

# The Art and Science of Pediatrics

Volume 10  
December 2012



**Pediatric Interest Group  
Weill Cornell Medical College**



Weill Cornell Medical College

Dear Weill Cornell Medical Students and Faculty:

One measure of the quality and success of a special event lies in the support it generates in subsequent years. The reviews of all of previous Pediatric Medical Student Research Days are overwhelmingly positive. The consensus of all in attendance at these events is that they are a tradition worth continuing.

On behalf of the Department of Pediatrics and the Pediatric Interest Group, it is a pleasure for me to welcome you to the Tenth Annual Pediatric Medical Student/Faculty Research Day. In the spirit of last year's Journal, this year's Journal, "The Art and Science of Pediatrics," contains original prose by students about their experiences in pediatrics and features on community service opportunities in addition to student, resident, fellow, and faculty research abstracts. The work presented in this journal and displayed at Pediatric Research Day is the product of a wonderful collaboration between our medical students, residents, and faculty committed to developing the next generation of pediatric scientists. What makes this work even more special is that our students accomplished this work in spite of the tremendous demands placed on their time by medical school. We believe this exposure to research early in one's medical career is an essential first step in not only launching a successful career in investigation but also in establishing a foundation for lifelong learning for those who choose to pursue clinical medicine.

As Chairman of the Department of Pediatrics, I congratulate the students and their faculty mentors on the success of their research efforts and acknowledge the strong leadership of the Pediatric Interest Group, Michelle Neely and Julia Kendall, and their advisors, Drs. Susanna Cunningham-Rundles and Thanakorn Jirasevijinda, on organizing and continuing this important pediatric program.

Sincerely,

A handwritten signature in black ink that reads "Gerald M. Loughlin".

Nancy C. Paduano Professor and Chairman  
Department of Pediatrics  
Weill Cornell Medical College

# The Art and Science of Pediatrics

December 5, 2012 • Volume 10 • Pediatric interest Group

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### **COVER IMAGE: “TONGUE DEPRESSOR MANDALA”**

Created by pediatric patients of the Phyllis and David Komansky Center for Children’s Health General Pediatric Unit, 6 North

# STUDENT WRITING

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FACULTY INTERVIEWS AND PERSONAL ESSAYS



## INTERVIEW WITH DR. SHIELA CARROLL

*Krisitin Oshiro, Weill Cornell Medical College Class of 2016*

Dr. Sheila Carroll, Assistant Attending Pediatrician at NewYork-Presbyterian Hospital and Assistant Professor of Pediatrics in the Division of Pediatric Cardiology at Weill Cornell, was kind enough to talk with me about her career and research in pediatric cardiology. She also serves as the director of Fetal Cardiology at Weill Cornell. Dr. Carroll has done considerable research on the genetics of inherited cardiac disease including Brugada syndrome, hypertrophic cardiomyopathy, and long QT syndrome. She is currently developing a fetal echocardiography database at NewYork-Presbyterian Hospital. Clinically, Dr. Carroll spends most of her time on the fetal and post-natal diagnosis of congenital heart disease and the management of post-open heart surgery or cardiac catheterization patients.



*Sheila J. Carroll, MD*

### **Journey to Becoming a Pediatric Cardiologist**

Dr. Carroll always wanted to work with children, and her interest in pediatrics stemmed from her genuine love of caring for children and their families. She was interested in a lot of different specialties during medical school, including medicine and emergency medicine, but she always remained true to her desire to care for children. She eventually chose cardiology for its technical nature, and she enjoyed the mixture of interventional procedures, ICU care, and continuity of care. Dr. Carroll was specifically drawn to cardiology because she was fascinated by the anatomy of the heart and embryology related to the development of the heart and other vital organs.

Currently, Dr. Carroll works primarily on cardiac imaging, such as fetal echocardiograms and transthoracic echocardiograms. During a typical week, Dr. Carroll works in the department's outpatient clinic, reads images, performs EKGs, and consults inpatient cases within the hospital. She finds the most rewarding part of her job is getting to know patients and their families and guiding them through difficult conditions and treatments. Dr. Carroll clearly expressed her love of children and their spontaneous personalities that bring light to any situation. However, she finds that the most challenging part of her job is dealing with noncompliant patients with sometimes serious conditions. Fortunately, noncompliance is not always an issue with pediatric cardiology because of the severity of most cardiac conditions.

### **Research – Fetal Echocardiography Database**

As the Director of Fetal Cardiology at Weill Cornell, Dr. Carroll is working on developing a fetal echocardiography database for NewYork-Presbyterian Hospital. She found that as the availability of fetal echocardiography expanded, she saw a large increase in the patient population. Dr. Carroll was interested in getting a sense of the conditions she was evaluating through this method to improve the delivery of care to her patients. Also, Weill Cornell sees a fairly large number of uncommon heart conditions, and the fetal echocardiography database will help centralize these rare cases. Dr. Carroll is using the fetal echocardiography database in conjunction with outside institutions to perform studies on rare congenital heart diseases. Overall, this fetal echocardiography database will serve as a reference for conditions seen at our hospital and as a way to monitor patient outcomes.

### **Research – Congenital Heart Disease**

In addition to developing the fetal echocardiography database, Dr. Carroll's research focuses on congenital heart disease outcomes, and she recently published an article with the help of a current medical student on the relationship between gestational age and congenital heart disease and

surgical outcomes. Dr. Carroll is also working on a multi-center study on a rare variant of a common congenital heart condition called Tetralogy of Fallot with absent pulmonary valve.

### **Advice for the Next Generation of Physicians**

Since Dr. Carroll has a wealth of knowledge and experience to share, I inquired about particular advice she would give to current medical students who are interested in pediatrics. Dr. Carroll suggested that medical students spend time with teams on the hospital floors through shadowing or attending conferences where the pediatric cardiology team discusses patient cases and images on a regular basis. She invites any interested medical students to either shadow or attend these conferences to gain more exposure to pediatric cardiology.

Dr. Carroll also shared some advice on interacting with pediatric patients and their families. She mentioned the critical importance of ensuring patient comfort throughout an encounter, either by standing back and watching more experienced clinicians in their encounters or by being cautious of the patient's reactions during the visit. Dr. Carroll also advised to be sensitive and understanding of parents and their experiences with their child's condition, no matter how serious. Throughout our conversation, Dr. Carroll's compassionate and thoughtful personality radiated through her responses, and she concluded our conversation by sharing, "I think it's really important to figure out what is the right field for you so you'll be happy with doing it everyday."



## INTERVIEW WITH DR. MAURA FRANK

*Laura Fitzpatrick, Weill Cornell Medical College Class of 2016*



**Maura D. Frank, MD**

“The message I have to students and to all medical professionals is to take [obesity prevention] seriously,” says Dr. Maura Frank. “This is as important as listening to the heart.” In 2006, Dr. Frank—director of Ambulatory Pediatrics in the Division of General Academic Pediatrics at NewYork Presbyterian Hospital and medical director of the General Pediatric and Adolescent Practices—started the Health for Life (H4L) program to stem the growing tide of pediatric obesity. Along with their parents, participants—most of whom are on Medicaid—commit to a 10-week intensive encouraging healthy habits and behavioral change. Working with a multidisciplinary team—including doctors, residents, medical students, dietitians, physical therapists, exercise trainers and social workers—the kids meet weekly for exercise, discussion and a healthy snack. Dr. Frank spoke about the program’s philosophy, obesity and policy, and the rewards of her work. (Note: transcript has been edited for length.)

### **What approach does H4L take to managing obesity?**

The best approach is prevention. But that ship has sailed. We don’t want to make kids feel bad, but the sequellae of obesity are so severe that we have to figure out a way to [help].

We never talk about weight. The discussion focuses on food choices. We use the “Go, Slow, Whoa” model. There are foods you can eat all the time: Go. There are foods you have to think about, such as avocado, which is healthy but a little fattening: Slow. And then there are cakes and ice cream—the Whoa foods.

The physical activity curriculum includes activities people can do easily at home or in the park [such as walking or playing outside], not things that take a lot of money. It has become clear that there’s just so much we can do without major policy changes—similar to cigarette smoking.

### **What policy changes are needed?**

I think [NYC Mayor Michael] Bloomberg’s idea of limiting soda size is great.

[Another component is] having more easily accessible real foods as opposed to packaged foods—fruits, vegetables. Parents have to be on board. There have to be changes in the school and the community.

In the [H4L] program, we make every effort to be culturally sensitive, so [at first] I didn’t feel we could interfere with certain foods. Finally we said, let’s try it. And we have lots of people who started eating brown rice. [We need to come at the problem] from more than one angle and see the whole ecology of obesity.

[As for local] policy: in the building where I work, Helmsley [Tower], the doors are locked at every floor. Many of us would take the stairs more, but it’s not feasible. That’s a fairly easy policy change that could affect a lot of people.

### **You mentioned the “ecology of obesity.” What’s the role of medical professionals?**

The key thing is to see yourself as a change agent. Making small suggestions can go a long way. One policy change we’re talking about is better reimbursement for visits relating to lifestyle modification. I think that will happen in the future.

**You mentioned that you encourage H4L participants to play outside for exercise. What do you tell families who live in unsafe areas?**

We have many families in that category in our program. We [ask], on the weekends, can they take a train somewhere together and be in a park? Can they walk to a safer area? We problem-solve. That's where the social worker comes in.

**Have you researched whether H4L is getting results?**

For the first 12 groups we found that the vast majority of kids either stayed the same or decreased their BMI z-score [a finer measurement than BMI]. Prior to that [their scores] had been going straight up. So that's a success.

We also demonstrate great behavior changes in just about every area. The numbers were enough to make us feel we were doing something valuable. The physical fitness tests are part of a joint research project with the Hunter College graduate program in physical therapy.

It's amazing how much [parents] say they got out of the program. That's something you can't measure easily with numbers.

**What's most rewarding about your job? What's most challenging?**

Most rewarding is when something we've done for a family has made a big difference—whether it's making lifestyle changes, helping their teenager through a difficult time, or identifying eczema and treating it properly. Most challenging is getting people to make the changes.

Many of us started with the notion that in certain communities it's more acceptable to be at a higher weight than in others. While I think there's some truth to that, many of those kids feel stigmatized. There's a high rate of bullying. To see some [H4L participants] grow into swans—they feel so good about themselves, like they've accomplished a tremendous feat. And they have.

**What advice do you have for students interested in pediatrics?**

Get as much exposure to pediatrics as possible, whether in a clinical experience—come shadow us—or in a program like H4L, big buddies or Camp Phoenix, or working on a research project that puts you in touch with children and their families. The more concrete experience you have, the better you will be able to make an informed decision about your path in medicine.

*Medical students may contact Dr. Frank about assisting with new research projects, analysis of existing data, volunteering for H4L or shadowing in the general pediatrics group. She can be reached at [mdfrank@med.cornell.edu](mailto:mdfrank@med.cornell.edu).*

## WHERE YOU ARE

*Megan Riddle, MD-PhD student, MS3*

“There's nowhere you can be that isn't where you're meant to be.” John Lennon

I have a confession to make: I probably am not supposed to be there. It is Saturday and, officially, I am “on call” for surgery, which meant I was to start the morning rounding with my team – transplant surgery – and then join the surgical consult team to bounce around the hospital dealing with various cases of newly distended abdomens, absent bowel sounds, and right upper quadrant pains. Instead, I stayed with my team. In addition to transplant, we are covering pediatrics. In the morning I have scrubbed on two pediatric surgeries, playing what seems to be my two key roles as a third year on surgery – alternating between staying out of the way and being careful not to drop things I am told to hold.

Now it is 6 pm and we are rounding. I admit to being tired –I realize I haven't had a meal since breakfast at 5:30am and can feel any remaining reservoirs of enthusiasm draining. We enter the NICU and approach one of the carefully monitored incubators lining the wall.

I begin to assume my anonymous post, a few steps back, white coat pockets packed with gauze and tape, just in case I can spring forward and be of service in some way, but otherwise simply prepared to watch and listen. Yet I am caught off guard by the father, standing next to the incubator in his hospital-issued yellow gown. He knows the resident; they have already exchanged greetings – now he reaches forward towards me, in a combination of gesture and handshake, “Hello, my name is Anthony. Here, come, you can stand right here. This is Carl.” He is moving away from the side of the bassinet, and I realize he is gesturing to me, pulling me from my anonymity and assuming I am an important part of the team. I step closer.

Something is wrong about the baby; he looks like a wax figure that has been set too close to a candle, his features flattened slightly and stretched – his neck too wide, his face too flat. Yet his father is smiling, beaming really. He looks so proud. This is *his son* and he wants us to see. I want to smile back with great reassurance, to say, *what a beautiful baby* because I know that, to this father, he is. But I fear I am mute; I manage a smile, a nod. The father and resident patter back and forth – the resident is a young father as well, with an eighteen month old he has shown me videos of earlier in the day, and, as the two men exchange words about their children, you can see the hopefulness on Anthony's face; he wants to see his son at 18 months, 18 years old, to talk about a future. Right now it is all so tenuous.

In minutes, we are gone. Such is the nature of rounds.

Two weeks pass, and I have finished my time on transplant, switching over into electives – which again brings me to the pediatric surgery service; it is my first day and we are headed to the NICU on morning rounds. The resident pauses outside the door, glances at his list, “This is baby Carl.” As he goes on to relay the hospital course in a few quick sentences. I am both saddened and relieved – saddened Carl is still here in the NICU, but relieved, maybe even surprised, that he is here at all. As the resident finishes his summary, though, there is a pause. Then, quietly “I don't think he is going to make it.”

It is early, and Anthony is not there. The nurse is concerned; we are all concerned. Carl does not look much different, but his organs are slowly, quietly, giving out. We leave quickly, moving to another incubator in the room, a baby girl who is recovering well from abdominal surgery.

The next morning, in the NICU, the baby girl continues to improve. But Carl's incubator is gone.

"Where's Carl?" the resident asks a nurse.

She pauses, "He died this morning."

Later, we learn the parents decided to remove life support. They were both there. He had passed away two hours before we had arrived for rounds. The surgeon, on hearing the news, requests we print out a new patient list, with Carl's name removed. That is done immediately.

I will hold myself together for the day – maintain my composure through morning surgery, through afternoon clinic, through the telling of a family that their little girl who they thought was healthy two days ago likely has stage four cancer.

Then I will get home. And there I will finally let myself cry. For Carl and his father, for the future so quietly snuffed out, and for the little girl and her family who, with our – and here, I realize, I now include myself – help, still have potential for tomorrow. Then I will wipe away the tears and realize that, sometimes, you are exactly where you are supposed to be.

## THE MOST IMPRESSIVE JUGGLER YOU'VE NEVER IMAGINED

*Michelle Neely, Weill Cornell Medical College, Class of 2015*

As part of my thesis research in college, I was entrusted with the odd and slightly unnerving task of judging children's intelligence. My research (examining the neural correlates of children's detection and appreciation of humor) fell within a much larger investigation of children and humor, which included how the use and appreciation of humor might relate to cognitive faculty. Starting in infancy, children prefer to attend to stimuli that are marginally discrepant from their existing capabilities and knowledge. The phenomenon of humor (from childhood through adulthood) usually arises from the act of detecting incongruity. Thus, the development of a sense of humor is almost a proxy for growing perceptual and cognitive mastery.

As one of the many hats I wore for my research, I was responsible for administering cognitive assessments of children between the ages of six and twelve. The instrument used was the Weschler Abbreviated Scale of Intelligence (or, for the acronymically inclined, the WASI). Among other measures of cognitive ability, the WASI has a verbal component in which children are asked to define a list of words. Each definition is scored between 0 and 2 points, depending on its appropriateness and thoroughness. For example, defining "lunch" as "a break" is, while not completely incompatible, a rather unsatisfactory definition (0 points); offering "you eat it" as a definition is somewhat closer to the mark (1 point); and "a meal between breakfast and dinner" is comprehensively correct (2 points). By the time I had completed my thesis research, and had administered over twenty of these assessments, I had honed an acute sense of the spoken word and its potential for precision and accuracy. I no longer had to consult the WASI manual for scoring guidelines; I internally rattled off a "0," "1," or "2" as kids sat across the table from me and offered their best explanations of the gamut of words from "bird" to "trend."

As an unexpected consequence, I refined an impressively stoic poker face that I oftentimes had to assume and maintain throughout the course of the assessment. Bill Cosby may have said it first, but my thesis research was living proof that kids say the darndest things.

There was the eight-year-old girl that told me that "decade" meant "years and years," and, upon prompting, expanded on her definition by explaining that "decades ago, dinosaurs roamed the earth!" Externally, I nodded to accept the definition and proceed with the next word; internally, I lamented the plight of the poor Tyrannosaurs Rex who, with his powerful haunches enrobed in bell-bottoms and his lower claws stuffed into platform shoes, surely must have felt inadequate when his comically short upper limbs limited the range of his Point Disco Roll-it dance moves.

Then there was the eleven-year-old boy who unintentionally revealed some *unique* methods of self-introspection by defining "tradition." It's "something you do each time something happens," he explained, "...like on Christmas when you open presents *after* you wake up and *before* you eat breakfast...or on Sundays when the mail doesn't get delivered so you have to write letters to yourself." How inconsiderate of me not to write to myself after all these years, I thought.

But my favorite definition-related anecdote came from a seven-year-old girl responding to the question I'd asked in a number of similar encounters—question #24: "What does 'entertain' mean?"

"I don't know."

The WASI protocol indicates that this first dismissal is not to be scored. Instead, the proctor encourages the child to *attempt* a definition. I gently suggested that she try her best. Her eyebrows furrowed with focus, her fingers drummed on the table between us.

“Well...it’s like a juggler,” she ventured, looking up at me, her eyes widening and her arms gesturing. “And he’s juggling...*one hundred* chairs...each with a baby on top of it!”

She went on to describe how the audience would enjoy the performance, and I had to hand it to her: certainly I couldn’t think of anything more entertaining than that. And I don’t think either of us could have predicted how apt a definition hers would prove to be; I have been entertaining people with her definition of ‘entertain’ for years, now.

Throughout my journey from premed to medical student, I’ve had many more encounters with children in more medical settings; and while some of these encounters have been far less humorous and much more painful, I’ve always been struck, and moved, by the power and beauty of interacting with kids. Their sincerity is disarming—their honesty, humbling; they can crack you up with one breath and break your heart with the next.

I decided to go into medicine for a multitude of reasons. I deeply value the preciousness of life and the intricate symphony of physiological processes that underwrite it. I’m hopelessly fascinated, moved, and inspired by people—enchanted by the richness of their lives’ narratives and drawn by an ineffable desire to contribute to them in meaningful ways.

But if we go into medicine to help others, to contribute, to give, I think we are most convinced to stay because of what we can take away—how we learn from our experiences and how they change us, and renew us, again and again. Interacting with children is always revitalizing. Children are unapologetically frank, which keeps you alert, grounded, and on your toes. Furthermore, they offer you a peek at a distant mirror of yourself, when curiosity and imagination lay unbridled by the weight of adulthood. And while this same reflective quality can make it unbelievably difficult to see children in pain and burdened by illness, caring for them challenges us to reclaim that creativity, earnestness, and inventiveness—so that we, too, may easily conjure in our minds a juggler juggling one hundred babies, each perched upon one of one hundred chairs.

# RESEARCH ABSTRACTS

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MEDICAL STUDENTS



## SCIENCE AND MEDICINE ENHANCEMENT PROGRAM

*Rolake Alabi, MD-PhD Student, Weill Cornell Medical College*

**Background:** In the spirit of the Student National Medical Association's Youth Science Enrichment Programs (YSEP), the Science and Medicine Enhancement Program (SMEP) provides middle school students with hands-on opportunities to learn about health and disease through a multi-subject approach. In a series of sessions held at the Weill Cornell Medical College, groups of 3-4 students led by medical students work on hands-on group and individual activities designed to reinforce basic concepts in basic biology, physiology, pathophysiology and healthy living related to the diseases and health conditions that most affect the students' communities. The primary project goal is to engage middle school students from groups underrepresented in medicine in active learning opportunities designed to emphasize the cross-disciplinary applicability of medicine. We hope this active engagement with material and with our SNMA member volunteers and other WCMC volunteers provides SMEP students with an exciting and memorable experience that inspires them to pursue careers in medicine.

**Methods:** SMEP focuses on active learning, exposing SMEP students to students from similar backgrounds farther along the pipeline, and introducing SMEP students to the cross-disciplinary applicability of science and medicine. The program's current primary modes of evaluation are pre-tests (administered prior to the start of teaching) and post-tests (administered after teaching sessions are completed), which are designed to measure how effectively the curriculum achieves its content objectives.

**Results:** Preliminary results suggest the current curriculum improves students' grasp of key concepts tested in the pre- and post-tests. Results also show that curricular changes made between the 2011 and 2012 SMEP years have improved student performance.

**Conclusions:** We believe that SMEP may be a program on which a new subset of YSEP programs that closely collaborate with local magnet schools with curricula and activities already focused on science and medicine can be modeled. We hope that, just as WCMC's Health Professions Recruitment and Exposure Program for high school students, has served as a model for Student National Medical Association chapters throughout the nation, SMEP will also serve as a model for special programming focused on middle school students interested in science and medicine.

