eBrief
Summer 2017

SPOTLIGHT ON University of Minnesota!

The University of Minnesota Medical School boasts one of the top programs in the nation, and has an especially rich history of transplant innovation. After performing the world's first deceased donor pancreas transplant in 1966, the University of Minnesota's Transplant Team went on to found the first nationally accredited transplant fellowship training program (1970), perform the world's first living donor pancreas transplant (1979), perform the world's first total pancreatectomy with islet cell autotransplant (1977), establish the world's first non-directed living kidney donor program (1999), and perform the Midwest's first 'breathing lung' transplant (2013). The University continues to rank highly in research funding and is consistently among the top 10 public universities for annual research expenditures and the top three universities within its division for annual new research award funding.

Both research and quality healthcare are provided to patients through a diverse network of hospitals, outpatient clinics, and specialty locations on both the University's East and West Bank campuses. Known as MHealth, this network is comprised of the University of Minnesota Medical Center (UMMC), the Transitional Care Unit, and the new Clinics and Surgery Center. UMMC, located on the East Bank campus, has over 300 beds with the entire 3rd floor devoted to operating rooms, the entire 4th floor devoted to intensive care units, and multiple additional levels and wings devoted to acute patient care. The 500 bed Transitional Care Unit, on the West Bank campus, provides intensive, prolonged care for patients who have been recently hospitalized or are in need of rehabilitation services. Combined, these facilities ensure that patients are given adequate time to recover after a hospitalization, and ultimately reduces the burden of unnecessary hospital stays.

In addition to these inpatient locations, the recently completed MHealth Clinics and Surgery Center also provides outpatient services. This state-of-the-art facility is home to more than 50 specialty clinics and resource centers, boasts one of the most technologically advanced patient-tracking systems, and was designed to facilitate and bolster clinical research. As one of the first studies to test the Center's research capacity, the CASG-BKV Natural History participants and coordinators have blazed a trail for research in this new facility. Through a collaborative effort with the CSC's research staff, coordinators have developed a nearly seamless process for completing research visits and providing subjects the best experience possible.

Dr. Jo-Anne Young

Rachel Sweet

Casey Dahl

MHealth Center

MHealth Clinics and Surgery Center

Meet the Minnesota Team

Jo-Anne Young (née van Burik), M.D., is a Professor of Medicine and Medical Director of the Program in Adult Transplant Infectious Disease. She joined the faculty at the University of Minnesota in 1999. She received both her B.A. and M.D. from Case Western Reserve University and completed a residency in Medicine at Vanderbilt University Medical Center. Her fellowship in Infectious Disease and several years of junior faculty service were at the University of Washington with the Fred Hutchinson Cancer Research Center. Dr. Young's primary area of interest is bringing diagnostic and treatment opportunities to the bedside for both solid organ transplant patients, as well as leukemia patients and hematopoietic stem cell transplant recipients. She has worked on developing diagnostic testing for complicated fungal infections of the immunocompromised host. Currently, she is lead investigator at the University of Minnesota for multiple clinical trials on bacterial, viral, and fungal agents, as well as vaccines, for transplant patients. Dr. Young very much enjoys the consent discussion with patients (and their significant others) who are starting on the BK virus natural history study, because it is a virus that many folks have not heard about before. Quickly going through the story of when the virus was discovered, when diagnostic testing evolved, that it is not the "Burger King" virus, and what is involved in clinical care today regarding this virus seems to hold everyone's attention!

Jaime Green, M.D., (not pictured) is an Assistant Professor of Medicine and Assistant Director of the Program in Adult Transplant Infectious Disease. She joined the faculty at the University of Minnesota in 2012. She attended medical school at the University of Medicine and Dentistry of New Jersey, Newark, NJ. She had further internal medicine residency training at the University of Virginia, Charlottesville, VA. Her fellowship in Infectious Disease was completed at the University of California, San Diego. For fun she enjoys being out of doors with her dogs Dakota & River.

Rachel Sweet started in clinical research this past September, and was formerly a Public Health student at the University. After emphasizing in infectious disease for her Master's degree, she's found working on the BKV Natural History to be both interesting and personally rewarding. Being involved in a viral study has allowed her to learn more about the intersection between health research and clinical practice, and she's excited to see how the study's results may affect patient care in the future.

