Retrospective 6903/6904 data entry completed for total patients

June 30, 2017