## A SURVEY OF THE ETIOLOGY OF IMMUNE THROMBOCYTOPENIA (ITP)

*Valerie Arias, Candidate for MD, 2014 U Chicago<sup>1</sup>, Ehsan Shabbir, MD<sup>2</sup>, Daniel Victorio, Candidate for BS, 2013<sup>2</sup>, Emily Sperling, Candidate for BA, 2014<sup>2</sup>, Naznin Haq, BA<sup>3</sup> and James B Bussel, MD<sup>4,5</sup>*

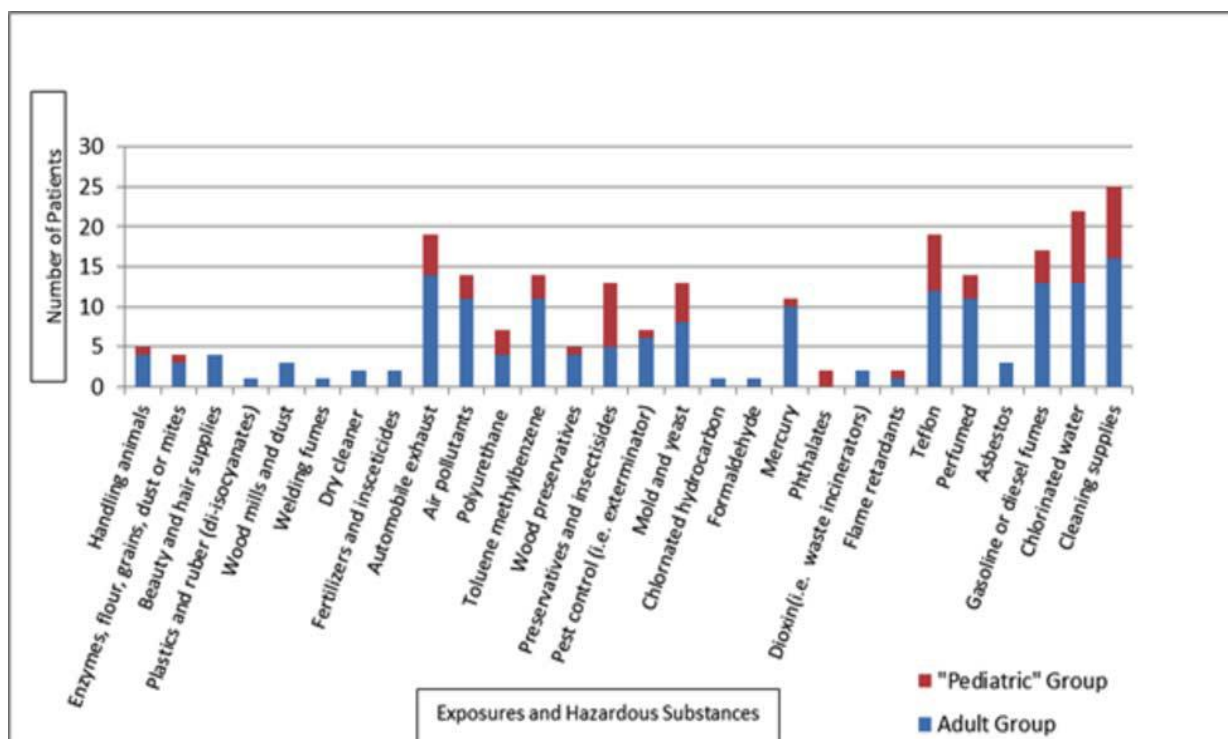
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**Background:** Socioeconomic, environmental, lifestyle and genetic factors play a role in the etiology of ITP but are poorly understood. A self-reported questionnaire was designed to study these relationships and how these factors prior to the diagnosis of ITP relate to treatment response and disease progression in order to gain insight into the etiology of ITP.

**Methods:** To design the questionnaire that would address topics of interest: 1) 60 ITP patient interviews were performed and 2) the questionnaire was reviewed by project coordinators, nurse practitioners, Platelet Disorder Support Association (PDSA) members, and hematologists. The input was incorporated into a further-revised questionnaire, which was then administered to both “pediatric” (patients <18 years of age at the time of diagnosis) and adult ITP patients from the Platelet Disorders Center at Weill Cornell-NewYork Presbyterian Hospital. Formal statistical analysis to relate responses to one question to responses of another to define subgroups of patients is ongoing.

**Results:** 109 patients were enrolled. Ages ranged from 2-78 years of age; median age was 55 years, with 21 females and 33 “pediatric” patients. The most frequent environmental exposures in adults were automotive exhaust (n=14) and Teflon (n=12). In pediatrics, preservatives and insecticides (n=8) and Teflon (n=7) were most common. The most prevalent hazardous substances in both groups were cleaning supplies (n=16 adults, n=9 “pediatric”) and chlorinated water (n=13 adult, n=9 “pediatric”). 13 adults also had exposure to gasoline or diesel fumes. Refer to figure 1. 51(47%) patients reported at least one infection prior to diagnosis with ITP. The most common were Strep throat (n=12); influenza (n=9), and respiratory tract infections (n=8). Twenty-four (22%) patients reported at least one autoimmune disease, including celiac (n=2) and discoid lupus (n=2). Twenty-one patients reported a family history of Type II diabetes, 12 Type I diabetes, 13 osteoarthritis and 10 rheumatoid arthritis. Eight (7%) patients reported at least one inflammatory disease including: Crohn’s disease (n=3), Inflammatory bowel disease (n=7), Systemic lupus erythematosus and Vitiligo (each n=1). Thirty-seven (34%) patients reported surgeries prior to diagnosis of ITP, especially: appendectomy (n=8) and tonsil removal (n=8). Twenty-three patients traveled close to date of diagnosis, 58 patients reported more stress than usual (i.e. death of a relative, loss of employment); 13 patients reported a drastic change in diet (i.e. decreasing calories (n=7) or becoming vegetarian (n=5)). Vitamin supplementation for vitamin C and D (each n=17), E (n=12) and B (n=11) were common. In addition, 11 vitamin deficiencies were reported: vitamin D (n=5), vitamin B12 (n=3) and other (n=3). The most frequent allergic reactions included: 31 (28%) patients with hay fever, 9 patients with allergies to milk, 7 patients with poison ivy or skin irritation, 6 patients with eczema, and 4 with allergic rhinitis. Other medical conditions reported were: hypothyroidism (n=10), hyperthyroidism (n=9), high blood pressure (N=16), high cholesterol (N=14), and anemia (N=13) [9 additional patients included 4 with iron deficiency anemia and 5 with a family history of iron deficiency anemia]. Seven patients reported a lack of prenatal care in their mothers’ pregnancy and 7 were premature. Medications reported include: acetaminophen (n=53), antibiotics (n=36), antihistamines (n=22), and hormone therapy (n=17). Vaccinations received close to date of diagnosis include: flu vaccine (n=10) and T-dap (n=9). Prednisone was reported most frequently as both the best therapy to minimize symptoms (n=18) and the worst (n=16).

**Conclusions:** Our pilot study intended to capture critical information and to further development of the questionnaire. We can see if there are groups of patients in whom onset and other characteristics relate to outcomes including response to treatment. Following formal statistical analysis of the material acquired (in progress and anticipated by early September), the next step will be for a final updated version of the questionnaire to be posted on the PDSA web site in order to accrue responses from a much larger number of patients. The questionnaire will also be given to a non-ITP patient population to serve as controls.



# PRELIMINARY RESULTS FROM FOCUS GROUPS TO EVALUATE THE FEASIBILITY OF PARENT-TO-PARENT EDUCATION IN THE PEDIATRIC CLINIC WAITING ROOM

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**Background:** Pediatric obesity rates have tripled over the past 30 years, leaving children with a higher incidence of cardiometabolic risk and increasing vulnerability to cardiometabolic disease.<sup>1</sup> Childhood obesity is widely acknowledged to be a national public health problem, but pediatricians in general practice have limited time to provide counseling in this area.<sup>2</sup> Parent-to-parent education is a potentially effective, but underutilized, focal point of childhood obesity prevention and treatment.<sup>3,4</sup> Using focus groups, we explored the feasibility of and interest in implementing a program to deliver health information via a parent educator in the NYP-Cornell Pediatric Clinic. The parent peer educator would ideally share both factual and practical knowledge as well as provide emotional support and encouragement to parents.

**Design/Methods:** A sample of caregivers (N=15, F=14 M=1) who had previously participated in Health For Life (H4L), a 10-week health education program for children with BMI in the 85<sup>th</sup> percentile or greater and their caregivers, were interviewed in two focus groups in August 2012. Participants were recruited based on child attendance records and availability. Participants were asked to discuss a series of questions designed to evaluate satisfaction with and benefit of H4L; barriers to changing lifestyle habits; preferences regarding health information; logistics/feasibility of creating a parent-to-parent peer health education program; and parent receptivity to waiting room education. The use of focus groups allowed for exploration of the individual experiences of the participants and provided a venue for a thorough examination of “not only what people think but how they think and why they think that way” about nutrition counseling.<sup>5</sup> Sample questions included: How do you feel about sharing information about healthy choices and your experiences making healthy lifestyle changes with other parents?

**Results:** Groups were moderated, audio-recorded, and transcribed by a medical student research assistant. Transcripts were coded into specific topics and these codes were then grouped to reflect broader themes. Codes and themes were developed by the medical student and PI, both of whom also reviewed the coding results. A qualitative research specialist has been added as an investigator to validate the coding schema.

**Conclusions:** Initial results of focus groups indicate that parent-to-parent interaction is a viable platform for health education, either in the pediatric clinic waiting room or in a group format. In addition to coding participants’ verbal expressions of interest in the provision and receipt of support from other parents, it was possible to code for actual exchanges in which participants shared personal experiences, related emotionally to one another, and gave one another specific health/nutrition advice. Parents expressed a desire for professional guidance, either in the form of a curriculum or a moderator. Additionally, parents expressed interest in an internet-based forum to exchange ideas and success stories with professional oversight. We plan to continue gathering qualitative data through key informant interviews and to quantify parent opinions through a phone survey for all parents who participated in focus groups or interviews.

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## ENDOSCOPIC MANAGEMENT OF INTRALUMINAL URETERAL ENDOMETRIOSIS: A VIABLE TREATMENT MODALITY?

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**Background:** Endometriosis affects about 15% of premenopausal women and may present anywhere along the urinary tract. Although urinary endometriosis (UE) most commonly affects the bladder, the ureters are involved in  $\approx 1\%$  of patients; this is usually extrinsic involvement as intrinsic involvement is rare. Untreated UE may result in urinary obstruction and insidious renal failure. While surgical resection with or without hormonal suppression is the treatment of choice for extrinsic UE, there is scant literature on intrinsic UE. We present the largest experience on the ureteroscopic management of intrinsic UE causing ureteral obstruction.

**Methods and Results:** Our IRB-approved database was reviewed for patients who underwent ureteroscopic management of intrinsic UE from 1993-2012. Patients were diagnosed with ureteroscopic biopsy and underwent at least one ureteroscopic ablation of lesions with a Holmium YAG laser. Patients were followed for evidence of disease persistence, recurrence, or progression with interval laboratory evaluation and imaging. A total of 5 patients were identified. Mean age at initial diagnosis of hydronephrosis was 37.5 years (31.6-40.8) and management was a median time of 185 months (22-226). Three patients received hormonal treatment. One patient required nephroureterectomy for absent renal function at the time of diagnosis but had recurrent bleeding due to UE recurrence in the ureteral stump, successfully managed with laser ablation. Three of the other four had resolution of their hydronephrosis and are stent-free following laser ablation and hormonal therapy, although all three did develop ureteral strictures that required balloon dilation. The other patient continues to have intrinsic disease with an indwelling stent and is still on hormonal therapy. Overall definitive success rate was 80% with no treatment related complications.

**Conclusions:** Ureteroscopic management of ureteral obstruction due to intrinsic UE, often with concurrent hormonal therapy, is a viable alternative to nephrostomy or invasive surgical procedures. Follow-up imaging for resolution of hydronephrosis, ureteroscopic surveillance and retrograde urography are recommended to detect recurrence and/or progression of obstruction in these patients.

# AN INHERITED *TUBB2B* MUTATION ALTERS MICROTUBULE DYNAMICS AND CAUSES PRIMARY ERRORS OF AXON GUIDANCE

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**Background:** Despite the belief that aberrant brain connectivity leads to many genetic neurodevelopmental disorders, identifying and understanding primary errors of axon guidance has been complicated by the anatomical complexity of the central nervous system and the phenotypic complexity of disease processes. Congenital fibrosis of the extraocular muscles (CFEOM) is a rare, Mendelian complex eye-movement syndrome, which can be caused by primary errors of axon guidance. Since eye movements are controlled by anatomically well-defined and simple motor axons, CFEOM is a prototypic disorder that offers a unique opportunity to understand how human axon guidance goes awry. We previously described a family that segregates CFEOM, intellectual disability, polymicrogyria, and corpus callosum hypoplasia as dominant traits, but that lacks any mutations in known CFEOM genes. Here we identify the genetic, molecular, and neurodevelopmental features of this novel CFEOM subtype.

**Methods and Results:** We used linkage analysis followed by DNA sequencing to identify an inherited heterozygous missense mutation in *TUBB2B* that segregates with CFEOM, polymicrogyria, and intellectual disability. *TUBB2B* encodes b-tubulin, which, together with a-tubulin, forms microtubules. To determine whether this *TUBB2B* mutation causes primary axon guidance abnormalities, we first performed diffusion tensor imaging (DTI) of brains of affected family members. DTI reveals aberrations in the trajectories of commissural projection neurons, implying a paucity of homotopic connections; however, these aberrations could be secondary to diffuse brain malformation associated with polymicrogyria. Thus, we expressed exogenous Tubb2b-E421K in a small number of developing mouse callosal projection neurons, via *in utero* electroporation, and found this is sufficient to perturb homotopic connectivity, without affecting neuronal production or migration or causing any brain malformation. Finally, by introducing the human mutation into yeast b-tubulin, which is over 90% homologous with human b-tubulin, we find that TUBB2B-E421K alters microtubule dynamics.

**Conclusions:** These data provide evidence that *TUBB2B* mutations can cause primary axon guidance errors in the central and peripheral nervous system. Eight mutations in the closely related gene *TUBB3* also disrupt microtubule dynamics and result in CFEOM. The shared molecular and neurodevelopmental features of *TUBB3*-CFEOM and *TUBB2B*-CFEOM support a convergent mechanism of axon dysinnervation caused by abnormal dynamic properties of neuronal microtubules.



# THE IMPACT OF AN ARTS PROGRAM IN A CHILDREN'S CANCER AND HEMATOLOGY CENTER

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**Background:** The Arts in Medicine (AIM) program is an established, 13-year-old program in a major children's Cancer and Hematology Center that provides meaningful artistic opportunities to cancer patients and their families in inpatient and outpatient settings. To continue on its trajectory, a program evaluation of AIM's clinical effectiveness of its various art activities was necessary.

**Methods:** We report the results of a survey-based program evaluation assessing the clinical effectiveness of AIM-facilitated activities. The survey consisted of questions designed to assess patient familiarity with and participation in art opportunities, and was distributed in Texas Children's Cancer Center for one week in June 2010 during normal clinic hours. The survey was not intended for patients only, as many parents, siblings, cousins and friends accompanying patients benefit from the arts programming as well.

**Results:** The weeklong distribution of the Arts in Medicine survey yielded a large response, with 460 cancer and hematology patients and family members completing the survey and a patient return of 40%. Our survey evaluated the familiarity of patients and family members with various art programs under the umbrella of AIM; familiarity with each of the three programs is well below 40%. The survey also assessed previous program participation of patients and siblings (parents were asked to answer on behalf of their children) in AIM program activities. Survey responses revealed very high participation in arts and crafts, a daily activity in the clinic. The main goal of this program evaluation was to review the perceived benefit of art activities offered by AIM. Patients and family members were asked to rate the "helpfulness" of each activity on a Likert scale of 1 to 5, where 1 is extremely unhelpful and 5 is extremely helpful. An astounding 80.5% of patients and family members found arts and crafts to be very helpful. A stratification of perceived helpfulness by age was more illustrative, for even the oldest of patients (ages 19–25) rated all art activities to be very helpful, despite the tangible stigma against participation.

**Conclusions:** We report the results of a comprehensive survey evaluating the clinical effectiveness of AIM-facilitated activities. Among 460 patients and family members, we found low familiarity with the actual AIM program but high participation in and perceived benefit of AIM-facilitated activities. To raise awareness, implementing a daily activity schedule and providing AIM program information to all newly diagnosed patients and families is recommended. Teenagers perceived art activities to be especially beneficial. To increase older children's involvement in AIM activities, expanding performance arts and increasing specific efforts to engage teenager involvement should be considered.

<sup>1</sup>*Excerpted with minor changes from: Cowell, E., Herron, C., and Hockenberry, M. 2011. The impact of an arts program in a children's cancer and hematology center. Arts & Health, 3(2): 173-181*

# PROGNOSTIC VALUE OF PHYSEAL AND EPIPHYSEAL INVOLVEMENT METAPHYSEAL “CYSTS” IN LEGG-CALVÉ-PERTHES DISEASE USING MAGNETIC RESONANCE IMAGING

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**Background:** Metaphyseal radiolucencies described as “cysts” when viewed on standard pelvic X-rays are considered a radiographic risk factor in Perthes Disease. Magnetic resonance imaging with contrast can confirm “true cysts” and delineate their exact location and extension beyond the metaphysis into the physis and epiphysis. The presence of multiple (two) cysts can also be visualized.

**Objective and Aims:** 1) To determine the prognostic value of metaphyseal “cysts” that involve the physis and epiphysis in Perthes disease 2) To determine the prognostic value of multiple metaphyseal “cysts”

**Materials and Methods:** 68 patients (82 affected hips and 54 unaffected hips at presentation) with Legg-Calve-Perthes disease were followed up for an average of  $3.1 \pm 2.0$  years. Hips were imaged using T1-weighted, fat suppressed T2-weighted, and gadolinium-enhanced subtraction MRI. The lateral pillar classification and the deformity index (DI) were used to evaluate femoral head deformity.

**Results:** 42 hips developed metaphyseal “cysts.” 13 hips developed two “cysts.” 30 of these “cysts” were isolated to the metaphysis and 25 extended through the physis to involve the epiphysis. Presence of metaphyseal “cysts” was associated with significantly worse lateral pillar class ( $p=0.047$ ). The average DI was significantly greater ( $p=0.006$ ) for the hips with metaphyseal “cysts” compared to the hips without metaphyseal “cysts” ( $0.32 \pm 0.12$  vs.  $0.23 \pm 0.07$ ).

The location of metaphyseal “cysts” (isolated to metaphysis vs involving physis and epiphysis) was not associated with a significant difference in the lateral pillar class ( $p=0.56$ ). The average DI, however, was significantly greater for the hips with “cysts” involving the physis and the epiphysis ( $p=0.036$ ) compared to the hips with isolated metaphyseal involvement ( $0.36 \pm 0.12$  vs  $0.28 \pm 0.10$ ). Presence of multiple “cysts” in a hip did not correspond to significantly worse lateral pillar class. ( $p=0.27$ ). The average DI was  $0.31 \pm 0.10$  for hips with a single “cyst” versus  $0.35 \pm 0.15$  for hips with multiple “cysts” ( $p=0.39$ ).

**Conclusions:** Metaphyseal “cysts” extending through the physis into the epiphysis correlated with more severe femoral head deformity. The presence of multiple metaphyseal “cysts” was not indicative of worse femoral head deformity.

# MR PERFUSION INDEX AS A QUANTITATIVE METHOD OF EVALUATING EPIPHYSEAL PERFUSION IN LEGG-CALVE-PERTHES DISEASE (LCPD) AND CORRELATION WITH SHORT-TERM RADIOGRAPHIC OUTCOME: A PRELIMINARY STUDY

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**Background:** Current radiographic prognosticators of outcome of LCPD can only be applied after femoral head deformity has occurred. Quantification of femoral head perfusion using gadolinium-enhanced subtraction MR technique may serve as an early prognosticator of outcome.

**Objective:** The purposes of this study were 1) to develop a reproducible method to quantify femoral head perfusion using this MR imaging technique and 2) to determine if the perfusion at early stages of LCPD correlates with radiographic deformity after two-year follow-up.

**Methods:** 15 patients meeting the following inclusion criteria were studied: radiographs and perfusion MRI obtained at Waldenstrom's Stage I or early Stage II, age 6-12 years, and unilateral disease. MR perfusion index, a measure of perfusion in the epiphysis, was obtained using digital image analysis of subtraction gadolinium-enhanced MR images obtained using GE 1.5 Tesla scanner. Intra- and inter- observer reliability of this index were assessed by two independent observers. MR perfusion index obtained at the early stage of LCPD was correlated with deformity index (a validated radiographic measure of femoral head deformity) obtained after a minimum two-year follow-up. Pearson product –moment correlation test was used for statistical analysis.

**Results:** Intra- and inter-observer agreements for MR perfusion index were high. The intra-observer correlation coefficient for each observer was 0.97 and 0.98 respectively. The inter-observer correlation coefficients were 0.93 and 0.94. Substantial variability of MR perfusion index was found in the patients at the early stages of LCPD, ranging from 0 (no perfusion) to 0.70 (high perfusion). The deformity index at 2 year follow-up ranged from 0.18 (mild) to 0.62 (severe deformity), with inter-observer correlation coefficient of 0.82. MR perfusion index obtained at early stage LCPD showed moderate inverse correlation with deformity index at two year follow-up ( $r=-0.64$ ,  $p=0.01$ ), suggesting that a higher perfusion index at the early stages was associated with a less deformity later. Of 6 patients that received symptomatic non-operative treatment only, the correlation was strong ( $r=-0.87$ ,  $p=0.03$ ). Of 9 patients that received femoral varus osteotomy, the correlation was more moderate and not statistically significant ( $r=-0.58$ ,  $p=0.10$ ).