Casey Dahl also started in clinical research in September. She previously attended the University for both her Bachelor's and Master's biology programs. Working at the University allows her to draw from her past experience with cellular biology research and infectious disease diagnostics, and she really enjoys being closer to the human aspect of research.

Special Staff Highlights!

As a new feature in our eBriefs, we would like to highlight the accomplishments of your individual staff members! But we need your help! If you have great news to share about yourself or your colleagues, please email Dunia Ritchey (dritchey@peds.uab.edu) so it can be included in the next eBrief!

Congratulations to **Phil Wozniak**, former Study Coordinator at Nationwide Children's Hospital, on his Fulbright Fellowship! Phil will be conducting a pre-clinical trial of a novel means of RSV prophylaxis using medical nanotechnology, specifically polyanionic carbosilane dendrimers (synthetic biomolecules with multiple binding sites that have been shown to successfully interrupt interactions between the virus and the cell membrane). He will be working under Dr. Maria-Angeles Munoz-Fernandez at the Hospital General Universitario Gregorio Maranon in Madrid, Spain. When Phil returns to the U.S. in June, 2018, he will begin medical school at Ohio State University. Bravo, Phil! We are so proud of you!

Congratulations, also, to **Dr. Concetta Marsico**, who completed a Research Internship at the Central Unit before returning to Italy last month. Her abstract, *Blood Viral Load (VL) Not Clinically Meaningful in Symptomatic Congenital Cytomegalovirus (eCMV) Infection* was recognized among the top four abstracts submitted for ID Week 2017, and Concetta was given the Program Committee Choice Award to help defray the expenses of traveling to San Diego in October to present at ID Week 2017. Hooray, Concetta! We are so grateful to have worked with you!

Protocol Updates – Where Are We Now??

DMID 11-0067: The **Gan-Premie** study enrolled the first subject on March 4, 2014. We have 15 sites in the US (no global sites). This is our PK only study, no treatment. Eleven out of 15 sites have enrolled at least one subject. Our total enrollment is 15 at this point. Although the enrollment target was 32, it has been determined by our Central Unit Director of Clinical Pharmacology and our NIH Project manager that only nine more enrollments would be optimal for the data collected to meet the outcome measures outlined in the protocol. The current funding cycle ends 9/2017, with expectations of an extension of the next Options through 5/2019 to be announced soon.
We know all sites are actively screening, but we also understand that these babies are few and far between. We encourage you to continue your screening efforts.

DMID 11-0069: The **Valgan Toddler** study enrolled the first subject on August 14, 2015 at the Great Ormond Street Hospital (GOSH) site in London. A total of 14 subjects have been enrolled since then, two of which did not progress to the randomization phase due to negative Guthrie results. Twelve participants have been enrolled and randomized, with the most current enrollment at the site in Rochester, New York. Study enrollment has been slow, but steady. We know from what we hear on our monthly calls that it isn't from a lack of trying. Our sites have set wide nets to look for eligible study subjects and have shared their creative thoughts to increase our referral prospects. The screening efforts have been commendable, and there remains a bit of friendly "*across the pond*" competition. At this point we have enrolled six in the UK and eight in the US. We have nine US sites, and nine UK sites.
Our target enrollment number is 54. The current funding cycle ends 9/2018, with expectations of an extension for additional Options through 5/2019 to be announced soon. Your continued screening efforts are appreciated.

DMID 11-0070: The **GeneXpert** study began with the first subject enrolled on April 29, 2014. Investigational research teams have almost completely enrolled the study with 98% of subjects enrolled. Investigators are still actively recruiting for subjects.

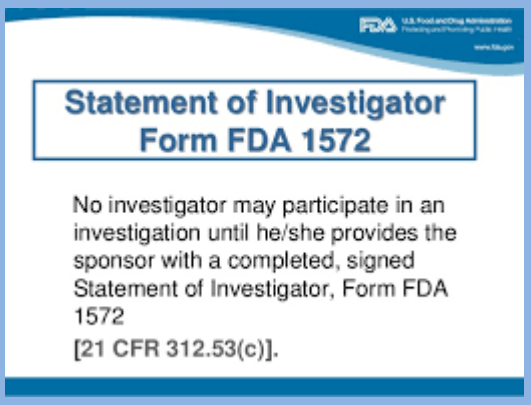
DMID 11-0071: The **BK Viremia** natural history study enrolled first subject on Feb. 5, 2015. Three sites are actively recruiting for subjects. Although the enrollment number varies daily, at the time of this ebrief, 245 subjects are enrolled. Included in the number of subjects enrolled are more than 30 subjects identified with BK viremia based on plasma BK viral load by PCR. The investigators participating in this study are continuing recruitment for potential subjects. The projected total enrollment number is 450 subjects.