**Conclusion:** MR perfusion index obtained from gadolinium-enhanced subtraction MR images has high reproducibility. A lower MR perfusion index at early stages of LCPD correlated with greater radiographic deformity at two-year follow-up.

**Significance:** The MR perfusion index appears to be a promising early prognosticator of outcome in LCPD. Further studies with a large sample size and longer follow-up are needed to determine its clinical applicability and usefulness.

# IMMUNE RECONSTITUTION INFLAMMATORY SYNDROME ASSOCIATED WITH EXTRAPULMONARY MULTI-DRUG RESISTANT TUBERCULOSIS IN AN HIV-INFECTED CHILD

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**Background:** We report a case of Immune Reconstitution Inflammatory Syndrome (IRIS) with extrapulmonary multidrug-resistant (MDR) tuberculosis (TB) in an HIV+ child. Haiti has the highest TB rate in the Western Hemisphere (estimated prevalence of 314 per 100 000.<sup>1</sup> MDRTB is a growing global concern, with 10-15% of cases occurring in children.<sup>2</sup> Furthermore, IRIS, a paradoxical clinical deterioration characterized by marked inflammatory phenomena after antiretroviral therapy (ART), is frequently observed with the expanding use of ART in developing countries.

**Case report:** An 11-year-old, HIV-positive girl presented with a 6-month history of cough, weight loss and diarrhea and a 2-month history of fever. She was severely emaciated weighing 47 pounds (<<5<sup>th</sup> percentile) with a CD4 count of 8 cells/mm<sup>3</sup>. After initiation of ART and treatment for multiple opportunistic infections, she improved significantly with good weight gain and an increase in CD4+ cell count to 95 cells/mm<sup>3</sup>. However, she remained febrile with a once daily peak to 39°C, night sweats, persistent complaints of abdominal pain, and a limp when walking. An abdominal CT scan demonstrated a left sided retroperitoneal multi-loculated fluid collection walled off with a thick capsule near the psoas muscle with partial obstruction of the left kidney and beginning of fistulization to the lower back subcutaneous tissue. Greater than 1 L of purulent bloody material was drained via percutaneous aspiration and sent for culture/ pathology. Ziehl-Neelsen stain showed 3+ acid-fast bacilli and GeneXpert amplified large amounts of *M. tuberculosis* complex DNA with rifampicin resistance. The patient started an empiric MDRTB regimen based on national resistance patterns with levofloxacin, ethionamide, kanamycin, para-aminosalicylic acid, pyrazinamide and pirodioxine and finally defervesced within a week.

One month after MDRTB treatment initiation, the patient began having febrile episodes with rapid growth of large, red, tender inguinal, axillary and supraclavicular lymph nodes which fistulized to the skin, draining caseating material. All were confirmed as due to MDRTB. Viral load was undetectable ruling out antiretroviral resistance. This paradoxical worsening was attributed to IRIS likely occurring as a result of recovery of T-cell immune response to persisting TB antigens, after ART or TB treatment.<sup>3</sup> Her symptoms were managed with surgical drainage of fistulizing nodes and non-steroidal anti-inflammatory drugs. The patient was discharged on MDRTB therapy after 11 months and has continued to show great clinical improvement in follow-up, with consistent weight gain and increase in CD4 number up to 326 cells/mm<sup>3</sup> one year after diagnosis.

**Conclusion:** Although extrapulmonary MDRTB is difficult to diagnose and treat in an HIV+ child, a good outcome can be obtained, even in resource poor settings. Research has focused on TB in adults, to the relative neglect of children. While very vulnerable to severe disease, children have an incredible ability to overcome it and merit greater focus as suggested by this case.

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# RADIOULNAR SYNOSTOSIS-HEMATOLOGY (RUS-H) SYNDROME: DESCRIPTION OF THE NEW SYNDROME AND COMPARISON TO SIMILAR SYNDROMES

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**Background:** Congenital radioulnar synostosis (RUS) is a rare anomaly characterized by fusion of the radius and ulna. RUS occurs more frequently in males than females, and is bilateral in 50% of cases. Since 1793, there have been > 400 cases reported. Literature review revealed 7 rare syndromes with RUS and hematologic problems including our newly named RUS-H Syndrome: 1) Diamond-Blackfan Anemia (DBA) associated with normochromic, macrocytic anemia in early infancy and erythroblastopenia; 2) Amegakaryocytic Thrombocytopenia Radioulnar Syndrome (ATRUS, HoxA11 mutation) with thrombocytopenia since birth requiring stem-cell transplantation; 3) IVIC Syndrome with mild thrombocytopenia and leukocytosis; 4) WT Syndrome involving a wide array of hematologic abnormalities including easy bruising, hypoplastic anemia, pancytopenia, Acute Lymphoblastic Leukemia (ALL), and Acute Myeloblastic Leukemia (AML); 5) Cohen Syndrome with neutropenia and fluctuating thrombocytopenia; 6) Noonan Syndrome with abnormal bleeding and easy bruising; and 7) RUS-H Syndrome (not involving HoxA11 mutations) associated with a spectrum of hematologic abnormalities including easy bruising, recurrent epistaxis, neutropenia, thrombocytopenia, ALL and aplastic anemia.

**Results:** This study addressed the association of RUS, other congenital abnormalities, and hematologic problems in previously described syndromes and in the novel RUS-H Syndrome. All 7 syndromes are associated with hand abnormalities.

Six of the 7 syndromes (not Cohen) are associated with hearing loss/ear abnormalities. Four syndromes (DBA, ATRUS, WT, and RUS-H) have an increased risk of hematological malignancy. DBA, IVIC, Cohen, and Noonan have abnormalities of the eye and genitourinary system. DBA, WT, Cohen, and Noonan Syndromes are associated with dysmorphic facial features. ATRUS, IVIC, Cohen, and Noonan Syndromes all exhibit lower limb abnormalities. DBA, Cohen, Noonan, and RUS-H are associated with short stature. DBA, IVIC, Noonan, and RUS-H Syndromes are associated with kidney abnormalities and structural heart defects.

Three Syndromes (DBA, IVIC, and Cohen) have cranial abnormalities. DBA IVIC, and Noonan Syndrome have structural defects of the shoulder. IVIC, Cohen, and Noonan Syndromes are associated with spinal anomalies. Two Syndromes (DBA and Noonan Syndrome) are associated with liver, spleen, and neck abnormalities. Cohen and Noonan Syndrome are associated with developmental delays. Lastly, WT and Noonan Syndrome are associated with skin abnormalities. DBA, Cohen, and Noonan Syndrome are the most common of the 7 syndromes, with DBA estimated at 5 per 1,000,000; Cohen Syndrome predicted to have a prevalence of <1,000; and Noonan Syndrome predicted to have a prevalence of <1 in 2,500; however, RUS in DBA, Cohen, and Noonan Syndrome is limited to case reports. RUS-H Syndrome has been identified in 12 families in the United

States, Canada, and England. IVIC and WT Syndromes have been reported in 4 families total, and ATRUS with an identified HoxA11 mutation has been reported in at least 2 families.

**Conclusions:** Since RUS may often be missed on routine physical examination, we recommend specific evaluation of pronation/supination in patients with hematological problems of unknown etiology. Additionally, we recommend that a targeted genetic panel be developed to detect mutations that are known for syndromes involving RUS, blood abnormalities, and other similar orthopedic entities that have cross-over manifestations like Thrombocytopenia-Absent Radii (TAR) Syndrome. This panel might consist of mutations associated with DBA (RPL5, RPL11, RPL35A, RPS7, RPS10, RPS17, RPS19, RPS24, and RPS26 mutations), with ATRUS (HoxA11 mutation), with IVIC Syndrome (SALL4 mutations), with Cohen Syndrome (8q22.2q22.3/COH1 deletion), with Noonan Syndrome (PTPN11, SOS1, RAF1, KRAS, NRAS, and BRAF mutations) and with TAR Syndrome (RBM8A null allele and noncoding SNP).

The causative mutations of WT and RUS-H Syndromes have yet to be discovered. Genetic analysis of 6 of the 12 families with RUS-H Syndrome did not reveal a HoxA11 mutation. Broader sequencing techniques are underway for all 12 families in our RUS-H cohort, with hopeful detection of a new candidate gene as the unifying causative factor for the abnormalities in limb formation and hematopoiesis.

**Background:** Acute lymphoblastic leukemia (ALL) is the most common childhood malignancy and remains a leading cause of childhood cancer death. At present, there is great interest in utilizing novel genomic approaches such as whole genome sequencing to characterize the genetic alterations that lead to the development of cancer, approaches which to our knowledge have only begun to be applied to the area of childhood leukemia. As pedigrees with familial childhood leukemia (our target subjects, defined as families with more than one member with childhood leukemia) are rare, the International Familial Childhood Leukemia Registry was created as a global registry for eligible families to participate in our study.

**Methods:** Our project is still in the process of comprehensively characterizing the phenotypic and genetic features of leukemia in these pedigrees. Through whole genome sequencing, we will investigate the genetic factors that these index cases share to determine how such genes may be involved in leukemogenesis.



# IL-18-MYD88 SIGNALING AXIS IS IMPORTANT IN THE ATTAINMENT OF A ROBUST VIRUS-SPECIFIC EFFECTOR NK CELL RESPONSE

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**Background:** Cytomegalovirus (CMV), a member of the herpes virus family, is the most common congenital viral infection in the developed world. The clinical manifestation of CMV infection varies upon the host, with significant morbidity and mortality in the neonate and immunocompromised population. Natural killer (NK) cells, sentinels of the innate immune system, are critical in the control of CMV infection in humans and mice. Recent studies have demonstrated that NK cells can become long-lived and can contribute to secondary immune responses similar to members of the adaptive immune system, which may prove to be an advantageous strategy for therapy or vaccination against CMV infection. Pro-inflammatory cytokines, such as IL-18, have been suggested to play an important role in the early response of NK cells to mouse cytomegalovirus (MCMV) infection, although previous studies relied on global ablation of cytokine signaling. Moreover, studies exploring the effects of these pro-inflammatory cytokines on the generation of NK cell memory have not been done. Our work seeks to define the influence IL-18 and its signaling molecule, MyD88, on the activation, expansion, and generation of the long-lived virus-specific NK cell response to MCMV infection.

**Methods:** Using mice deficient in the IL-18R, IL1R, and MyD88 we generated bone marrow chimeric mice and employed an adoptive transfer system to study the role of these signaling pathways in the early and long-term NK cell response against MCMV infection

**Results:** We demonstrate that IL-18 receptor-deficient NK cells exhibit a defect in NK cell expansion following MCMV infection; however, the generation of IL-18 receptor-deficient memory NK cells was unaffected, as IL-18 receptor-deficient and wildtype NK cells were detected greater than 5 weeks following MCMV challenge. NK cells deficient in MyD88, the adapter protein which mediates signaling downstream of the IL-1 and IL-18 receptors, also showed a similar defect in expansion. No defect was observed in IL-1 receptor-deficient NK cells.

**Conclusions:** These data together highlight the importance of an IL-18-MyD88 signaling axis in NK cell priming, and in the attainment of a robust virus-specific effector NK cell response. Understanding the full contribution of inflammatory cytokines and the signals necessary for a protective NK cell response against viral infection will be of interest in the development of vaccines and therapeutics.

# THE NEURAL CORRELATES OF HUMOR IN CHILDREN<sup>1</sup>

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**Background:** Humor is a vital component of human well-being. Neuroimaging studies conducted with adults indicate that humor activates specific brain regions including the temporo-occipito-parietal junction (TOPJ), involved in incongruity resolution, and mesolimbic regions, involved in reward processing. However, no study to date has used neuroimaging to examine humor in typically developing children. Here we illuminate the neural network involved in the detection and appreciation of humor in childhood.

**Methods:** Fifteen typically developing children ages 6-12 were invited to watch and respond to video clips while neural activity was imaged with a 3T GE Discovery MR750 scanner. Prior to presentation during functional imaging, the clips were evaluated by age-matched controls and were representative of three categories: Funny, Positive (enjoyable but not funny), and Neutral (not intended to evoke any emotional response).

**Results:** We found TOPJ and mesolimbic activation in children's response to humor, suggesting these regions may form a humor-essential neural network already present in childhood. Furthermore, in a novel comparison of Funny stimuli to Positive stimuli, we found that bilateral TOPJ activation may be specific to humor processing and not part of a general constellation of neural activity in response to reward. Finally, we observed greater activation in the inferior frontal gyrus and NAcc in younger participants, indicating humor activation intensity changes during development.

**Conclusions:** By providing a crucial link in studying the neurodevelopment of humor processing across the lifespan, our findings contribute valuable information about the evolution of how children understand their world.

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<sup>1</sup> This research was published in The Journal of Neuroscience, 2012 Feb 1;32(5): 1784-1790

# BRAIN MAST CELLS IN NEONATAL HYPOXIA-ISCHEMIA: ISOLATION AND CHARACTERIZATION

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**Background:** Perinatal hypoxic-ischemic (HI) brain damage is a major cause of mortality & chronic neurologic morbidity in infants and children. To date early hypothermia of asphyxiated term newborns is the only effective intervention; there is a need for additional interventions. There is increasing evidence that mast cells (MC) play an integral role in the pathophysiology of HI brain damage, including interaction/activation of microglia, neurons, astrocytes, and oligodendrocytes. MC synthesize and secrete a variety of mediators but the specific phenotype may differ according to the stimulus. Cell-cell interactions and phenotype are best studied *in vitro*; previous studies have relied on MC isolated from gut or bone marrow or MC lines which may behave differently from brain MC. Isolation of MC from rodent brain has not been reported. The objective of these studies was to develop a procedure for the isolation of brain mast cells from the immature rat.

**Methods:** P11 Wistar rats of both sexes were subjected to hypoxia-ischemia (HI), hypoxia alone (H), or control, room air (RA) and sacrificed 18 hrs. later. HI brains were split into contralateral (HC) & ipsilateral (HI) hemispheres. Brains from each group were extracted, weighed and placed in incubation buffer. MC were isolated on OctoMACS Magnetic Sorting Columns with FcRI linked MACS microbeads. Aliquots of MC-rich suspensions were stained with toluidine blue, photographed, and counted. Additionally, an aliquot was stained with CD45, CD11b, and FcR1 and ran of the Becton-Dickinson FACScan for flow cytometry analysis.

**Results:** We isolated  $5.01 \times 10^5$  mast cells/g brain from control, compared to  $1.36 \times 10^7$  /g (H),  $1.67 \times 10^6$  /g (HI),  $1.58 \times 10^6$  /g (HC), supporting our *in vivo* observations of increased brain MC in H and HI. Additionally, flow cytometry analysis of our samples indicated that there was only 10% microglial contamination.

**Conclusion:** To our knowledge this is the first example of mast cell isolation from the immature rat brain. This novel method will allow us to further elucidate the role that MCs play following HI.

# RESEARCH ABSTRACTS

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RESIDENTS, POSTDOCTORAL FELLOWS, FACULTY

# A-TYPE PROANTHOCYANIDINS FROM CRANBERRIES TARGET ACUTE MYELOGENOUS LEUKEMIA STEM CELLS

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**Background:** Acute myelogenous leukemia (AML) is a fatal disease in which the majority of patients relapse and die even after attaining initial complete remission. AML is thought to be initiated and maintained by chemoresistant leukemia stem cells (AML-SCs). Therefore, identifying therapies that can eliminate AML-SCs is a priority. Iron is crucial to normal cell metabolism and plays a role in multiple cellular activities, including promotion of processes required for maintenance of malignancy, such as oxidative phosphorylation, nucleotide synthesis, and Wnt signaling. An important regulator of intracellular iron is ferroportin, an iron exporter.

**Methods and Results:** Using a publicly available gene expression dataset for AML patients (GEO accession #GSE6891), we found that low levels of ferroportin correlate with poor outcomes ( $p = 0.018$ ). We investigated the levels of ferroportin in AML-SCs and discovered that ferroportin levels are significantly lower in AML-SCs than in their normal counterparts ( $p=0.008$ ). Based on these findings, we hypothesized that aberrant iron metabolism may be an important feature of LSC biology that could be targeted by a novel therapeutic agent. To this end, we investigated the activity of known natural products with iron chelation activity in AML-SCs, specifically focusing on proanthocyanidins found in cranberry extracts. Many of the reported health benefits of cranberries, including their antimicrobial functions, are associated with a unique class of proanthocyanidins referred to as A-type PACs (A-PACs). We tested the effects of a commercially available cranberry extract (Cysticran 40; CYS) and A-PACs in 15 primary AML and 5 normal CD34+ cord blood specimens and found potent and specific anti-LSC activity.

Primary AML samples were shown to be highly sensitive to CYS, with a mean LD50 of 180.6  $\mu\text{g/ml}$  (110.2 – 251.1  $\mu\text{g/ml}$ , 95% CI;  $n=9$ ). Purified A-PACs demonstrated even greater potency (mean LD50= 82.51  $\mu\text{g/ml}$ ; 57.07–107.9, 95% CI;  $n=11$ ). The sensitivity to PACs and CYS was also observed in phenotypically described progenitor and stem cell populations from the AML samples. Sensitivity to CYS and A-PACs was not confined to AML with specific cytogenetic abnormalities or known mutations, suggesting potency across AML subtypes. Importantly, we did not observe any overt effects on purified CD34+ cells from healthy cord blood samples. Functional stem cell assays showed ablation of AML-SCs with A-PAC treatment. Specifically, primary AML samples treated with 62.5  $\mu\text{g/ml}$  demonstrated more than 75% decrease in colony forming activity relative to vehicle control ( $n=5$ ). In contrast, there was less than 2 fold decrease in colony formation in CD34+ CB cells treated with 125 $\mu\text{g/ml}$  of PACs ( $n=4$ ). Xenotransplant assays showed significantly decreased human AML engraftment after treatment with 62.5 $\mu\text{g/ml}$  A-PAC (90.6% decreased engraftment,  $n=3$ ,  $p<0.001$ ), while normal CD34+ cells retained engraftment capability in immunodeficient mice ( $n=4$ ).

**Conclusions:** We observed that treatment with CYS and PACs resulted in caspase-3 activation, evaluated by immunoblots and flow cytometry. Furthermore, pre-treatment with antioxidants or holo-transferrin partially protected AML cells from A-PAC induced cell death ( $p<0.01$ ). In addition, A-PAC treatment induced changes in cellular iron metabolism and increased ROS levels. Interestingly, gene expression analysis revealed that A-PACs upregulated chemokine and NF- $\kappa\text{B}$  pathways ( $p= 1.2 \times 10^{-5}$ ), which is uncharacteristic of anti-LSC compounds discovered to date and suggests a novel mode of AML-SC ablation that bypasses NF- $\kappa\text{B}$  signaling to achieve AML-SC ablation. Together, our results suggest that cranberry A-PACs represent a novel class of compounds with therapeutic potential to ablate leukemia stem and progenitor cells, with minimal effects on normal hematopoietic stem cells.

## IMPLEMENTATION AND UTILITY OF MENTAL HEALTH SCREENING

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**Background:** Mental health (MH) conditions are more prevalent than chronic physical conditions, yet often unrecognized. Validated screening tools are feasible in pediatric practice and increase recognition of MH concerns. Yet they are rarely used and implementation studies are few. HEADSS assessments are routinely used with adolescents; accuracy has not been compared to MH screens.

**Objective:** To assess implementation of MH screening and compare screens to routine HEADSS assessment in detecting MH problems in adolescents.

**Design/Methods:** A retrospective chart review of all patients aged 12 to 19 years was conducted in an urban academic pediatric clinic 1 year after universal screening was implemented. The PSC-Youth Report (PSC Y) was implemented for all patients 13-19 years of age. The Patient Symptom Checklist (PSC 17) was used for patients 12 and below. A score of 30 (of 37 items) is positive score for MH referral for the PSC-Y while 15 a positive screen for the PSC 17. Elevated scores on subscales for internalizing, externalizing, and attention disorders can also indicate a MH issue. The HEADSS (Home, Education, Activity, Drugs, Sex, Suicide) assessment was completed during patient visit. A HEADSS assessment was considered positive impairment if any category was endorsed.

**Results:** 327 charts were reviewed. Average age of subjects was 14 years. Only 41% of subjects received screening. 52% of those screened had results documented in the medical record. HEADSS assessment was administered to 95% of subjects. 42% of HEADSS were positive; 12% were positive for the MH question. MH screen total score was positive in 6% of cases; an additional 3% were positive in at least 1 subscale. Using screening tools as a standard to evaluate HEADSS, sensitivity was 67%, specificity 63%, PPV 11% and NPV 97%. HEADSS was inadequate in detecting internalizing (75% missed), attention (100% missed), and externalizing symptoms (33% missed). Unfortunately only 50% of positive screens had appropriate referrals made.

**Conclusions:** Standardized MH screening instruments increased recognition of MH issues compared to HEADSS assessment among adolescents. Screens were administered at low rates during practice acclimation to a new initiative and increased recognition only lead to a referral 50% of the time. Although use of a screening tool involves challenges, efforts to increase rates of screening are essential, as HEADSS assessment alone missed one-third of patients with MH issues.

## RESIDENT ATTITUDES, KNOWLEDGE AND EXPERIENCE WITH COMMUNITY PEDIATRICS

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**Background:** Academic pediatric societies including the Academic Pediatric Association and the American Academy of Pediatrics, as well as the Accreditation Council of Graduate Medical Education endorse residency training in community pediatrics to develop essential skills to effectively engage in communities outside of traditional medical settings. Pediatric residents' knowledge of the communities they serve has been previously shown to be limited; their comfort in community settings and attitudes towards their training in this arena are not well described.

**Objectives:** Describe pediatric residents' attitudes, knowledge and experiences regarding community pediatrics.

**Design/Methods:** Web-based, self-administered survey of pediatric residents in a medium-sized urban academic training program. Small incentive provided. Survey questions assessed demographics, attitudes, knowledge, and behaviors regarding community pediatrics. Chi square analysis was used.

**Results:** N = 52, Response rate = 83%, Resident providers: 32% PGY-1, 36% PGY-2, 30% PGY-3. Resident continuity clinics: 95% government insured. Career plans: 58% sub-specialty, 39% general pediatrics. 94% of residents reported comfort (13% strongly agree) counseling children and families in community-based settings, 74% described adequate training (8% strongly agree). Knowledge of community metrics was low; for example: 34% knew the percentage of children in the state living below poverty line (13% underestimated, 51% overestimated). Experience in the community varied widely: 70% had not participated in parent group discussions, 41% had not participated in community health screening activities, 39% had not previously given a talk in the community. Resident attitudes, knowledge and experience did not vary by planned career choice or by year of training.

**Conclusions:** Most residents reported comfort with counseling children and families in community-based settings and felt they received adequate training. Despite these attitudes, resident knowledge regarding their community was low and their level of community experience was limited. These data highlight the importance of further research designed to assess experiential learning strategies that may close the gap between residents' attitudes and knowledge of the communities they serve.

**Support:** AAP/Met Life Community Pediatrics Training Initiative Obesity Prevention Residency Training Funds



# THE USE OF SONOGRAPHIC MEASUREMENT OF OPTIC NERVE SHEATH DIAMETER TO PREDICT RAISED INTRACRANIAL PRESSURE IN CHILDREN WITH VENTRICULOPERITONEAL SHUNTS

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**Background:** Children with ventriculoperitoneal shunts (VPS) require frequent radiologic imaging to assess for elevated intracranial pressure (ICP) when shunt malfunction is suspected. Computed tomography (CT) is the preferred imaging technique, and thus children with VPS incur increased lifetime exposure to ionizing radiation. The role of radiation exposure in developing fatal malignancies is well reported in medical literature. Bedside sonography of the optic nerve sheath diameter (ONSD) has been shown to predict elevated ICP in adult patients. Optic nerve (ON) sonography provides a portable, rapid, non-invasive modality, with no ionizing radiation exposure. There are limited studies on the use of ON sonography to predict elevated ICP in children. None have specifically examined this measurement in children with VPS in the emergency setting.

**Objective:** Our objective was to evaluate the accuracy of physician-performed bedside sonographic measurement of ONSD to predict elevated ICP in children with suspected VPS malfunction in the pediatric ED.

**Design/ Methods:** We included all children age 0-21 years with suspected VPS malfunction presenting to an urban pediatric ED from January 2011 to present who required an imaging study. We excluded subjects with ocular or facial trauma, ON disease, unstable vitals or requiring emergent neurosurgery. A cohort of pediatric emergency physicians underwent a standard training session in ON sonography. Trained physicians performed bedside ON ultrasound on eligible subjects. ONSD was measured twice and the average diameter recorded. We defined (+) US (elevated ICP) as ONSD > 4mm in subjects < 12 months, and > 4.5mm in subjects  $\geq$  12 months of age. We compared US findings to a gold standard for elevated ICP (head CT or MRI). We recorded practitioner clinical impression for VPS malfunction prior to ON ultrasound.

**Results:** We studied 23 subjects in this pilot study as shown in tables.

**Table 1:** Sensitivity 100%; Specificity 57%; PPV 18%; NPV 100%.

	(+) ICP	(-) ICP
(+) US	2	9
(-) US	0	12

**Table 2:** Sensitivity 50%; Specificity 60%; PPV 11%; NPV 92%.

	(+) ICP	(-) ICP
(+) Clinical Impression	1	8
(-) Clinical Impression	1	12

**Conclusions:** Optic sonography was more accurate than clinical impression in predicting elevated ICP in children with suspected VPS malfunction. It may be a useful screening tool in the emergency setting to guide who does not require CT imaging.

# THE CLINICAL IMPACT OF THE REVISED 2011 AAP GUIDELINES FOR UTI IN FEBRILE INFANTS

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**Background:** In 2011, the American Academy of Pediatrics (AAP) released clinical practice guidelines (revised from 1999) for the diagnosis and management of urinary tract infection (UTI) in febrile children age 2 to 24 months. These revisions may impact future care and practice in the emergency setting.

**Objective:** Our objective was to compare the evaluation of UTI in febrile children based on the 2011 AAP guideline to the previous standard approach based on the 1999 guideline.

**Design/Methods:** We performed a review of children age 2 to 24 months who presented to an urban pediatric ED from January 1, 2007 to present with a diagnosis of UTI or suspected UTI (fever and urine test) identified by ICD9 codes. We excluded subjects <2mos of age, no fever, no urine test, urogenital abnormality or surgery, immunosuppressed or with an underlying medical condition. We recorded clinical parameters for eligible subjects; vital signs, fever history, gender, ethnicity, circumcision status, urinalysis, urine culture results and treatment.

We compared whether subjects who met criteria to be tested for UTI would be tested based on the revised 2011 guideline, that recommends urine testing only for children determined to be at >2% risk of UTI. We also categorized patients as having a positive or negative UTI based on both the 1999 definition (>105 cfu) and the 2011 definition (>5x10<sup>4</sup> cfu and pyuria), and examined whether the 2011 guideline would modify the care plan.

**Results:** We reviewed 363 medical records and identified 131 eligible subjects.

Table 1 illustrates 77/109 (71%) subjects who met criteria for UTI testing based on 1999 guideline would have been tested based on 2011 guideline. Thus, 29% would not have been tested in 2011.

	(+) Testing 1999	(-) Testing 1999
(+) Testing 2011	77	0
(-) Testing 2011	32	0

Table 2 illustrates 103/128 (80%) overall agreement between 1999 and 2011 definition of UTI. There is 74/78 (95%) agreement for (-)UTI, but only 29/50 (58%) agreement for (+) UTI. Thus, 42% defined as having UTI based on 1999 guideline would not have met criteria for UTI based on 2011 guideline. Of these 21 subjects, the mean age was 12 mos, and all 21 had no pyuria on urinalysis.

	(+) UTI 1999	(-) UTI 1999
(+) UTI 2011	29	4
(-) UTI 2011	21	74

**Conclusions:** There are substantial variances in both testing and treatment recommendations in this cohort of subjects with UTI based on the 1999 AAP guidelines when the 2011 guidelines are applied.

## ACCURACY OF COMMUNITY DIAGNOSIS OF AUTISM SPECTRUM DISORDER

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**Introduction:** The importance of accurately identifying individuals with autism has never been greater, particularly given the growing prevalence, considerable family and societal costs, and recognized importance of early diagnosis and intervention. Accurately diagnosing autism is of utmost importance also in the research of autism, since inaccurate diagnosis could lead to erroneous implications. We used the Autism Diagnostic Observation Schedule (ADOS) as a validated tool to examine the accuracy of community Autism Spectrum Disorder diagnosis (ASD).

**Methods:** 70 subjects (average age of 7.1 years, range 2.3 to 16.5 years), with reported diagnosis of Autism Spectrum Disorder were evaluated using the ADOS. 66 Subjects were evaluated using module 1, 2 or 3 and were included in our analysis. An assessment of non-verbal intellectual ability using the DAS (differential ability scale), as well as the Vineland Adaptive Behavior Scales, Second Edition (Vineland-II) were also performed.

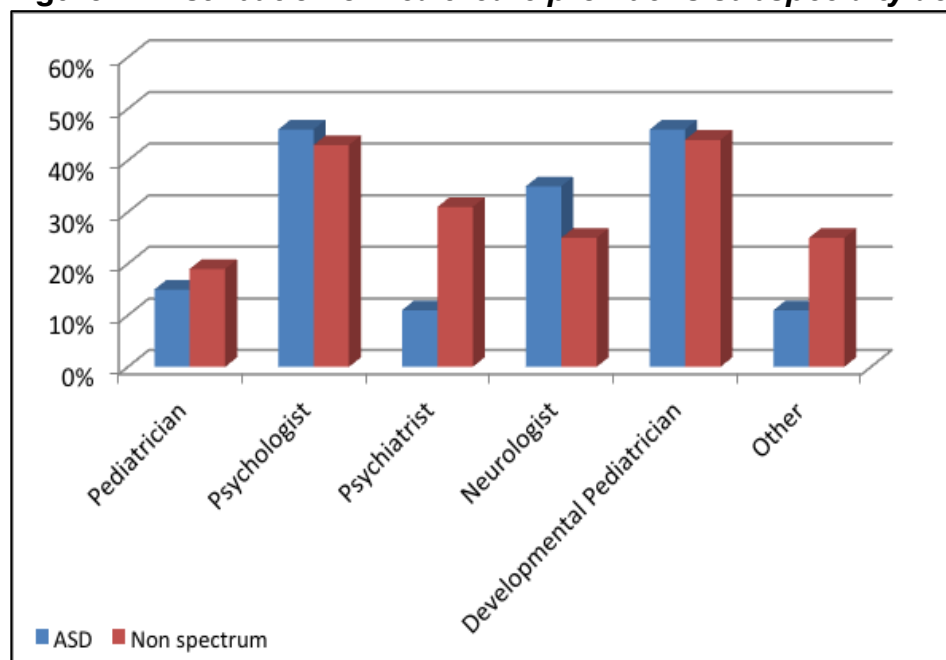
**Results:** 49% of the sample was reported to have a diagnosis of PDD-NOS, 43% was reported to have a diagnosis of Autism, and 8% was reported to have a diagnosis of Asperger syndrome. 23% of subjects who received a community diagnosis of Autism, PDD-NOS or Asperger, were classified as non-spectrum on the ADOS. Non-spectrum and spectrum subjects did not differ on age. Subjects enrolled with community diagnosis of PDD-NOS were significantly more likely to be classified as non-spectrum on the ADOS than subjects with diagnosis of autism or Asperger (38% versus 10%,  $p < 0.05$ ). Language impairment was the most common Overall Diagnosis in the non-spectrum group (68%). Calibrated Severity Scores differ significantly among the 3 groups ( $p < .001$ ). Post-hoc analyses indicated that non-spectrum subjects received the lowest CSS, whereas autism subjects received the highest CSS. ( $1.8 \pm 1.1$  versus  $8.3 \pm 1.4$ ,  $P < 0.001$ ). CSS was efficacious in predicting ADOS outcome (positive predictive value of 100%, negative predictive value of 93%). Non-verbal IQ scores were higher in the non-spectrum group compared to the ASD group. ( $105.9 \pm 26.5$  vs.  $81 \pm 21$ ,  $P = 0.009$ ). No difference in Vineland Scores was demonstrated between groups.

**Conclusion:** We demonstrated high rates of inaccurate ASD community diagnosis as confirmed by ADOS. These findings suggest that community diagnosis of ASD, which maybe dated or based on inadequate data, may not be accurate enough to serve as the basis for enrolling subjects into research studies. Parent reports of PDD-NOS appear to be particularly unreliable.

**Table 1- subject characteristics**

Diagnosis based on ADOS	Autism / Autism Spectrum Disorder	Non spectrum	P value
No. of subjects	54	16	
Male sex % (N)	90% (49)	68%(11)	
Age of first concern (months)	17.34± 9.9	17.33± 7.4	NS
Age at evaluation (months)	87.4± 49.4	88.1± 67	NS
Health care provider who made the diagnosis:			
Pediatrician	15%	19%	
Psychologist	46%	43%	
Psychiatrist	11%	31%	
Neurologist	35%	25%	
Developmental pediatrician	46%	44%	
Other (OT, PT)	11%	25%	
Non Verbal IQ	81± 21	105.9± 26.5	0.009
Vineland adaptive behavior composite score	66.2 ±12.6	74.2± 10.8	0.02
Vineland Communication Standard Score	73.2 ± 12.1	75.6 ± 16.1	NS
Vineland Socialization Standard Score	65.3 ± 10	66.7 ±11.2	NS
Vineland Daily living skills Standard Score	71.7±14.7	69.4±11.9	NS
Comparison Score	7.8 ± 1.6	2.19 ± 1.86	<0.000

Data are presented as mean ± SD. NS= non-significant

**Figure 1- Distribution of healthcare provider's subspecialty according to Diagnosis**

**NOTE:** Data did not include: Community evaluation included the following: ADOS (26%), WISC-III or WISC-IV (8.5%), ADI-R (4.3%), Stanford-Binet test (7.1%), Vineland Adaptive Scale test (30%), chromosomal testing or CGH (24%), fragile x testing (15.7%), 15/70 had an additional diagnosis besides ASD.

# THE INFLUENCE OF GESTATIONAL AGE ON SERUM CALCIUM, PHOSPHATE AND MAGNESIUM LEVELS

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**Background:** Calcium (Ca), phosphate (PO<sub>4</sub>) and magnesium (Mg) are essential for bone mineralization and basic cellular functions. Premature infants are at increased risk for electrolyte abnormalities secondary to incomplete nephrogenesis and immature renal function. Currently, normal values based on gestational age (GA) do not exist.

**Objective:** To determine whether serum Ca, PO<sub>4</sub>, and Mg levels vary with GA or maternal factors. Hypothesis: Infants of lower GA will have lower levels of Ca but higher levels of PO<sub>4</sub> and Mg.

**Methods:** Retrospective chart review (n=226) of all infants admitted to the Neonatal Intensive Care Unit (NICU) from December through June 2010. Exclusion criteria included asphyxia, congenital anomalies and outborn infants. Data collected included: GA, birth weight (BW), Ca, PO<sub>4</sub>, & Mg at 24-48hrs of life, and maternal magnesium administration.

**Results:** Mean GA was  $33.1 \pm 1.6$  weeks and BW  $1915.7 \pm 743.7$  grams. Mean Ca was  $8.22 \pm 0.78$  mg/dL (albumin adjusted Ca  $9.28 \pm 0.78$  mg/dL), PO<sub>4</sub>  $5.78 \pm 0.97$  mg/dL and Mg  $1.81 \pm 0.63$  mg/dL. When cohorted into groups based on GA, there was a negative correlation between PO<sub>4</sub> and Mg levels and GA. There was no significant difference in Ca among the groups. [table1] 89.4% and 52.8% of infants 24-27 and 28-31 weeks, respectively vs 24.7%, 22.6% and 11.5% for infants 32-34, 35-37 and >37, respectively had exposure to maternal Mg infusion.

**Conclusions:** PO<sub>4</sub> levels decrease with increasing GA. Mg levels are influenced by maternal Mg exposure and the observed change may not be related to GA. Ca levels are unaffected by GA, although there is a trend for increasing values with increasing GA. This data suggest that clinicians should expect higher PO<sub>4</sub> levels with increasing degrees of prematurity, and low phosphate levels in extreme prematurity are atypical and require a thorough evaluation.

**Figure1**

GA (wks)	Mean Ca (mg/dL)	Mean PO <sub>4</sub> (mg/dL)	Mean Mg (mg/dL)
>37 (n=23)	8.29	4.99	1.42
35-37 (n=31)	8.33	5.42	1.61
32-34 (n=103)	8.22	5.99	1.63
28-31 (n=51)	8.23	5.68	2.32
24-27 (n=18)	7.98	6.45*	2.28*

\*P= <0.001

# PEDIATRIC INTEREST GROUPS

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## and FIELD PROGRAMS

# Big Buddies Program

**Christopher Robinson**

The Big Buddies Program is a student-run program that matches individual Weill Cornell medical students with a child or teenager from New York City Community. While the children may have ongoing medical needs, the focus of the program is for the medical student to serve as role model and mentor. The interactions give program participants an opportunity to see the students without their white coats and stethoscopes and the medical students the chance to see their Little Buddies as individuals rather than patients. Big Buddies have the opportunity to spend one-on-one time with their Little Buddies or participate in group events.

The activities are guided by the Big Buddy/Little Buddy pair, and are meant to meet their unique interests. The relationship of the pair develops over the year, as they meet up about once a month, as well as keep in touch via phone calls and email. Examples of past activities are trips to sporting events or the zoo, picnics, skating in Central Park, and trips to the movies. Group events have included Halloween and Thanksgiving parties.

From both pair activities and group events, the pairs come away with more than just a good time: The Little Buddies benefit from having a caring adult to look up to and confide in, as well as someone to share their love (or loathing) of the Yankees, their passion for Pokemon, or their dislike of algebra. Much of medicine is taught through a mentor/mentee system, with those who have less experience learning from those with more, the Big Buddies program provides a fun opportunity for students to practice being a mentor, to learn to listen carefully, and be a sounding board for a young person's ideas, while also providing guidance and support. It is a chance to put down the textbooks and connect with others, establishing relationship that can leave a lasting impression on all involved.

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# Camp Phoenix

Molly Ketcham and Pat Maher

Every year, almost one million American children are burned. Fortunately, advancements in trauma and resuscitative care have improved the treatment and survival of these young patients. Despite these medical and surgical advances, the psychosocial care of pediatric burn victims continues long after discharge. These children often return home with scars as permanent reminders of their trauma and the aftermath of surviving a serious burn usually includes considerable stress, diminished self-esteem, and difficulty creating positive social relationships. Camp Phoenix, the first burn camp in the United States run by medical students, was founded in 2000 by Paul Mullan, a 2004 Graduate of Weill Cornell Medical College. Since then, Camp Phoenix has provided a safe environment for pediatric burn survivors and their siblings to interact with their peers and share their experiences.

Camp Phoenix sponsors three one-day events and one overnight camping trip each year. Past events have been held at the Intrepid Museum, the Bronx Zoo, Lucky Strikes Bowling, Sony Wonder Technology Lab, Chelsea Piers, New York Knicks games, the Museum of Natural History and NYC Firehouses, amongst many others. We have worked with over 250 children at these events, with an average of 30 campers and 25 volunteer counselors at each event. Camp Phoenix activities are designed to build confidence, emphasize teamwork, initiate friendship, and maximize fun.

Last June, a group of almost 80 campers and volunteer counselors spent an incredible three days at Camp Glen Spey in Port Jervis, NY. The overnight camping trip is always especially memorable. Campers are introduced to new activities such as rope courses, archery, canoeing, and hiking. For many of our campers, this is their first time away from home and outside of an urban setting. Campers are divided into cabins, where they work together and quickly develop their sense of community and camaraderie. They create cabin names and cheers and group enthusiasm is rewarded as the cabins participate in one of Camp Phoenix's favorite traditions, the Messy Olympics. Campers compete for cabin pride in games such as the "Human Ice Cream Sundae," and "Spaghetti Speed Race."

In addition to helping the campers and their families, Camp Phoenix offers a unique educational experience for the medical students involved. Our volunteers serve as mentors for children with a range of medical and psychosocial issues, allowing them to hone their skills as leaders, role models, and caretakers. Positive experiences at the day events and overnight camp weekend have inspired many volunteers to develop interest in Pediatrics and Burn Surgery.

Camp Phoenix aims to give future physicians opportunities outside of the classroom to better appreciate the art of compassionate and empathetic care for complex patients. Started in 2011 our shadowing program allows medical students to spend time with the pediatric team in the burn unit. We expect to enhance this shadowing program further with the 2013 implementation of burn surgery shadowing. These experiences will help students learn about the inpatient and surgical experiences of our campers and relevant psychosocial issues. These experiences are meant to educate all interested students about what our campers went through during the rehabilitation phase of their burn care and to have any questions and concerns fully addressed by experts.

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# Chemistry for Kids

**Christopher Robinson**

Chemistry for Kids exists to give underprivileged young students the opportunity to experience science in fun and exciting ways. We hope that through our interactive experiments, we can provide young students an avenue to explore their interests in science, and inspire them to become future scientists and doctors. Overall, our main priority is to show students that science can be fun!

# The Heads Up! Pediatric Literacy Program

**A Project of the Weill Cornell Medical College Department of Pediatrics,  
Division of Child Development**

Economic disadvantage and limited parental education mean that children born into poverty are susceptible to delays in language development. These children routinely lag behind their peers before pre-school or kindergarten even begin.<sup>1</sup> In most cases, this gap continues to widen in elementary and middle school as children with poorer educational foundations fall further below school standards. Weakness in language and reading skills can lead to poorer educational and health outcomes, such as school failure, low self-esteem, troubled behavior, and substance abuse.<sup>2</sup> In contrast, recent studies have shown that reading aloud to children from early on in life has positive effects on children's language and pre-literacy skills.<sup>3</sup>

In an effort to improve early literacy, the Heads Up! Pediatric Literacy program has initiated a mild intervention mediated by pediatric primary care physicians. Doctors are the professional constituent with the most access to children and parents before school begins. By having physicians alert parents to the need to read to their young children—and by giving an age-appropriate book as part of the physical exam—we make the promotion of early language and literacy development a standard part of primary pediatric care.

Beyond encouraging language development and school readiness, books can also be used for assessment in the exam room. Books can help physicians see whether a four month-old reaches for objects or if a child who moves to accept a book has a normal gait. At some sites, including WCMC, trained volunteers help children select more books and conduct parent outreach in the waiting room. Heads Up! targets pediatric clinics that serve needy populations. At all of our 12 clinic sites—pediatric outpatient clinics affiliated with WCMC, Lincoln Hospital, St. Barnabas Hospital, Methodist Hospital, and New York Hospital Queens—at least 85% of patients qualify for Medicaid. In 2010-2011, Heads Up! distributed 40,391 brand-new books and corresponding literacy guidance to nearly 20,000 children.