DMID 16-0061: Our newest study is the Observational Neonatal HSV PK study. We expect to have 17 sites involved in this study, all in the US. One site has been activated and they have enrolled two subjects in the negative HSV Group 2. We encourage all potential sites to be working diligently to expedite contract approvals and move towards site activation.

Our Recent NIH Site Visit

In May, the NIH Project Officer, Dr. Walla Dempsey, and the NIH Contract Officer Swee Teo, who is responsible for the two newest NIAID contracts, conducted an annual site review during a two-day visit to the Central Unit at UAB. The visit included presentations by staff and discussions related to enrollment status and challenges, study timelines, and plans for the next year. Based on the review, Dr. Dempsey recommended **performance date extensions for the five studies initiated in 2012**. These date extensions (September 2018, 2019 or 2020 depending on the study) will be provided to the sites as soon as they are approved and processed by NIH. For more details on all studies, see the protocol summaries above.

Recent Questions Concerning FDA Form 1572



Recently, a question arose related to which laboratories should be entered into Section 4 of the FDA Form 1572. Guidance on this from the FDA is somewhat vague. Per DMID, the following is the interpretation of Section 4 that DMID has directed us to adhere to: "For Section 4, only clinical laboratory facilities need to be included. Research laboratories must be identified in the Protocol, but not on the FDA Form 1572." So for example, when we (CASG) prepare our protocols, we always describe in the protocol the management of laboratory specimens that will be sent to the UAB Virology Lab (and would if we used another central lab). For this reason, this lab (the Central Lab) does not have to be repeated in Section 4 of the sites' 1572.

Human Subjects Protection Training (HSP) and Good Clinical Practices (GCP)

NIH and NIAID require any site staff who are involved in the design, conduct or oversight of clinical research to receive HSP and GCP training. Although the Central Unit only collects training certificates for principal and co-investigators, the site is still responsible for filing training certificates in the Project Notebook for *anyone* on the Study Personnel Signatures/Responsibility Log. This includes lab and pharmacy personnel, and should be documented on the Protocol/Other Training Log. The monitors will look for these training certificates when they visit your site.

Subrecipient Monitoring, Risk Assessment and Invoicing

As you and/or your site administrator know, UAB recently began the full implementation of the subrecipient monitoring and risk assessment process that is now required for all federal grants and contracts. Under these new federal regulations, UAB must insure that the "subrecipients", i.e. our sites, are appropriately spending, invoicing and completing the work specified in the subcontracts. The process is as follows:

- BEFORE we can send a subcontract, you/your site must complete the Subrecipient questionnaire that includes questions related to accounting practices, conflict of interest policies, etc. This form covers ALL subcontracts with your site.
- For **each** new protocol-related subcontract, there is a specific Letter of Intent that must be signed by the institution which includes a summarized budget and more questions.
- Before subcontract amendments are sent out, we/the Central Unit staff must complete a Review form verifying that you are sending invoices "IN A TIMELY MANNER", meeting the requirements of the study, etc.

WHAT DOES THIS MEAN FOR YOU?

- You MUST return all forms to the Central Unit as soon as possible. (Forms for the two newest studies (16-0061 and 16-0095) were sent to all sites within the past 2-3 months; to date, we have only received them back from about half of the sites.
- Site staff need to work with your accounting and administrative offices to make sure **invoices are sent on a frequent, regular basis**. The subcontracts specify monthly invoices for the older studies, but if that is not possible, we should be getting them at least quarterly. All subcontracts include the statement that payment is contingent upon the availability of funding, and, given the early "clawback" of funds by NIH last year, and other NIH issues, there is always the possibility that we could not provide payment for invoices that include requests for activities that occurred months or years previously.