Books are purchased using funding from two sources. Every year Heads Up! renews a grant with Reading Is Fundamental (RIF), in which RIF promises to pay over 75% of our book purchases provided Heads Up! spends the stated budget. In 2011-2012 the RIF book-purchasing budget is \$129,938. Of this, Heads Up! is required to provide only \$28,050 in “matching” funds, most of which is obtained through private donations, corporate gifts, or hospital auxiliary funds. The program also receives support from Reach Out and Read, which helps us secure additional books.

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# Health For Life

**Reya Liili**

Health for Life is a program run by the NYPH Department of Pediatrics that works with overweight children. A team of pediatricians, physical therapists, social workers, nutritionists, and medical student volunteers help children and teens ages ~9 - 18 learn about how to lead a healthier life. The 10 week program has 2 major components: exercise and nutrition. During the exercise sessions, participants discover fun new ways to incorporate physical activity into their lives. As part of this, all participants receive pedometers that they carry around for the duration of the program. The nutrition sessions focus on learning about which foods are healthy and which ones should be eaten only rarely, and how to change dishes you like.

Each medical student volunteer is paired with a program participant. In addition to attending the weekly nutrition sessions, mentors help their mentees stay on track with the program by offering encouragement and advice through weekly phone conversations between sessions. In return, volunteers get to be role models and make an impact on a child's life, and have a great time!

**Faculty Advisor:**

Maura Frank, MD

# Health Professions Recruitment & Exposure Program (HPREP)

**Zebib Abraham, Reya Liilii, Avinash Maganty, and Yoanna Pumpalova**

The Health Professions Recruitment & Exposure Program (HPREP) is part of the Pipeline Mentoring Institute of the Student National Medical Association (SNMA). HPREP aims to expose high school students from underrepresented minorities to science, medicine and the health professions. The overarching goal is to encourage minority students to pursue a career in medicine. During the three month after school program, the students attend a variety of lectures, participate in an anatomy lab dissection, receive assistance on their college application and essay, write a research paper on a topic of their choice and build a lasting relationship with a medical student mentor. We typically accept 80 high school students every year and engage 40 medical students from across all classes to be mentors and role models for the high-schoolers. This program began here at Cornell and has subsequently spread to many other medical colleges around the country.

# Kids in Chronic Care Support (KICS)

Eileen Koh and Michelle Neely

KICS is a student run program with the New York Presbyterian department of pediatric hematology/oncology that creates one on one matches between Weill Cornell medical students and children or adolescents currently receiving therapy. The focus of the program is to provide support for the children and their families; it gives the kids an opportunity to form a close, consistent relationship with someone outside of their treatment team. The pediatric oncology team interviews medical students and personally matches them with patients interested in having a buddy. Once a patient is matched, the student will make the initial contact with the patient during a clinic visit. After this, matches can spend time together whenever it is best for both, this can be during hospital visits or outside of the hospital. The relationship really develops on their own terms.

For the kids, the hospital can be an intimidating place associated with pain, sickness, and not to mention the terrible effects of chemotherapy. Medical students can help make it just a little better by having fun with the kids. Knowing they get to meet up with their match, play a game of Connect Four, or paint with watercolors might just make the hospital a little friendlier. Especially in pediatrics, the diagnosis of cancer can have a major impact not only on the patient but also on the patient's family. For parents, KICS can take just a little of pressure off of the situation and give them a needed break. For the medical students, the opportunity gives them insight into what it is like to be a child with a severe chronic illness.

The program is currently being restarted and is slowly but surely rebuilding to its previous state. Past members of the program have had positive experiences and spoke highly:

*"At first I thought, he's on chemo, I'm going to feel bad for him. But although his illness was always in the background that wasn't all there was to him, and you can lose sight of that when you're a doctor. You can forget the humanistic side, putting a person in the context of their life."*

*"It's nice for the kids to have someone who's relatively young; not their parent or a sibling, just somebody who wants to hang out with them. It distracts them from their treatment. We're medical students, but we're not there for any medical purpose... We just want to talk to them and have a little fun."*

*"In the first two years you spend so much time learning basic sciences, it can be a real drag. Being able to take yourself out of that, to put a face to what you're doing, really motivates you."*

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# Komansky Center Initiatives

## Family Advisory Council

The Komansky Center Family Advisory Council (FAC) is a group of dedicated parents and family members of pediatric patients who are committed to working with Komansky Center hospital staff and administration to provide family-centered care to all patients. Our vision is to achieve a level of care where patient and family involvement is expected and welcomed by all. Among the Council's many current initiatives are:

### ***Family Education and Orientation Workgroup***

The goal of the Workgroup is to improve care while at the hospital by helping patients' families and Hospital staff communicate more effectively. The *Family Education and Orientation Workgroup* tries to identify ways to 1) Orient family members to the Hospital with written and verbal communication tools; 2) Enhance communication skills of new and current Hospital staff members; 3) Improve communication between Hospital staff and families and, d) Revise preoperative procedures for outpatient surgeries.

### ***Family Experience Workgroup***

A child's stay in the hospital is often very stressful for his or her family. *The Family Experience Workgroup* is committed to creating a pleasant environment for patients and their families. Workgroup members identify different ways to improve and expand the infrastructure and recreational services currently offered at the Hospital. Recent activities have included distribution of gifts during the holidays, participation in the Thanksgiving festivities hosted by Child Life, and engaging local school children to create holiday cards for hospitalized children.

### ***Family Support Workgroup***

By sharing experiences, families can help each other through a tumultuous and traumatic time. The *Family Support Workgroup* is committed to identifying ways to provide support to families and to managing that support systematically. *Family Support* is focused on three areas: 1) The development of a resource center for families; 2) the creation of a parent-to-parent directory; and 3) the development of a mentoring program so that current families can seek advice from families who have "graduated" from the hospital.

### ***Family Faculty Program***

The *Family Faculty Program* works with hospital staff and administration to incorporate FAC parents in orienting and educating new residents on the topic of family-centered care. FAC parents help residents learn by sharing their own stories within the healthcare system. The *Family Faculty Program* hopes to expand their activities to student education.

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# Motivating Action through Community Health Outreach (MACHO)

Crystal Castaneda, Nicole Ramsey

Overview: Motivating Action through Community Health Outreach (MACHO) is a Weill Cornell Medical College student-led, community-centered response to the alarmingly increasing rate of childhood obesity, particularly within minority and socioeconomically disadvantaged communities. We target East Harlem children ages 7 to 13 with the goal of establishing healthy nutritional, fitness, and personal habits early in life to encourage children to achieve their fullest potential.

Mission: The goal of MACHO is to empower youth with the knowledge and practical tools to take control of their health and their lives through proper nutrition, fitness and personal development. We aim to accomplish this goal by:

*Motivating Action by building a community of empowered youth* through dissemination of information that inspires the adoption of healthy living habits,

*Motivating Action by pursuing a holistic, adaptive, and individualized approach* towards addressing poor nutrition and sedentary lifestyles, and

*Motivating Action by partnering with community organizations to build a supportive network* of empowered individuals and families.

History: MACHO was established in the fall of 2009 by a handful of Weill Cornell Medical College students who recognized the desperate need for education and resources to fight the obesity epidemic. By pairing with Settlement Health, a nonprofit community health center in East Harlem, MACHO initiated a pilot-phase program to teach kids how to make healthy nutrition and fitness choices within their community. The pilot program met once a week for ten weeks. In 2010-2011, the program was expanded to a full-year curriculum that met once a week during the school year and every day in the summer. The scope of MACHO was broadened to include a pilot mentoring program, educational field trips, and assessments to track knowledge and fitness progress. The lessons from the first three years have served as a foundation for the revamped organization and new initiatives for the 2012-2013 year.

Program: The structure of the curriculum consists of biweekly after-school sessions coupled with a weekend mentoring and personal development component. For the after-school program, our volunteer graduate and undergraduate teachers lead the nutrition, physiology and exercise classes with the help of teaching assistants, who include high school students and former program participants. The Mentor program includes our personal development curriculum, where we use a multi-generational group-mentoring model: mentor teams are composed of college students who mentor high school students, who then serve as mentors to our middle school and elementary school participants. The mentor teams work on group projects to be presented at the end of each semester based on a specific theme surrounding health.

Day 1			Day 2			Day 3		
Snack + HW	Exercise	Nutrition	Snack + HW	Exercise	Physiology	Exercise	Group Project	P.D. Curriculum

For the 2012-2013 year, we run sessions at St Marks the Evangelist School in Harlem and the Silberman School of Social Work at Hunter College. We have 40 participants, ages 7 to 13 and guardians.

Members: MACHO volunteers include students from WCMC, Cornell University, Columbia University, Hunter College, high school students from Cristo Rey High School in East Harlem, and young professionals. We are overseen by faculty advisors from New York-Presbyterian Hospital Pediatrics department, WCMC, Hunter College, and Hunter School of Public Health and Social Work. Our community health outreach partners include the Boys' Club of New York, Settlement Health, Harlem Center for Healthy Living, and Choosing Healthy and Active Lifestyle for Kids (CHALK)

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**Motivating Action  
through  
Community Health Outreach**



**Empowering our Youth.**



# MENTORING AND RESEARCH --- OPPORTUNITIES IN PEDIATRICS

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# RESEARCH OPPORTUNITIES IN PEDIATRICS

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Field(s) of Interest: Pediatric hospitalist and outpatient medicine, health services research, healthcare safety and quality research

Research Title: Health services research, healthcare safety and quality research

Project Description: Medication Safety

I am working on several studies looking at improving outpatient medication safety. One involves studying the impact of electronic prescribing on medication safety among community providers in New York State. Another involves improving patient safety for patients transitioning from the inpatient to the outpatient setting.

Students' Role in the Projects:

Students will learn how to consent patients, perform structured interviews in the hospital, and perform follow-up phone calls using surveys to detect whether a patient has experienced harm from a medication. Students would have the opportunity to participate in research team meetings where we discuss study design, data collection, analysis and manuscript writing.

Preferred Experience: None required

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**Adele Boskey, Ph.D.**

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Field(s) of Interest: Mineralization, matrix formation, bone development and repair.

Research Title: Mineral analysis in bones of animals with developmental abnormalities

Project Description: The goals of one of the major projects in this laboratory is the determination of how matrix proteins regulate biomineralization. As such we study the effects of these proteins in solution, in culture, and when they are ablated or over expressed in transgenic animals. The project would be based on one of the models currently under investigation, where the student would do the histology, and work on the infra red imaging analysis of the bones of animals of different ages.

Students' Role in the Project: Infrared and microCT analyses of bones and teeth of a specific KO or TG animal. Student will learn about the ablated protein and perform IR Imaging and microCT

Preferred Background/ Experience: Student should have computer skills

### References:

- Mochida Y, Parisuthiman D, Pornprasertsuk-Damrongsri S, et al. Decorin modulates collagen matrix assembly and mineralization. *Matrix Biol.* Nov 18 2008.
- Boskey AL, Roy R. Cell culture systems for studies of bone and tooth mineralization. *Chem Rev.* Nov 2008;108(11):4716-4733.
- Verdelis K, Ling Y, Sreenath T, et al. DSPP effects on in vivo bone mineralization. *Bone.* Aug 16 2008.
- Boskey AL, Spevak L, Weinstein RS. Spectroscopic markers of bone quality in alendronate-treated postmenopausal women. *Osteoporos Int.* Sep 4 2008.
- Gourion-Arsiquaud S, West PA, Boskey AL. Fourier transform-infrared microspectroscopy and microscopic imaging. *Methods Mol Biol.* 2008;455:293-303.
- Ward DF, Jr., Williams WA, Schapiro NE, et al. Focal adhesion kinase signaling controls cyclic tensile strain enhanced collagen I-induced osteogenic differentiation of human mesenchymal stem cells. *Mol Cell Biomech.* Dec 2007;4(4):177-188.
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### **James B Bussel, MD**

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### Field(s) of Interest: Hematology/ Oncology

- *Antenatal Management of Fetal Alloimmune Thrombocytopenia*
- *Experimental treatments of Refractory ITP*

Project Description: Diagnosis, counseling, and entry into a multi-center randomized clinical trial. We design and coordinate this study, which is intended to prevent intracranial hemorrhage from immune thrombocytopenia in fetuses and neonates by administering treatment to mothers while they are who have a platelet antigen incompatibility with their husbands.

Children and adults with difficult to treat ITP are enrolled on treatment protocols of various agents including thrombopoietic agents, anti-CD20 including standard and augmented versions, anti-D, IV gammaglobulin, and inhibitors of syk and other novel agents. All of the studies have various research components (collaborative laboratory studies) connected with them.

### Students' Role in the Project:

A) Helping to collect data. This entails contacting other centers to ensure that the various components of the trial are sent to us: consents and IRB paperwork; infusion related data, lab work (maternal data and fetal sonos), and follow up information on the neonates and infants. B) Helping to analyze the data that has been collected. C). Design and contribute to special projects related to AIT study.

1. Monitor the individual ITP patients to ensure that their visits and studies occur as per protocol and that the appropriate information is collected.
2. Help to develop new studies connected with individual protocol agents and/or help to develop novel studies of new agents .
3. Ongoing analysis of data to determine progress with protocols.
4. Facilitate laboratory studies by pulling freezer specimens to be batched and sent off

Preferred Background/ Experience: None requested



References:

Bussel Kuter et al AMG531 Treatment of ITP NEJM, 10/20/2006  
Bussel JB, Cheng G, Saleh MN, et al. Eltrombopag for the treatment of chronic idiopathic thrombocytopenic purpura. N Engl J Med. Nov 29 2007;357(22):2237-2247.  
Scaradavou A, Cunningham-Rundles S, Ho JL, Folman C, Doo H, Bussel JB. Superior effect of intravenous anti-D compared with IV gammaglobulin in the treatment of HIV-thrombocytopenia: results of a small, randomized prospective comparison. Am J Hematol. 2007;82(5):335-341  
Psaila B, Bussel JB. Fc receptors in immune thrombocytopenias: a target for immunomodulation? J Clin Invest. Aug 2008;118(8):2677-2681.  
Kuter DJ, Bussel JB, Lyons RM, et al. Efficacy of romiplostim in patients with chronic immune thrombocytopenic purpura: a double-blind randomised controlled trial. Lancet. Feb 2 2008;371(9610):395-403.  
Bussel JB, Kuter DJ, Pullarkat V, Lyons RM, Guo M, Nichol JL. Safety and efficacy of long-term treatment with romiplostim in thrombocytopenic patients with chronic ITP. Blood. March, 2009

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**BJ Casey, PhD**

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Field(s) of Interest: Developmental cognitive neuroscience

Research Title: Research in Developmental Psychobiology

Project Description:

Work on developmental brain imaging studies using functional magnetic resonance imaging and fiber tracking with diffusion tensor imaging to examine limbic forebrain regions implicated in addiction and impulsivity.

Work on attention and reading training interventions and how they impact behavior and neural systems testing pre and post-training effects with functional magnetic resonance imaging and diffusion tensor imaging. This work is relevant for the disorders of ADHD and reading disorders.

Work on developmental brain imaging studies using functional magnetic resonance imaging and fiber tracking with diffusion tensor imaging to examine limbic forebrain regions implicated in addiction and impulsivity.

Work on attention and reading training interventions and how they impact behavior and neural systems testing pre and post-training effects with functional magnetic resonance imaging and diffusion tensor imaging. This work is relevant for the disorders of ADHD and reading disorders.

Students' Role in the Project: Students would be provided with background reading, IRB and HIPAA training, image analysis, behavioral testing, programming and scientific discussions. Typically students are exposed to every aspect of the study and depending on contributions in the lab can be a co-author on a paper or conference presentation and as such get writing experience too. The student is jointly mentored by a team of investigators including pre and post-doctoral fellows and a faculty PI.

Preferred Background/Experience: Yes, some general computer experience would be very helpful.

References:

Casey BJ, Getz S, Galvan A. The adolescent brain. Dev Rev. 2008;28(1):62-77.  
Hare TA, Tottenham N, Galvan A, Voss HU, Glover GH, Casey BJ. Biological substrates of emotional reactivity and regulation in adolescence during an emotional go-nogo task. Biol Psychiatry. May 15 2008;63(10):927-934.  
Casey BJ, Jones RM, Hare TA. The adolescent brain. Ann N Y Acad Sci. Mar 2008;1124:111-126.  
Casey BJ, Nigg JT, Durston S. New potential leads in the biology and treatment of attention deficit-hyperactivity disorder. Curr Opin Neurol. Apr 2007;20(2):119-124

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Field(s) of Interest: Autoimmune Disease; Immunoregulation

Research Title: Regulation of the Immune Response in Autoimmune Disease

Project Description: The laboratory studies the human immune system in healthy individuals and patients with systemic lupus erythematosus to better understand the triggers and mediators of autoimmunity and inflammation in that disease. Students are welcome to participate in ongoing laboratory projects, or initiate their own projects, that use cell culture, flow cytometry, real-time PCR, cell transfection, protein analysis, and other approaches to study mechanisms of autoimmunity.

Preferred Background/ Experience: None, although laboratory experience helps.

References:

Crow MK. Collaboration, genetic associations, and lupus erythematosus. N Engl J Med. Feb 28 2008;358(9):956-961.  
Crow MK. Anticyclic citrullinated peptide antibody-negative rheumatoid arthritis: clues to disease pathogenesis. Curr Rheumatol Rep. Jul 2008;10(3):165-167.  
Niewold TB, Adler JE, Glenn SB, Lehman TJ, Harley JB, Crow MK. Age- and sex-related patterns of serum interferon-alpha activity in lupus families. Arthritis Rheum. Jul 2008;58(7):2113-2119.  
Kariuki SN, Crow MK, Niewold TB. The PTPN22 C1858T polymorphism is associated with skewing of cytokine profiles toward high interferon-alpha activity and low tumor necrosis factor alpha levels in patients with lupus. Arthritis Rheum. Sep 2008;58(9):2818-2823  
Aringer M, Crow MK. A bridge between interferon-alpha and tumor necrosis factor in lupus. J Rheumatol. Aug 2008;35(8):1473-1476

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**Susanna Cunningham-Rundles, PhD**

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Field of Interest: Cellular Immunology, host response to pathogens, development of immune response, cytokine regulation

### Research Titles:

1. Role of beta glucans in immune response and hematopoiesis
2. Development of Neonatal Immune Response

### Project Descriptions:

Role of beta glucans in immune response and hematopoiesis: The overall objective of our studies in collaboration with the MSKCC Research Center for Botanical Immunomodulators (NIH P50) is to identify botanicals with potential bioactivity for enhancement of immune function and reconstitution of hematopoietic and immune function after cancer chemotherapy, and to investigate botanicals that have adjuvant activity for cancer immunotherapy.

Development of neonatal immune response: The increased susceptibility of neonates to infections stems from the immaturity of the immune system at birth. Hematopoiesis and host defense in the neonate are developmentally immature. Studies focus on the role of microbes both commensals and potential pathogens on neonatal immune response in the regulation of proinflammatory response.

Students' Role in the Project: Student will participate in all aspects of the studies including experimental design and hypothesis testing and will learn relevant technology.

Preferred Background/Experience: Knowledge of basic laboratory skills and sterile technique.

### References:

- Lin, H., Cassileth, B., She, Yu-Hing, Sirotnak, F., and Cunningham-Rundles, Ph.D. 2004 Maitake beta-glucan MD- fraction enhances bone marrow colony formation and reduces doxorubicin toxicity in vitro International Immunopharmacology 4: 91-99.
- Lin, H., Cheung, S.W.Y., Nesin, M., Cassileth, B.R., and Cunningham-Rundles, S. 2007 Enhancement of umbilical cord blood cell hematopoiesis by Maitake beta glucan is mediated by G-CSF production. Clinical and Vaccine Immunology 14: 21-27
- Mohamed MA, Cunningham-Rundles S, Dean CR, Hammad TA, Nesin M. Levels of pro-inflammatory cytokines produced from cord blood in-vitro are pathogen dependent and increased in comparison to adult controls. Cytokine 2007 39(3): 171-177.
- Tatad, A.M. F., Nesin, M, Peoples, JD, Cheung, S W-Y, Lin, H., Sison, C, Perlman J.M, and S. Cunningham-Rundles Cytokine expression in response to bacterial antigens in preterm and term infant cord blood monocytes (adv e pub 12.19.2007) and Neonatology 2008; 94:8-15
- Peoples, JD, Cheung, S W-Y, Nesin, M, Tatad, AMF, Lin, H, Hoang, D, Perlman, J, Cunningham-Rundles, S. 2008 Neonatal cord blood subsets and cytokine response to bacterial antigens Am J Perinatology 9: 647-57
- Lin, H , De Stanchina, E, Zhou, XK, She, Y-H, Hoang, D 4, Cheung, S W-Y, Cassileth, B R., Cunningham-Rundles, S 2008 Maitake Beta-Glucan enhances umbilical cord blood stem cell transplantation in the NOD/SCID mouse Exp Biol Med 234:342–353 PMCID: 19144872
- Lin, H, De Stanchina, E, Zhou, XK, Hong, F, Seidman, A, Fornier, M, Xiao, WL, Kennelly, E J. Wesa, K, Cassileth, B R, Cunningham-Rundles, S. 2010 Maitake beta-glucan promotes recovery of leukocytes and myeloid cell function in peripheral blood from paclitaxel hematotoxicity Cancer Immunology Immunotherapy Epub. Feb 6. PMC: 20140432
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Field (s) of Interest: Medical Genetics

Research Title: Student can work on one of two projects, these include study made in adolescent patients with Marfan syndrome and or parental attitudes re: newborn screening.

Project Description: Both studies will involve the use of questionnaires. We are in the process of developing a questionnaire for IRB approval re: Newborn screening. The aim is to determine what information pregnant women and their partners have about newborn screening and the NYS Screening program in order to determine their needs as well as to develop an educational program about this subject in face of the expanded test panel. The educational program will be aimed at patients but will include a professional component. We plan to develop a questionnaire for adolescents with Marfan syndrome to learn more about their views on their asthenia appearance and life activities.

Students' Role in Project: Students can help develop and modify the questionnaires. Student will learn interview techniques.

Preferred background/Experience: None

**References:**

Offit K, Kohut K, Clagett B, Wadsworth EA, Lafaro KJ, Cummings S, White M, Sagi M, Bernstein D, Davis JG.: Cancer genetic testing and assisted reproduction. Oct 10; 24(29): 4775-82. 2007.  
Carter EM, Davis JG, Raggio CL.: Advances in understanding etiology of achondroplasia and review of management. Current Opinion in Pediatrics. Feb; 19(1): 32-7. 2007.  
Sills ES, Burns MJ, Parker LD, Carroll LP, Kephart LL, Dyer CS, Papenhausen PR, Davis JG. Further phenotypic delineation of subtelomeric (terminal) 4q deletion with emphasis on intracranial and reproductive anatomy. Feb 12;2:9. 2007.  
Giampietro, P.F., Raggio, C., Davis, J.G.: Marfan Syndrome: orthopedic and genetic review. Current Opinion in Pediatrics 14(1): 35-41, 2002.

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Field(s) of Interest: Hematology, disorders of iron metabolism, anemia of inflammation, beta-thalassemia.

Research Title: Investigating the role of cytokines and hepcidin in a mouse model of anemia of inflammation

**Project Description:** Anemia of inflammation (AI) is the second most common form of anemia, affecting patients with chronic illnesses, such as infections, autoimmune diseases, or cancer. The aim of the project is to better characterize the complex pattern of inflammatory cytokines that is responsible for AI, with the purpose of identifying new therapeutic targets for this condition. It has already been shown that interleukin-6 is increased in AI, activating the production of the iron regulatory hormone hepcidin in the liver. Through hepcidin, IL-6 ultimately affects iron metabolism reducing the availability of iron for erythropoiesis, and thus generating the anemia. However, together with IL-6, other cytokines (e.g. IFN- $\gamma$ , TNF- $\alpha$ ) have been shown to alter iron metabolism and erythropoiesis, with mechanisms that still need to be fully elucidated.

**Students' Role in the Project:** Student(s) will participate in all aspect of the above-described research, learning numerous techniques. These include: tissue samples collection, tissue iron analysis, flow-cytometry, ELISA, RNA extraction and analysis, quantitative PCR. Students will gain experience in many of the following experimental approaches:

1. Use of mouse models lacking the expression of hepcidin (Hamp KO) or specific cytokines (IL-6 KO, IFN-  $\gamma$  KO, and TNF- $\alpha$  KO), and generation of double knockout (e.g. IL-6/Hamp KO).
2. Induction of AI by injection of heat-killed *Brucella abortus* antigen (HKBA).
3. Study of iron metabolism by expression profile analysis of iron-related genes, and comparison of results to tissue and serum iron levels in HKBA-treated and control mice.
4. Study of erythropoiesis with the goal of elucidating the mechanisms responsible for anemia in mice.
5. Inactivation of specific cytokines by treatment with cytokine inhibitors to selectively analyze the effect of the numerous cytokines involved in AI.

**Preferred Background/Experience:** Basic knowledge of molecular biology and laboratory techniques. Literature review skills. Interest and motivation are required.

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**Field(s) of Interest:** Developmental and Evolutionary Biology

**Research Title:** Evolutionary conservation of notochord gene expression in the ascidian, *Ciona intestinalis*.

**Project Description:** Our lab is interested in identifying the components of the gene regulatory networks underlying notochord development and evolution. This particular project consists in determining whether genes that are expressed in the vertebrate notochord are also expressed in the notochord of larvae of the sea squirt, *Ciona*. The ultimate goal of these experiments is to establish how many of the genes found in the vertebrate notochord are also present in the *Ciona* notochord, the most primitive notochord experimentally available. A better understanding of the nature and characteristics of the minimum complement of genes necessary to build a functional notochord is crucial for understanding how the vertebrate notochord develops and, in turn, controls proper development of floor plate, liver, pancreas, and, ultimately, the correct formation of the vertebral column.

**Students' Role in the Project:** The student would be synthesizing RNA probes to be used for whole-mount *in situ* hybridization experiments on *in vitro* fertilized *Ciona* embryos.

Preferred background/Experience: Good will and some basic knowledge of developmental and molecular biology

References:

Capellini, T.D.\*, Dunn, M.P.\*, Passamaneck, Y.J., Selleri, L. and Di Gregorio, A.: Conservation of notochord gene expression across chordates: insights from the Lepreca gene family. *Genesis Special Issue on Chordate Origins and Evolution*. 2008. In press. (\*equal contribution)

Kugler, J.E., Passamaneck, Y.J., Feldman, T.G., Beh, J., Regnier, T.W. and Di Gregorio, A. Evolutionary conservation of vertebrate notochord genes in the ascidian *Ciona intestinalis*. *Genesis - Special Issue on Chordate Origins and Evolution*. 2008. In press.

Capellini, T.D., Zewdu, R., Di Giacomo, G., Asciutti, S., Kugler, J.E., Di Gregorio, A. and Selleri, L.: - Pbx1/Pbx2 govern axial skeletal development by controlling Polycomb and Hox in mesoderm and Pax1/Pax9 in sclerotome. *Dev. Biol.* 2008. In press.

Passamaneck, Y.J., Hadjantonakis, A.-K., and Di Gregorio, A.: Dynamic and polarized muscle cell behaviors accompany tail morphogenesis in the ascidian *Ciona intestinalis*. *PLoS ONE* 2007 Aug 8;2:e714.

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Field(s) of Interest: Uretal obstruction- renal histopathology and function

Field(s) of Interest: Uretal obstruction- renal histopathology and function

Project Descriptions:

Renal Dysfunction models: Hydronephrosis and polycystic kidney disease: In children, the most commonly detected prenatal anomaly is hydronephrosis, the dilation of the renal collecting system. Our laboratory has had a long-standing interest in the molecular mechanisms of damage to the kidney after obstruction, especially the fibrotic response, in which there is a pathologic accumulation of extracellular matrix proteins, which damage the kidney and reduce its function. One of the first events in the obstructed kidney is the build-up of pressure, which results from obstruction of the ureter. We have previously found that pressure activates important signaling pathways in the generation of Nitric Oxide, a cytokine with an important role in renal. Currently, we are investigating how pressure activates the fibrotic process in various cells in the kidney. These studies will use gene array, proteomic and metabolomic approaches to identify appropriate candidates. These studies will be important to determine if there are pathways which might be amenable to therapeutic intervention to halt or reverse renal damage in obstruction. We are also investigating an in vitro model of polycystic kidney disease. Using embryonic kidneys, we are studying different signaling pathways and examining their role in cAMP-mediated cyst formation.

Design of a Synthetic Bladder Augment Patch: Bladder dysfunction related to small, fibrotic bladders is a significant problem in children, resulting in high bladder storage pressures and low bladder volume. The high pressures that build up impact upon bladder function by inducing fibrosis and on quality of life because of incontinence; if left untreated, high bladder pressure can lead to renal failure and a lifetime of dialysis, or renal transplantation. The conventional surgical approach to increase bladder size is bladder augmentation

[ileocystoplasty], which is associated with significant morbidity. In our laboratory, we are interested in designing a synthetic bladder augmentation patch to increase the bladder storage capacity. This approach would reduce much of the current surgical morbidity, and would also eliminate the metabolic complications of ileocystoplasty. Studies are underway to determine the biocompatibility of the synthetic patch to determine its suitability for use in vivo.

Effect of Androgens on Development of Genitourinary Tissue : Congenital Adrenal Hyperplasia is an inherited deficiency of certain enzymes involved in the production of male hormones [such as androgens]. The most common deficiency is 21-hydroxylase, the enzyme involved in cortisol production. The deficiency of 21-hydroxylase not only decreases cortisol, but also stimulates adrenocorticotrophic hormone, leading to excess male hormones. In females, the result of this enzyme deficiency is virilization [the appearance of secondary male characters in the female], which begin in utero; these girls are born with genital ambiguity and an enlarged clitoris. The molecular mechanisms controlling androgen's action in the clitoris are unknown. Therefore, we are studying the in vitro expression of androgen and estrogen receptors in surgical waste tissue obtained from CAH patients. These preliminary studies will allow us to understand how androgens act on female genitalia, so that we may be able to design strategies to prevent female genitals from the negative effects of androgen excess in CAH.

Wound Healing: The healing of acute cutaneous wounds requires interactions among cytokines, immune cells, parenchymal cells, and components of the extracellular matrix. This process is dynamic and results in scar formation, which restores functional continuity in the affected area. Compromise of the wound-healing process contributes to significant morbidity and even death. Our laboratory has developed a model in which to study wound healing in full thickness human skin. This model was originally developed using pediatric foreskin and was used in several studies by our laboratory. We have recently expanded the model to use adult tissue and to study aspects of the immunology of wound healing in both adult and pediatric skin. We have further adapted this model for use in studies on squamous cell carcinoma.

Students' Role in the Project: Students will learn basic biochemical and molecular biology techniques including immunostaining, PCR, and western blot analysis. They will use these skills in experiments evaluating the effects of pressure on cells in the urinary tract.

Preferred Background/ Experience: Willingness to learn and work hard and committed interest are pre-requisites.

#### References:

Veerappan A, Reid AC, O'Connor N, Mora R, Brazin JA, Estephan R, Kameue T, Chen J, Felsen D, Seshan SV, Poppas DP, Maack T, Silver RB. Mast Cells are Required for the Development of Renal Fibrosis in the Rodent Unilateral Ureteral Obstruction Model. *American Journal of Physiology Renal*, in press, 2012. doi:10.1152/ajprenal.00562.2010

Carlsen I, Donohue KE, Jensen AM, Selzer AR, Chen J, Poppas DP, Felsen D, Frøkiær J and Nørregaard R. Increased cyclooxygenase-2 expression and prostaglandin E2 production in pressurized renal medullary interstitial cells. *Am. J. Physiol. Reg.* 299: R823 - R831, 2010. PMID: 20610829 PMC2944419

Broadbelt NV, Chen J, Silver RB, Poppas DP and Felsen D. Pressure activates epidermal growth factor receptor (EGFR) leading to the induction of iNOS via NFκB and STAT3 in human proximal tubule cells (HKC-8). *American J Physiol Renal* 297: F114-F124, 2009. PMID: 19403642 PMC2711717

Mizuguchi Y, Chen J, Seshan SV, Poppas DP, Szeto HH and Felsen D. A novel cell permeable antioxidant peptide decreases renal tubular apoptosis and damage in unilateral ureteral obstruction. *Am J Physiol, Renal* 295: F1545-F1553, 2008. PMID: 18784263 PMC2584902

Petratos PB, Chen J, Soslow RA, Bleustein CB, Poppas DP, Felsen D. Full-Thickness Human Foreskin Transplantation onto Nude Rats as an In Vivo Model of Acute Human Wound Healing. *Plast Reconstr Surg* 111:1988-97, 2003. PMID: 12711961

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**Maura D. Frank, MD**

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Field(s) of Interest: Obesity

Research Title: Effect of weight management program on weight/BMI, eating and physical activity behaviors, and quality of life.

Project Description: Data entry and management, study recruitment, medical student mentoring program, IRB proposal development.

Students' Role in the Project: Student will learn the basics of research project development, recruitment for research projects, formulation of an abstract.

Preferred Background/ Experience: Knowledge of Excel helpful, student will learn EndNote

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Field(s) of interest: Access to care, Pediatric mental health, Maternal literacy, Maternal depression, Medical Education.

Current Project Title: Addressing the Not-So-New Morbidity within Pediatric Medical Education

Principal Investigators: Dr. Susan Bostwick and Dr. Cori Green

Project Description: We are conducting a needs assessment of pediatric residents and program directors to assess their current training in pediatric mental health issues. A survey is being conducted of all Pediatric Program Directors and focus groups of residents are being run. This project will conclude with the creation of an educational intervention to better train pediatric residents to address mental health issues within the primary care setting. This intervention will be tested in further projects.

Students' Role in the Projects:

Students will learn how to create and help implement educational interventions. Students will be involved in creation of assessment tools, recruitment of resident subjects, analysis of data, and abstract writing.



Preferred Experience: None required

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**Daniel W. Green, MS, MD**

Hospital for Special Surgery  
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Field(s) of Interest: Pediatric Orthopedic Surgery and Scoliosis

Research Title: Selected clinical projects in pediatric orthopedic surgery

Project Description: Previous projects include: DDH, congenital muscular torticollis, discoid meniscus, scoliosis and kyphosis.

Students' Role in the Project: Literature review, radiograph review, data analysis

Preferred Background/ Experience: None requested

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**Barry Kosofsky, MD, PhD**

Department of Pediatrics, Division of Neurology  
The Weill Medical College of Cornell University  
525 East 68<sup>th</sup> Street, Room LC-6  
212-746-5942  
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Research Title: Alterations in Brain Development following Prenatal Exposure to Cocaine

Project Description: We have a multidisciplinary basic research program in mice to study molecular, neuroanatomic, and behavioral alterations induced in mouse brain development following prenatal exposure to cocaine.

Students' role in the project: Basic Research Skills, including molecular biology, neuroanatomy, and behavioral analyses.

Preferred Background/ Experience: Bench lab experience preferred (especially molecular biology or neuroanatomy).

References:

Tropea TF, Guerriero RM, Willuhn I, Unterwald EM, Ehrlich ME, Steiner H, Kosofsky BE. Augmented D1 dopamine receptor signaling and immediate-early gene induction in adult striatum after prenatal cocaine. *Biol Psych*. 2008;63(11):1066-74.  
Tropea TF, Kosofsky BE, Rajadhyaksha AM. Enhanced CREB and DARPP-32 phosphorylation in the nucleus accumbens and CREB, ERK and GluR1 phosphorylation in the dorsal hippocampus is associated with cocaine conditioned place preference behavior. *J Neurochem*. 2008;106(4):1780-90.  
Malanga CJ, Ren JQ, Guerriero RM, Kosofsky BE. Augmentation of cocaine-sensitized dopamine release in the nucleus accumbens of adult mice following prenatal cocaine exposure. *Dev Neurosci*. 2009;31(1-2):76-89.

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**Alfred N. Krauss, MD**

Division of Neonatology  
Department of Pediatrics  
Weill Medical College  
212-746-3530  
ank2005@med.cornell.edu

Research Title: Neonatal Lung Function

Preferred Background/ Experience: None requested

References:

Ballabh, P. ; J. Kumari,; A.N. Krauss, MD; J. Shin, ; A. K. Jain; P.A.M. Auld, and S. Cunningham-Rundles 2003 Soluble E-selectin, Soluble L-selectin and Soluble ICAM-1 in Bronchopulmonary Dysplasia and Changes with Dexamethasone. *Pediatrics* 111(3):461-8

Ballabh, P.; M. Simm; J. Kumari, C. Califano, Z. Aghai, Laborada, G., C. Sison, and S. Cunningham-Rundles. 2003 Respiratory burst activity in bronchopulmonary dysplasia and changes with dexamethasone *Pediatric Pulmonol* 35(5): 392-9

Ballabh, P.; M. Simm; J. Kumari, A.N. Krauss; A. Jain, PAM Auld, and S. Cunningham-Rundles. 2003 Lymphocyte Phenotypes in Bronchopulmonary Dysplasia. *Am J. Perinatol* 8:465-475

Ballabh, P.; M. Simm; J. Kumari, ; A.N. Krauss; A. Jain, C. Califano, M.L. Lesser, and S. Cunningham-Rundles 2004 Neutrophil and Monocyte Adhesion Molecules in Bronchopulmonary Dysplasia, and Effects of Corticosteroids *Arch Dis. Child* 89: 76-83

Dermendjian, M., Varma, S., Krauss, A.N., Auld, P.A.M.: Functional residual capacity (FRC) does not predict response to surfactant in preterm infants. *Am. J. Perinatology*, 2002;19:155-162.

Aghai, Z., Arevalo, R., Lumicao, L., Lesser, M., Shi, Q., Jain, J., Krauss, A.N., Auld, P.A.M., Hanauske-Abel, H.M.: Basement membrane biomarkers in very low birth weight premature infants. *Biology of the Neonate*, 2002;81:16-22

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**Nicole Kucine, MD**

Pediatric Hematology/Oncology  
Department of Pediatrics  
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Field(s) of Interest: Sickle Cell Disease, Anemia, Coagulation and Bleeding Disorders, Myeloproliferative disorders, Leukemia, Bone Marrow Failure/Abnormal Hematopoiesis

Potential Research Topics: I do not have currently established projects for students, however I have some ideas for survey-based projects that could be of interest to students whom I will mentor

1. Pediatrician assessment of menorrhagia – screening if and how pediatricians assess their female adolescent patients for menorrhagia, and their referral practices, with possible educational intervention after
2. Pediatric care providers and pain management – assessing boundaries in our institution to providing pain management for pediatric patients; possibly working with anesthesia to develop educational interventions

3. Thrombosis in Pediatric Inpatients – we are currently submitting an IRB for a retrospective chart review to look at incidence of thrombosis in our pediatric inpatients and to identify the most common risk factors in our population and possibly identify new risk factors for thrombosis in hospitalized children

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**Juhi Kumar, MD, MPH**

Pediatric Nephrology  
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Weill Cornell Medical College  
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Field(s) of Interest: Pediatric renal disease, vitamin D, cardiovascular outcomes of chronic kidney disease, kidney transport, Focal segmental glomerulosclerosis

Research Projects:

1. Vitamin D in children with chronic kidney disease (CKD): prevalence of deficiency and clinical correlates: This is a NIH funded ancillary study to the ongoing multicenter, prospective cohort study of children with CKD (CKiD). My study aims to define the prevalence and correlates of vitamin D deficiency. It will also prospectively evaluate the role of Vitamin D deficiency in growth failure, progression of CKD and cardiovascular outcomes.
2. Vitamin D supplementation in children with chronic kidney disease: Current guidelines for vitamin D supplementation in children with CKD are not evidence based and are extrapolated from adults. This study aims to evaluate the adequacy of the current KDOQI recommendations for treating vitamin D deficiency in these children.
3. Kidney transplant outcomes: This proposal aims to evaluate the effects of using a steroid free immunosuppression protocol on outcomes such as growth, allograft rejection and cardiovascular profile.
4. Focal segmental glomerulosclerosis (FSGS): FSGS is a devastating glomerulopathy that leads to end stage renal disease. It also tends to recur in 30-50% of patients after kidney transplantation, eventually leading to allograft loss. We have used Rituximab as a rescue therapy in our patients with recurrent FSGS with partial remission of proteinuria. We are collaborating with other centers in the US to evaluate the practice patterns for Rituximab use in recurrent FSGS.

References:

1. Sharief S, Jariwala S, Kumar J, Muntner P, Melamed ML. Vitamin D levels and food and environmental allergies in the United States: Results from NHANES 2005-2006. J Allergy Clin Immunol. 2011 May; 127(5):1195-202. Epub 2011 Feb 16. PMID: 21329969
2. Skversky Amy, Kumar Juhi, Abramowitz Matthew, Kaskel Frederick, Melamed Michal. Association of Glucocorticoid use and low 25-hydroxyvitamin D levels: results from the National Health and Nutrition Examination Survey (NHANES): 2001-2006. J Clin Endocrinol Metab. 2011 Sep 28. [Epub ahead of print] PMID: 21956424
3. Kumar Juhi, Furth Susan, Warady Bradley. The Pediatric Patient with Chronic Kidney Disease-Mineral Bone Disorder. Accepted for publication in the Clinical Reviews in Bone and Mineral Metabolism. Anticipated Publication date 12/2011
4. Melamed ML, Kumar J. Low levels of 25-hydroxyvitamin D in the pediatric populations: prevalence and clinical outcomes. Pediatric Health, February 2010, Vol. 4, No. 1, Pages 89-97.

**Thomas J.A. Lehman, MD**

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Pediatric Rheumatology  
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Field(s) of Interest: Pediatric rheumatic diseases

Project Description: Students have been involved in a variety of clinical research projects over the past years.

Students' Role in the Project: Chart review, data tabulation. We also teach basic aspects of clinical pediatric rheumatology/history.

Preferred Background/ Experience: None requested

References:

Lehmann HW, Lutterbuse N, Plentz A, et al. Association of parvovirus B19 infection and Hashimoto's thyroiditis in children. *Viral Immunol.* Sep 2008;21(3):379-383.  
Kieseier BC, Meyer Zu Horste G, Lehmann HC, Gold R, Hartung HP. Intravenous immunoglobulins in the treatment of immune neuropathies. *Curr Opin Neurol.* Oct 2008;21(5):555-562.  
Kuerten S, Javeri S, Tary-Lehmann M, Lehmann PV, Angelov DN. Fundamental differences in the dynamics of CNS lesion development and composition in MP4- and MOG peptide 35-55-induced experimental autoimmune encephalomyelitis. *Clin Immunol.* Nov 2008;129(2):256-267.  
Lehmann HC, Hartung HP. Complementing the therapeutic armamentarium for Miller Fisher Syndrome and related immune neuropathies. *Brain.* May 2008;131(Pt 5):1168-1170.  
Lehmann GM, Garcia-Bates TM, Smith TJ, Feldon SE, Phipps RP. Regulation of Lymphocyte Function by PPARgamma: Relevance to Thyroid Eye Disease-Related Inflammation. *PPAR Res.* 2008;2008:895901.  
Lehman HK, Ballow M. Immune deficiency disorders with autoimmunity and abnormalities in immune regulation-monogenic autoimmune diseases. *Clin Rev Allergy Immunol.* Apr 2008;34(2):141-145.

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**David C. Lyden, MD, PhD**

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Field(s) of Interest: Angiogenesis

Research Title: The role of bone marrow precursors in tumor angiogenesis and regeneration.

Project Description: Determine the role of VEGFR1 myeloid and VEGFR2 endothelial stem and progenitor cells in the formation of new vessels in tumor and Metastatic models and in wound healing studies such as burns and myocardial infarction.

Students' Role in the Project: The student will be responsible for leading one of several aspects in the study of neoangiogenesis.

Preferred Background/ Experience: None requested

### References:

Kaplan RN, Lyden D. Metastases: setting up shop. *Nature Reviews Cancer* 2006 6 (1): 3.  
Kaplan RN, Lyden D. Envoys of metastasis. *Nature Medicine* 2006 12 (1): 18. Jin DK, Kopp H, Petit I, Shido K, Young LM, Kanhai G, Amano H, Acevilla S, Heissig B, Hattori K, Zhang F, Hicklin DJ, Dunn A, Salari H, Werb Z, Hackett NR, Crystal RG, Lyden D, Rafii S.  
Cytokine-mediated Deployment of SDF-1 revascularization through recruitment of CXCR4+ hemangiocytes. *Nature Medicine* 2006 12 (5):557-567.  
Rafii S. and Lyden D. S100 chemokines mediate bookmarking of pre-metastatic niches. *Nature Cell Biology*. 2006 8:1321-1323.  
Gilheeney SW, Lyden DC, Sgouros S, Antunes N, Gerald W, Kramer K, Lis E, Meyers P, Rosen N, Thaler HT, Trippett T, Wexler L, Dunkel IJ. A phase II trial of thalidomide and cyclophosphamide in patients with recurrent or refractory pediatric malignancies. *Pediatr Blood Cancer* 2007 49(3):261-265.  
Rafii S and Lyden D. Cancer; A few to flip the angiogenic switch. *Science* 2008 319:163-164.  
Podolanczuk A, Kaplan RN, Psaila B, Rafii S, Lyden D. ?Targeting the Steps in Metastatic Progression? in *Bone and Cancer*. (In Press, February 2008).  
Shmelkov SV, Butler J, Hooper AT, Hormigo A, Kushner J, Milde T, St. Clair R, Murphy AJ, Valenzuela DM, Gale NW, Thurston G, Yancopoulos GD, Lyden D (corresponding author), Rafii S. CD133 identifies luminal differentiated epithelium and both CD133+ and CD133- cells initiate metastatic epithelial carcinomas. *Journal of Clinical Investigation*, Under 2nd Revision

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### **Catharine McGuinn, MD**

Pediatric Hematology/Oncology  
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Field(s) of Interest: Benign Hematology, Thrombosis, Coagulation, Thrombocytopenia

Research Title: Quality Improvement/ Outcomes in Pediatric Hematology Population

Description of Project(s): To be decided in conjunction with research team. Prospective survey or retrospective chart review format. Ideas include looking at sickle cell pain management pathway, anti-coagulation adherence, etc.

Students' Role in the Project: Flexible. Would be developed as project expanded

Preferred Background/ Experience: None requested Enthusiasm is important.

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### **W Beau Mitchell, MD**

Pediatric Hematology/Oncology  
Department of Pediatrics,  
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Laboratory Address: New York Blood Center Platelet Biology  
212-570-3280  
E-mail Address: bmittell@nybloodcenter.org

Fields of Interest: Clinical and laboratory aspects of bleeding, clotting, and platelet biology

Research Project 1: Bleeding complications in patients with connective tissue disorders.

Description of Project: We have seen a series of patients with connective tissue disorders who present with bleeding. This project will be a retrospective chart review to compile and analyze the bleeding characteristics of this population. Given the large sample size this project should provide unique information about bleeding in connective tissue disorders.

Students' Role in the Project: Chart review. Assistance with IRB process, scientific writing.

Preferred Background/ Experience: None

Research Project 2: A novel mutation resulting in an unusual type 2A von Willebrand Disease

Description of Project: We have identified a family with a novel mutation causing severe type 2A VWD. The mutation completely eliminates some aspects of von Willebrand factor function, but leaves others intact. Review of these patients' laboratory and clinical findings in concert with what is known of the VWF structure will likely reveal novel information about VWF structure and function.

Students' Role in the Project: Chart review. Assist with IRB submission. Review of literature. Scientific writing. Work with 3D structure imaging software.

Preferred Background/ Experience: None, although it would help if adept at computers.

Research Project 3: Morphology of platelets during thrombopoiesis

Description of Project: We are producing platelets from stem cells derived from umbilical cord blood cells. One critical question is whether the produced platelets are "normal". To determine this we are analyzing the platelets in several different ways. One of these ways is by morphology. We use both light and fluorescence microscopy to study the platelets as they are being produced in culture. This project will establish a baseline morphology by which to judge the effects of changes in the production techniques.

Students' Role in the Project: This will be primarily a visual cataloguing of microscopy images. The student will learn to use our imaging software and microscopes.

Preferred Background/ Experience: None, but will have to take the NYBC volunteer orientation.

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**Anne Moscona, MD**

**Matteo Porotto, PhD**

Pediatrics and Microbiology/Immunology

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Field(s) of Interest: Infectious diseases – Virology (specifically respiratory viruses and viral agents of bioterrorism).

Research Title: Molecular pathogenesis of human paramyxoviruses: parainfluenza virus type 3, and Hendra virus.

Project Description(s) The laboratory's research centers on molecular pathogenesis of human paramyxoviruses: parainfluenza virus type 3, and recently also the emerging pathogen Hendra virus. Parainfluenza virus is an important cause of lower respiratory tract infections in children, including croup and bronchiolitis, and there are currently no vaccines or antiviral agents for these diseases. Hendra virus is a highly fatal paramyxovirus is a potential agent of bioterrorism. We are interested in how viruses enter cells by fusing with the cells' envelope, and in how we might interfere with entry.

Molecular basis for human parainfluenza virus 3 infection. This laboratory has identified the role of the parainfluenza virus receptor-binding protein hemagglutinin-neuraminidase (HN) in the virus-induced fusion process whereby all paramyxoviruses enter host cells. HN's receptor binding is the critical first step towards HN's role in fusion promotion, and leads to activating or "triggering" of the fusion protein (F) to mediate fusion. Our parainfluenza projects focus on the molecular mechanisms for HN in the viral life cycle and in lung pathogenesis. Ongoing studies have led to novel antiviral strategies that are being tested, and to understanding mechanisms of resistance to antivirals.

Role of human parainfluenza virus 3 hemagglutinin-neuraminidase in immunopathogenesis of lung disease. The role of HN in pathogenesis of lung disease in vivo is being studied in a cotton rat model. Our group showed that mutations in HN that alter HN-receptor interaction (but do not affect replication) lead to dramatic differences in the disease in the cotton rat lung. We are determining whether HN's receptor affinity, its receptor-cleaving, or its F-triggering activities determine its virulence in the lung. We also are interested in identifying which immune response is altered by HN mutations that lead to enhanced disease.

Triggering of fusion by Hendra virus F protein: the role of G: In the Hendra virus projects, we apply our strategies for the study of paramyxovirus entry and fusion to an emerging and potentially fatal paramyxovirus that is viewed as a potential bioterrorism agent. For Hendra virus, the receptor binding protein (G) is required in order for the F protein to mediate fusion. Hendra G binding to receptor, like parainfluenza virus HN binding to sialic acid, "triggers" F protein to mediate fusion. The study of the mechanism of triggering/activation of F protein in Hendra virus should lead to strategies for interfering with this key step in viral entry.

Triggering Hendra F to fuse: peptides to interfere with fusion: Taking advantage of our finding that peptides that correspond to regions of HPIV3 F are superior to those derived from Hendra F at inhibiting Hendra fusion, we will determine whether inhibitory F-peptides bind to Hendra F, as would be predicted if the peptides are preventing the formation of the 6-helix bundle (6HB) believed to be required for fusion, or if inhibitory F-peptides bind to G and interfere with G triggering of F.

Innovative approaches to developing therapeutic and diagnostic reagents for Hendra virus. Insertion of F into the target cell membrane leads to fusion of the viral envelope with the plasma membrane and release of the nucleocapsid into the cytoplasm. Efficiency of F-triggering by G influences the extent of fusion, and provides a range of strategies for preventing viral entry. Based upon our studies of the paramyxovirus F-triggering process, peptides corresponding to heptad repeat regions of F can be used to prevent F from reaching its fusion-active state. It may also be possible to induce F to trigger "prematurely", thus becoming incapacitated before it reaches its target. Finally, molecules that inhibit receptor binding may prevent receptor interaction and all downstream events. Targeting several stages of the entry process simultaneously may provide synergism.

Students' Role in the Project:

Virology, molecular biology, biochemistry, structural analysis, immunology

Preferred Background/Experience.

Some lab experience preferred but not required. Interest and motivation are required.

References:

DeLaMora P and Moscona A. A daring treatment and a successful outcome: The need for targeted therapies for pediatric respiratory viruses. *Pediatric Transplan.* 11(2): 121-123, 2007.

Moscona A, McKimm-Breschkin J. News about influenza B drug resistance that cannot be ignored. *Journal of the American Medical Association (JAMA)* 2007 Apr 4;297(13):1492-3.

Palermo LM, Porotto M, Greengard O, and Moscona A. Fusion promotion by a paramyxovirus HN: modulation of receptor avidity of binding sites I and II by pH. *J. Virol.* 81 (17), 9152-9161, 2007

Porotto, M., Carta, P, Deng, Y, Kellogg, GE, Whitt, M, Lu, M, Mungall, BA, Moscona, A. Molecular determinants of antiviral potency of paramyxovirus entry inhibitors. *Journal of Virology* 81 (19): 10567-74, 2007.

Moscona, A. *CSI Microbiology: Emerging pathogens and a staged strategy for detection and discovery.* *Journal of Infectious Diseases* 196: 1727-8, 2007.

Aljofan M, Porotto M, Moscona A, Mungall BA. Development and validation of a chemiluminescent immunodetection assay amenable to high throughput screening of antiviral drugs for Nipah and Hendra virus. *J Virol Methods.* 2008 Apr;149(1):12-9.

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**Christine M. Salvatore, MD**

Division of Infectious Disease

Department of Pediatrics, Weill-Cornell

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Field(s) of Interest: Pediatric infectious disease

Research project 1: Serologic Response To High Dose Hepatitis B (HBV) Vaccine In HIV Infected Children

Project Description: The project is divided in 2 parts. Part 1) Is a retrospective chart review of all children/adolescents followed at our HIV Clinic to evaluate the response to the initial HBV vaccine. For each patient the following information will be collected: date of birth, age, gender, CDC clinical stage, nadir CD4 count, age at different doses of HBV and CD4 count at time of each dose if available, antiretroviral treatment history and in particular if on highly active antiretroviral therapy (HAART) at time of vaccination. Part 2) Is a prospective evaluation of antibody response after re-vaccination with a high dose of HBV vaccine. All subjects will have the HBV titers checked at baseline (week 0); if identified as "non-immune" the subject will receive a new series of HBV vaccine. Again CD4 count and percentage, CD19 count and percentage and viral load will be recorded and antiretroviral regimen will be reviewed.

At Week 24 from the vaccine booster the HBV titers and/or "immune"/"non-immune" status will again be rechecked in all subjects receiving the new dose to evaluate immune response.

The purpose of the study is to identify the possible risk factors that predispose HIV positive children to have a reduced immune response to HBV vaccine and to evaluate if administering a higher dose would improve the immune response

Students' Role in the Project: Learn to review and collect the most important data from a medical history. Help creating a database, analyzing the data and eventually submitting an abstract to a national meeting.



Preferred Background/ Experience: None in particular. A lot of enthusiasm and willingness to spend some time looking into the charts and possibly interacting with a particular group of children with special needs.

Research project 2: Infectious Complications After Spine Surgery in Children

Project Description: Retrospective chart review. The medical records of pediatric patients who required from 2000 to 2010 a surgical spine fusion will retrospectively be reviewed. The medical records of pediatric patients who developed infections and required irrigation and debridement (I&D) will retrospectively be reviewed in detail. Among the data that will be collected are: underlying disease, the time of diagnosis of the infection from the surgery, antibiotics at time of surgery, organisms isolated, antibiotic therapy and length of therapy, outcome. The purpose of the study is to identify possible risks factors and most frequent microorganisms involved so to recommend the most appropriate prophylactic antibiotic regimen at time of the surgery.

Students' Role in the Project: Learn to review and collect the most important data from a medical history. Help creating a database, analyzing the data and eventually submitting an abstract to a national meeting.

Preferred Background/ Experience: None in particular. A lot of enthusiasm and willing to spend some time looking into the charts

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**Snezana Nena Osorio,MD**

General Academic Pediatrics  
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Field(s) of Interest: Obesity and Medical Communication skills

Title of Research Project: Medical Communication Skills and Exploratory cancer project

Project Descriptions: The project includes goals for empirical evaluation of the family-centered care program. There are two projects on Medical Communication Skills. A Third project is focused on the natural history of pre-malignancy and the metastatic niche.

The first project will assess parent satisfaction with patient care before and after the introduction of Family-Centered Rounds. Parent perceptions of clinical care will be assessed among all families of hospitalized pediatric service patients upon admission. Time series analyses will be used to evaluate changes in patient satisfaction in response to the new strategy for bedside rounds.

The second project is a study to evaluate the impact of Family Centered Rounds on medical communications skills among pediatric residents. The study was designed with the directors of pediatric resident training at KCCH to introduce standardized scales to assess resident communication skills by parents, nurses, and supervising physicians. I will use the existing data from education files without identifiers from two time periods to assess the utility of a new clinical program of family-centered rounds. I am also working on developing communication curriculum for pediatric residents.

The third project is collaborative with Dr. David Lyden. This is an investigation of profiles of angiogenic and metastatic parameters in children with and without cancer. Emerging evidence suggests that bone marrow-derived , hematopoietic stem progenitor cells (HPC's) and endothelial progenitor cells (EPC's) contribute to tissue vascularization during both embryonic and postnatal physiological processes. Identification of cellular

mediators and tissue-specific chemokines, which facilitate selective recruitment of bone marrow-derived stem and progenitor cells to specific organs, may provide insight into the mechanisms by which the pre-metastatic niche develops in patients with pediatric malignancies. In this study, we seek to compare peripheral levels of circulating chemokines and progenitor cells in healthy pediatric controls to those of age-matched patients with pediatric malignancies. My role in this project involves recruiting and profiling blood samples from children who do not have cancer. Obtaining this information will be crucial in defining norms for the measures to be gathered among cancer patients. We will analyze blood samples gathered as "extra" blood when children already are undergoing blood testing. From these samples, we will measure plasma levels of growth factor and chemokine profile. This profile includes VEGF (vascular endothelial growth factor), PlGF (Placental derived growth factor), FGF (fibroblast derived growth factor), and SDF-1 (stromal derived growth factor). We have obtained IRB approval for this project, which also is approved by the WCMC CTSC.

I am also expanding my research to study angiogenesis and vasculogenesis among children who are overweight, as it is well known that the population of obese pediatric patients faces a future that includes elevated risk for cancers and cardiovascular problems. Research in adults has demonstrated that angiogenic factors are elevated in overweight and obese individuals. Furthermore, previous research demonstrated that coupling of adipogenesis and angiogenesis is essential for differentiation of adipocytes in obesity and that vascular growth factor (VEGF) is a key mediator. We will explore what genetic variants are responsible for this effect and possibly predict which subtypes of obesity are more prone to cancer. This research can be enhanced by studying other family members with obesity and malignancies to determine the genetic factors involved in the pre-metastatic setting.

Students' Role in the Project: 1. Medical Communication skills and patient satisfaction projects will provide the student with opportunities to learn how to develop questionnaire as an assessment tool, IRB process, how to analyze data. The third project is now centering on obesity-data collection, data entry, data analysis in collaboration with Dr. Lyden's lab.

Preferred Background/ Experience: None

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**Jeffrey Perlman, MD**

Department of Pediatrics, Division of Neonatology  
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212-746-3530

Field(s) of Interest: Neonatology, Brain development, Resuscitation

Title of Research Project: Evaluation of the Ergonomics of Chest Compressions in a Neonatal Manikin Model

Project Description: Evaluate the influence of compression rates on the depth of compressions including decay over time as well as the potential influence of surface location and gender.

Students' Role in the Project: Assist in the evaluations of data following a session and help to develop strategies to enhance CPR in the neonatal period

Preferred Background/ Experience: None

References:

Christman C, Hemway RJ, Wyckoff MW, Perlman JM The Two Thumb is Superior to the Two Finger Method for Administering Chest Compressions in Newly Born Infants. *Arch Dis Child Fetal Neonatal Ed* 2011;96:F99-F101

Hemway RJ , Huynh T, Perlman JM Chest Compressions in a Neonatal Manikin Model Vary in Depth and are Modulated by Duration, Height and Gender: Potential Implications for Asphyxial Arrest When Ventilation is Minimized. AHA Sessions 2011 Orlando Florida 2011

Huynh T, Hemway RJ, Perlman JM . The Two Thumb rather than the Two Finger (TF) Technique Using an Elevated Surface Rather than the Floor Should be the Preferred Method of Teaching Infant CPR Anytime™ PAS meeting. Denver 2011

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**Cathleen L. Raggio, MD**

Hospital for Special Surgery  
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Project Description: Pediatric, clinical and lab research. Spine Osteogenesis Imperfecta, Skeletal Dysplasia

Students' Role in the Project: Patient interaction, dissection, x-ray review, computer work

Preferred Background/ Experience: Good work ethic and enthusiasm

References:

Giampietro PF, Peterson MG, Schneider R, et al. Bone Mineral Density Determinations by DualEnergy x-ray Absorptiometry in the Management of Patients with Marfan Syndrome-Some Factors Which Affect the Measurement. *Hss J.* Feb 2007;3(1):89-92.

Carter EM, Davis JG, Raggio CL. Advances in understanding etiology of achondroplasia and review of management. *Curr Opin Pediatr.* Feb 2007;19(1):32-37.

Raggio CL. Sexual dimorphism in adolescent idiopathic scoliosis. *Orthop Clin North Am.* Oct 2006;37(4):555-558.

Giampietro PF, Raggio CL, Reynolds C, et al. DLL3 as a candidate gene for vertebral malformations. *Am J Med Genet A.* Nov 15 2006;140(22):2447-2453.

Ghebranious N, Burmester JK, Glurich I, et al. Evaluation of SLC35A3 as a candidate gene for human vertebral malformations. *Am J Med Genet A.* Jun 15 2006;140(12):1346-1348.

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**Stefano Rivella, PhD**

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Research Title:

- 1) Development of new strategies to cure beta-thalassemia
- 2) The role of iron in cancer and anemia of inflammation

Project(s) Description:

*Gene therapy of beta-thalassemia*

*Abnormal erythropoiesis and iron metabolism in beta-thalassemia*

*The role of iron metabolism in cancer and anemia of inflammation*

The projects include:

- Design and generation of retro or lentiviral vector harboring genes involved in abnormal hematopoiesis and iron disorders
- Design and generation of retro or lentiviral vector with genomic elements to regulate gene expression
- Test of the system *in vitro*
- Test of the system *in vivo* (infection of hematopoietic stem cells, embryonic stem cells, bone marrow transplantation and/or generation of transgenic animals)
- Generation of new tumor models and their correlation with inflammation, anemia and tumor progression

Students' Role in the Project:

Microbiology: bacteria transformation, plasmid DNA preparation

Molecular Biology: generation of recombinant DNA vectors, Southern blot analysis

Tissue Culture: maintenance and expansion of primary and secondary tissue culture cell lines; retroviral production, viral transduction

Mouse handling: analysis of hematopoietic parameters (CBC), facs, iron, gene and protein analyses, gene transfer in the bone marrow and liver, tumor induction and analysis

Preferred Background/ Experience: Basic and good knowledge of molecular biology and laboratory techniques; good skills in reviewing and summarizing scientific literature. The subjects that the candidate will review include: retrovirus, RNA interference, tetracycline controlled gene expression system, mouse embryonic stem cells. Good organization skills; computer literate.

References:

Breda L. and Rivella S. "Gene Therapy in Thalassemia and Hemoglobinopathies". Invited review: *Mediterranean Journal of Hematology and Infectious Diseases*. Epub 2009 Nov

Rivella S. and Rachmilewitz E "Alternative therapies for thalassemia". *Expert Review of Hematology*. Epub 2009 Oct

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**Heidi Stuhlmann, PhD**

Developmental Biology

Department of Cell & Developmental Biology

Department of Pediatrics (secondary)

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Research Title: Vascular Endothelium – A Life Line During Development And In The Adult

Development of a functional circulatory system in the vertebrate embryo is crucial for delivery of nutrients and oxygen to the embryo. Defects in the development of blood vessels result in death before birth or in congenital cardiovascular abnormalities. During physiological angiogenesis in the adult organism such as wound healing and during pregnancy, endothelial cells are stimulated to form new vessels, a process termed neo-angiogenesis. Similarly, during pathological processes such as ischemia, myocardial infarct, repair of injured tissue and tumor growth, endothelial cells become activated to sprout, migrate, and undergo remodeling. Thus, endothelial cells constitute a dynamic system that changes in response to environmental stimuli. Research in my laboratory focuses on understanding the molecular mechanisms that orchestrate these processes, using the mouse as a model system.

In a genetic screen for early developmental genes, we identified two novel genes that play important roles in vascular development and homeostasis. One of these, Vascular endothelial zinc finger 1 (Vezf1) encodes an endothelial transcription factor that plays essential, dosage-dependent roles in vascular system development. Vezf1KO embryos die at midgestation due to vascular remodeling defects and hemorrhaging. Unexpectedly, we found that heterozygous embryos display lymphatic vessel abnormalities that are reminiscent of the human congenital malformation syndrome, nuchal edema. We are presently collaborating with clinicians in the Fetal-Maternal Medicine Division at New York Presbyterian/Weill Cornell Medical College to investigate if human fetuses with nuchal edemas carry mutations in the VEZF1 gene.

A second gene identified in our screen, EGF-like domain 7 (Egfl7), is an early embryonic marker for endothelial cells and their progenitors. EGFL7 is a unique angiogenic factor: it is secreted specifically by endothelial cells, acts as a chemoattractant, and binds to the extracellular matrix. Importantly, we showed that EGFL7 interacts with and antagonizes endothelial Notch, a key vascular signaling pathway component. Overexpression or knockdown of Egfl7 in mouse embryonic stem cells, primary endothelial cells, mouse embryos and the post-natal retina results in defects in vascular sprouting, proliferation, and migration. Our ongoing studies indicate that Egfl7 expression is induced by hypoxia and Vascular endothelial growth factor, VEGF, and that it may play important roles in physiological angiogenesis during pregnancy. Specifically, we are examining its possible role in implantation and placentation, and how it may be involved in the development of preeclampsia

#### Students' Role in the Project:

The student would get "hands-on" lab experience. Initially, the student would work together with a research scientist in the lab to learn and master the required techniques, and later work more independently. The laboratory techniques could involve: Extraction of protein from tissue sample; protein gel electrophoresis; Western blot analysis Extraction of DNA from tissue samples; PCR amplification, DNA gel electrophoresis, preparation of sample for DNA sequence analysis  
Dissection of mouse embryos; embedding and sectioning, immunostaining/immunofluorescence analysis

Preferred Background/ Experience: Basic lab skills, knowledge in molecular and developmental biology, strong interest in research

#### References:

- Lewis, J.D., Destito, G., Zijlstra, A., Gonzalez, M.J., Quigley, J.P., Manchester, M., and Stuhlmann, H. (2006). Viral nanoparticles as tools for intravital vascular imaging. *Nat. Med.* 12(3): 354-360.
- Gowher, H., Stuhlmann, H., and Felsenfeld, G. (2008). Vezf1 regulates genomic DNA methylation through its effect on expression of DNA methyltransferase Dnmt3b. *Genes Dev.* 22: 2075-2084.
- Zou, Z., Ocaya, P.A., Sun, H., Kuhnert, F., and Stuhlmann, H. (2010). Targeted Vezf1-null mutation impairs vascular structure formation during embryonic stem cell differentiation. *Ather. Thromb. Vasc. Biol.* 30:1378-1388.
- Durrans, A. and Stuhlmann, H. (2010). A role for Egfl7 during endothelial organization in the embryoid body model system. *J. Angiog. Res.* 2(4):1-12.
- Nichol, D., Shawber, C.J., Fitch, M.J., Bambino, K., Sharma, A., Kitajewski, J., Stuhlmann, H. (2010)\*. Impaired angiogenesis and altered Notch signaling in mice overexpressing Egfl7. *Blood* 116(26):6133-6143.
- \*Commentary: Davis, G. (2010). Vascular balancing act: EGFL7 and Notch. *Blood* 116 (26):5791-5793.

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#### **Sima Toussi, MD**

Division of Infectious Disease  
Department of Pediatrics, Weill-Cornell  
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Field(s) of Interest: Pediatric Infectious Diseases

Research Title 1: *Clostridium difficile* colonization in infants and young children

Project Description: *Clostridium difficile* can cause diarrhea and severe illness in children and adults. *C. difficile* infection is likely under-recognized in the young pediatric population. Infants and young children are often not evaluated for *C. difficile* infection because it is thought to colonize their gut. However, it is unknown how commonly it colonizes the stool of young children. The rates published are extremely wide ranging and reported as being anywhere from 10-100% during the first year of life. The objective of this study is to describe the prevalence of *C. difficile* colonization in infants and young children and to assess possible risk factors.

Students' Role in the Project: The student's role will be the recruitment of study subjects in the inpatient and outpatient settings. This would involve learning how to consent and enroll patients with one of the co-investigator's and then eventually doing this independently. Part of the student's role will also be entry of the information into the database.

Preferred Background/ Experience: Interest in participating in clinical research.

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**Chani Traube, MD**

Pediatric Critical Care Medicine  
Department of Pediatrics, Weill-Cornell  
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Field(s) of Interest: Pediatric Critical Care Medicine; pediatric neuro-intensive care

Research Title: Detection of Pediatric Delirium: Validation of a Rapid, Observational Assessment Tool

Project Description: Delirium in critically ill children represents acute brain dysfunction, with short- and long-term health implications. There is an emerging literature suggesting that this is a common, serious, and under-diagnosed problem in seriously ill children. Evidence-based assessments of outcomes and interventions for pediatric delirium are lacking, largely due to the absence of a simple and reliable screening tool.

My research partners and I have developed a novel screening tool for the detection of delirium in this population, and have completed a pilot study confirming its feasibility, and suggesting a prevalence of >25% in our subjects. Once validated, this tool will allow for rapid and accurate identification of delirious children, facilitate appropriate interventions, and may improve long-term functional outcomes.

Students' Role in the Project: Students will have the opportunity to join a multidisciplinary team engaged in several projects regarding pediatric critical illness and its implications on brain function. They will participate in research study design, data collection, and manuscript writing. Students will learn how to obtain informed consent, conduct chart reviews, analyze data, and perform follow-up phone calls using surveys to detect whether a patient has experienced long-term effects from delirium.

Preferred Background/ Experience: None required. Interested students should be friendly, comfortable interacting with children and their families, and demonstrate organizational skills and attention to detail.

Research is ongoing, with active clinical trials in progress, others pending IRB approval, and others in planning stage.

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**Susan J. Vannucci, PhD**

Neonatology  
Department of Pediatrics, Weill-Cornell  
212-746 1446  
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Field(s) of Interest: Developmental Brain Injury/Hypoxic Ischemic Encephalopathy/Hypoglycemia/Neonatal Seizures

Research Title: Hypoxia-Ischemia in the Immature Brain

Project Description: Hypoxic-Ischemic (HI) brain damage resulting from asphyxia in the neonatal period is a major cause of death of premature and term infants and responsible for permanent neurologic handicap in the survivors. We have developed an animal model to study this injury in the newborn rat and utilize this model in both preterm and term-equivalent rodents. HIE is a major cause of seizures yet there is continued debate as to whether these seizures contribute to or merely reflect the severity of brain damage. We have recently extended our HIE model to include the detection of behavioral and electrographic seizures to test several of these relevant questions. A second project using this model will continue to look at the role of mast cells in promoting inflammation and cell death following HI in the immature brain.

Students' Role in the Project: The student can assist in performing the surgeries to induce the hypoxia-ischemia, as well as in the recording of the video EEG. It is important that the student is comfortable working with animals and in survival surgeries as well as in euthanasia of the animals to study the effects on brain development and injury. In addition, the student could participate in the study of the role of mast cells in mediating the inflammatory cascade as well as potentially contributing to the tissue repair.

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**Maria Vogiatzi, MD**

Metabolic Bone Disease  
Pediatric Endocrinology  
Department of Pediatrics  
212-746-3462 or 212-746-3486  
mvogiatz@med.cornell.edu

Research Topics:

Studies of osteoporosis in thalassemia: Thalassemia is a congenital hemolytic anemia that is associated with high rates of osteoporosis. The etiology of osteoporosis in this disease is poorly understood. Our project examines the etiology of bone disease in thalassemia, by doing both clinical and animal studies. We use a mouse model of thalassemia to determine the effect of certain medical interventions (such as PTH and bisphosphonates). The methodology that is used includes imaging, such as micro-CT, histology for assessment of bone remodeling and other basic science techniques.

Effect of erythropoiesis on mesenchymal differentiation: In this project, we use the thalassemia mouse as a model to study the effect of hematopoiesis on bone remodeling. Our results so far support the hypothesis that hematopoietic progenitors affect mesenchymal differentiation leading to decreased osteogenesis. In addition,

we have identified that this process involves erythropoietin (EPO). Cell cultures and co cultures, other basic science techniques and other mice models are used to examine the interactions of EPO and autocrine/paracrine factors on bone remodeling.

The role of iron in the development of osteoporosis: This project involves studies in iron overloaded mice, and the effect of iron overload on bone remodeling. The methodology that is used includes imaging, such as micro-CT, and histology for assessment of bone remodeling. Cell cultures and other basic science techniques are used to determine the role of iron on mineralization and the osteoclast.

Inflammatory response to iron excess: Iron excess has been thought to lead to increased oxidative stress. Our animal data support the presence of ROS and an inflammatory response. Our lab is in the processing of delineating the molecular mechanism by which iron excess triggers an inflammatory cascade. This is done by performing animal experiments using techniques such as flow cytometry.

Studies of diabetes in iron overload and thalassemia: Iron excess is associated with a number of endocrinopathies including diabetes. This project determines the development of insulin resistance and diabetes in our murine diabetes model as well the role of oxidative stress and inflammation in this process. In addition, we are conducting clinical studies that examine glucose abnormalities in iron overloaded patients with thalassemia by using continuous glucose monitoring by glucose sensors.

Studies of vitamin D supplementation on calcium excretion in thalassemia. This project studies the effect of various vitamin D doses on serum vitamin D concentrations and calcium excretion in regularly transfused patients with thalassemia. The study is supported by Cooley's Anemia Foundation grant.

Students' Role in the Projects: The student can be exposed to imaging techniques such as microCT, bone histology and dynamic histomorphometry for assessment of bone remodeling and basic science techniques including cell cultures and flow cytometry. The student will also have the opportunity to participate in clinical research in the area of diabetes and osteoporosis.

Preferred Background/ Experience: The student must be familiar with basic laboratory procedures. Biology majors preferred

#### References:

- M.G. Vogiatzi, E.A. Maclin, E.B. Fung, E. Vichinsky, N. Oliveri, J. Kwiatkowski, A. Cohen, E. Neufeld and P.J. Giardina for the Thalassemia Clinical Research Network. Prevalence of fractures among the thalassemia syndromes in North America. *Bone*, 2006; 38: 571-575.
- M. G. Vogiatzi, E.A. Macklin, E.B. Fung, A.M. Cheung, E. Vichinsky, N. Olivieri, M. Kirby, J.L. Kwiatkowski, M. Cunningham, I.A. Holm, J. Lane, R. Schneider, M. Fleisher, R.W. Grady, C.C. Paterson, P.J. Giardina. Bone disease in thalassemia: a frequent and still unresolved problem. *J Bone Min Research*; 2009 Mar;24(3):543-57.
- M.G. Vogiatzi, E.A. Macklin, F.L. Trachtenberg, E.B. Fung, A.M. Cheung, E. Vichinsky, N. Olivieri, M. Kirby, J.L. Kwiatkowski, M. Cunningham, I.A. Holm, M. Fleisher, R.W. Grady, C.M. Peterson, P.J. Giardina PJ; Thalassemia Clinical Research Network. Differences in the prevalence of growth, endocrine and vitamin D abnormalities among the various thalassaemia syndromes in North America. *Br J Haematol*. 2009 Sep;146(5):546-56. Epub 2009 Jul 13.
- J. Tsay, C. Pomeranz, A. Hassoun, S. O. Zandieh, J. Rutledge, M.G. Vogiatzi, S.E. Oberfield, R. Motaghedi, Screening Markers of Impaired Glucose Tolerance in the Obese Pediatric Population. *Hormone Research*. 2010; 73 (2): 102 – 107
- J. Tsay, C. Pomeranz, A. Hassoun, S. O. Zandieh, J. Rutledge, M.G. Vogiatzi, S.E. Oberfield, R. Motaghedi, Screening Markers of Impaired Glucose Tolerance in the Obese Pediatric Population. *Hormone Research*. 2010; 73 (2): 102 – 107



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**Mary Jo Ward, PhD**

Division of Child Development  
Department of Pediatrics  
The Weill Medical College of Cornell University  
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Field(s) of Interest: Development: infants, children, mother-child interaction

Research Title: Infant feeding skills, parental feeding practices, and growth disorders

Project Description: We will evaluate the effectiveness of an intervention delivered to the parents of infants from birth to 6 months of age. The study will include 75 families in a standard care group and 75 in an intervention group. The first group (standard care group) will receive routine well-child care on the schedule recommended by the American Academy of Pediatrics. The second (intervention group) will receive routine well-child care plus an intervention focused on teaching parents about age-appropriate infant nutrition and infant feeding skills. Group assignment will be made on the basis of historical cohort membership: the standard care group will be enrolled first and the intervention group enrolled approximately 3 months later. Subjects in both groups will be followed for 6 months. Outcome measures include parent feeding practices, infant diet, infant feeding skills, and infant overweight. Measures will address cultural and familial biases in favor of overweight children.

The following hypotheses will be tested:

- Compared to parents in the standard care group, more parents in the intervention group will report feeding only single-grain infant cereal and Stage 1 fruits and vegetables to their 6 month-olds. In contrast, more parents in the standard care group will report feeding Stage 2 and 3 foods, snacks, juice, and table foods.
- At 6 months, the rate of infant weight for length above the 75th percentile will be higher in the standard care versus intervention group.
- Parents in the intervention group will be more likely to report receiving accurate information about infant feeding and nutrition from their pediatricians than parents in the standard care group.
- More infants in the intervention than standard care group will use a cup for drinking and fewer will have been fed solid food in a baby bottle.

Student's role in the project: Students will be trained to conduct standardized interviews, to gather anthropometric data on adults and children, and to monitor delivery of the intervention, according to the research protocol.

Preferred Background/ Experience: Skills in interacting with adults from varied cultural backgrounds, interest in infant growth and development and primary care intervention models.

References:

Gray, J.D., Punsoni, M., Tabori, N.E., Melton, J.T., Fanslow, V., Ward, M.J., Zupan, B., Menzer, D., Rice, J., Drake, C.T., Romeo, R.D., Brake, W.D., Torres-Reveron, A., Milner, T.A. (2007). Methylphenidate administration to juvenile rats alters brain areas involved in cognition, motivated behaviors, appetite, and stress. *The Journal of Neuroscience*, 27, 7196-7207.

**Stefan Worgall, MD, PhD**

Pediatrics / Genetic Medicine

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Field(s) of Interest: Cystic fibrosis / host defense in lung / gene therapy

Research Titles:

Lung antigen presenting cells in cystic fibrosis

Respiratory syncytial virus vaccine using capsid-modified adenovirus vectors

Project Descriptions:

1. Cystic fibrosis lung disease is characterized by exaggerated inflammation and increased susceptibility to infections. Although the CFTR protein is primarily thought to be expressed by epithelial cells we and others have studied the expression of CFTR in non-epithelial cells, in particular antigen presenting cells in the lung. This project studies the abnormalities of lung dendritic cells derived from CF knock-out mice. Our data so far indicates that abnormal CFTR expression lung macrophages and dendritic cells is related to abnormalities in innate immune responses. These findings are important in understanding lung disease in CF and also to identify new targets for therapy of this severe disease.

2. Infections with RSV are one of the major causes for viral lower respiratory tract illness, especially in young children. Our laboratory has been working on the development of genetic vaccines for pulmonary pathogens. This project aims to analyze the immunological properties of a novel anti-RSV vaccine using a capsid-modified adenovirus vector. Protection against RSV could be achieved with an efficient vaccination strategy inducing neutralizing humoral immunity as well as a Th1-dominant cellular response. Adenovirus gene transfer vectors can be used to evoke robust systemic and mucosal immunity against an immunogen expressed as a transgene and Ad functions as a potent adjuvants. The Ad modifications include the addition of a RGD motif to the fiber knob, a modification known to enhance infection of antigen presenting cells and to increase Th1-type immune response, as well as the addition of RSV epitopes into the Ad capsid. These modified vectors will be assessed to induce immunity and protection against RSV in adult and neonatal mouse models. The study will evaluate if a modified Ad vector expressing the RSV F protein engineered to increase activation and infectivity of antigen presenting cells could be useful as a RSV vaccine.

Students' Role in the Project: Design of new and continuation of the present experiments. Student will be involved in cell culture studies and flow cytometry analysis of lung dendritic cells (project 1) and adenovirus vector construction and immunological analyses (project 2).

References:

- Worgall S, Heguy A, Luettich K, Harvey BG, Quadri LE, Crystal RG. Similarity of Patterns in Gene Expression of Human Alveolar Macrophages Evoked by *Pseudomonas aeruginosa* and *Burkholderia cepacia*. Infect Immun 2005; 73: 5262-8
- Krause A, Joh J H, Hackett NR, Roelvink PW, Bruder JT, Wickham TJ, Kovesdi I, Crystal RG, Worgall S. Epitopes expressed in different adenovirus capsid proteins induce different levels of epitope-specific immunity. J Virol 2006; 80: 5523-30
- Worgall S, Krause A, Qiu JP, Joh J, Hackett NR, Crystal RG. Protective immunity to *Pseudomonas aeruginosa* induced with a capsid-modified adenovirus expressing *P. aeruginosa* OprF. J Virol 2007; 81: 13801-13808
- Skaricic D, Traube C, De B, Joh J, Boyer J, Crystal RG, Worgall S. Genetic delivery of an anti-RSV antibody to protect against pulmonary infection with RSV. Virology 2008; 378:79-85

Xu Y, Tertilt C, Krause A, Quadri LN, Crystal RG, Worgall S. Influence of the cystic fibrosis transmembrane conductance regulator on expression of lipid metabolism-related genes in dendritic cells. *Resp Res* 2009; 10:26

Tertilt C, Joh J, Krause A, Chou P, Schneeweiss K, Crystal RG, Worgall S. Expression of B cell activating factor enhances protective immunity of a vaccine against *P. aeruginosa*. *Infect Immun* 2009; 77:3045-3055

Krause A, Xu Y, Joh J, Hubner R, Gess A, Ilic T, Worgall S. Overexpression of sonic hedgehog in the lung mimics the effect of lung injury and compensatory lung growth on pulmonary Sca-1 and CD34 positive cells. *Mol Ther* 2010; 18: 404-412

# PROGRAM MATCHING

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# CLASS OF 2012 PEDIATRIC RESIDENCY MATCHES

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NAME	PROGRAM	INSTITUTION	CITY, STATE
Boyle, Katherine	Pediatrics	U Washington Affil Hosps	Seattle, WA
Elizondo, Leah	Pediatrics	Mt Sinai Hospital	New York, NY
Frank Benjamin	Pediatrics	U Colorado SOM-Denver	Aurora, CO
Gilbert Kristin	Family Medicine	Oregon Health & Science Univ	Portland, OR
Greene Brandon	Pediatrics	Univ of Chicago Med Ctr	Chicago, IL
McLaren Son	Pediatrics	NYP Hosp-Weill Cornell Med Ctr	New York, NY
Prieto Monica	Pediatrics	NYP Hosp-Columbia Univ Med Ctr	New York, NY
Samuels Stephanie	Pediatrics	Yale-New Haven Hosp	New Haven, CT
Smith Mariel	Pediatrics	NYP Hosp-Weill Cornell Med Ctr	New York, NY
Timberlake April	Pediatrics	SUNY HSC Brooklyn	Brooklyn, NY
Vernov Mary	Pediatrics	NYP Hosp-Weill Cornell Med Ctr	New York, NY
Walsh Cora	Family Medicine	Univ of Minnesota-North Memorial	Minneapolis, MN

## DEPARTMENT OF PEDIATRICS

### GRADUATE MEDICAL EDUCATION CLASS OF 2012

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Michael Alfonzo	Emergency Medicine - Yale
Vidhya Annavajjhala	Cardiology – Texas Children's
Selene Bantz	Allergy/Immunology - Yale
Tiffany Dy	Allergy/Immunology - Montefiore
Timothy Brennan	Addiction Medicine – St. Luke's Roosevelt
Joanne Chiu	Cardiology – NYP Columbia/Cornell
Amira El-Sherif	General Pediatrics – Hope Mills Pediatrics, North Carolina
Alexis Feuer	Endocrinology – Cornell
Hannah Frait	Cardiology – NYP Columbia/Cornell
Elisa Hampton	Chief Resident – NYP/Cornell
Lystra Hayden	Pulmonary – Boston Children's
Lazaro Hernandez	Cardiology – University of Minnesota
Jennifer Hughes	Hematology/Oncology – Stanford
Christine Joyce	Chief Resident –NYP/Cornell
Doan Le	General Pediatrics – Access Community HealthCare Network, Chicago
Mary Palomaki	Tulare Community Health Clinic, Tulare, CA
Steven Quatela	Hematology/Oncology – MSKCC
Melissa Rose	Gastroenterology – Cornell
Helen (Nelly) Schottel	General Pediatrics – St. Barnabas Hospital, NY
Claire Zar-Kessler	Gastroenterology – Massachusetts General

#### Chief Residents 2011-12

Lindsey Greene	Pediatric Hematology/Oncology, CHOP
Jaspreet Loyal	General Academic Pediatrics, Yale