

SIGNAL

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Raising Awareness about Rare Diseases

October 2011 was the tenth National Niemann-Pick Disease Awareness Month. In order to raise awareness on this rare genetic disorder, the Center for Rare and Neglected Diseases hosted Mrs. Karen Quandt and her son Ty in October. They spoke with members of CRND and with students of the class "Developing Health Networks in Rare and Neglected Diseases." In September Mr. Sean Recke and his son Adam also spoke with students and faculty as part of a visit sponsored by the College of Science.

Lessons from the Quandt visit

Mrs. Karen Quandt, RN, MSN is the Chair for the National Niemann Pick Disease Foundation (www.nnpdf.org/). It is a non-profit organization

dedicated to supporting research and to providing support services for families. In addition to organizing annual family meetings, the foundation provides advocacy services, educational resources, and service referrals.

Both Mrs. Quandt and Ty delivered presentations. Ty shared a photo essay of friends and family and linked it with an electronic dialog that he wrote using an iPad. Mrs. Quandt then presented her epidemiological research that set out to determine whether families with Niemann Pick Type C Disease are susceptible to other genetically-linked

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Mrs. Karen Quandt with her son Ty

diseases. Three organizations assisted with her work, National Niemann-Pick Disease Foundation, The Niemann-Pick Disease Group of the United Kingdom and the Ara Parseghian Medical Research Foundation. Mrs. Quandt plans to expand her research by recruiting families from the International Niemann Pick Disease Alliance.

Lessons from the Recke visit

Mr. Sean Recke visited Notre Dame with his son Adam and his father

(Grandfather Recke). As part of their visit, the Recke team attended several sports events, including the football game against Michigan State and a soccer game.

Mr. Recke visited campus with the primary goal of raising awareness about Niemann Pick Type C disease and how it affects families. He talked about how long it took physicians to diagnose the

disease in his son and how they mismanaged communicating it to the family. By sharing his story, he wanted pre-professional students to be cognizant of issues facing families. He works tirelessly to support his son through awareness campaigns and monthly fundraisers. Mr. Recke can make a difference because he *believes*.

(Please visit www.RaceForAdam.org for more information.)



Mr. Sean Recke (in "I believe" shirt) with his son Adam (in green ND jersey)

Mrs. and Dr. Koehler visit Notre Dame and CRND



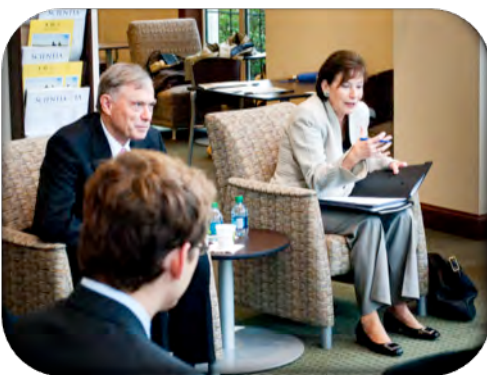
Mrs. Eva Luise Koehler (pictured in upper left panel on the left) is the former First Lady of the Federal Republic of Germany and Patroness of the German Alliance for Chronic Rare Diseases (ACHSE). She and her husband Dr. Horst Koehler, (former President of Germany and shown in the right panel on the left) met with students and CRND faculty on Friday, September 30th (<http://nd.edu/~crnd/>).

Both Mrs. and Dr. Koehler are leading advocates for rare diseases and established the Eva Luise and Horst Koehler Foundation in 2006. Mrs. Koehler wants to raise awareness on rare diseases because 5% of the population has a rare disease. Since 2004 Mrs. Koehler has been Patroness of ACHSE, an alliance of over 100 patient organizations.



The English translation of the German word ACHSE is axle. It describes their mechanism to promote awareness, especially in the political and scientific arenas. Mrs. Koehler provided an example of a “push” mechanism, whereby the Koehler Foundation and ACHSE sponsor a €50,000 prize to support scientific research on rare diseases. To promote public policy in rare diseases, ACHSE has built strong ties with many different international organizations, such as the German Federal Ministry for Education and Research, the European Organization for Rare Diseases, the European Medicines Agency, and the U.S. Food and Drug Administration.

The Koehlers, ACHSE, and CRND strive to make rare diseases “non-rare.”



Top of page left panel from the left, Mrs. Koehler, Father James Foster, Wei Lu, Jennifer Van Trieste.

Top of page right panel from the left, Dr. Horst Koehler, Brianna McSorley, Michael Clark, Aaron Patzwahl and Natalie Bott.

Bottom of page, top left panel: Dr. Horst Koehler, Aaron Patzwahl and Mrs. Koehler.

Bottom of page, top right panel: Marisa Truong, Natalie Bott, and Brianna McSorley. Michael Clark;

Bottom of page, bottom left pane, clockwise from left: Dr. Nitesh Chawla, Dr. Edwin Michael, Dr. Jeff Schorey, Dr. Pamela Tamez., Mr. Michael Clark.

Bottom of page, bottom left pane, clockwise from left: Dr. Basar Bilgicer, Dr. Jesus Izaguirre, Marisa Truong.



Undergraduates contribute to clinical research and publish

Undergraduate students who registered for the class “Developing Health Networks in Rare and Neglected Diseases” performed clinical research and published their results in the peer-reviewed, open access journal *PLoS One*. For access to the manuscript titled, “Defining Natural History: Assessment of the Ability of College Students to Aid in Characterizing Clinical Progression of Niemann-Pick Disease, Type C”, please visit <http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0023666>.

CRND course development and clinical research is in collaboration with physician-scientist Dr. Forbes D. Porter, nurse practitioner Nicole Yanjanin (both at the Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health). It is also linked to the Clinical Translational Seminar Series, which allows additional expert clinicians and researchers to interact directly with the students and Notre Dame community.

Sixty-four students were expertly trained in one rare disease, Niemann Pick Type C disease (NPC). This disease, which affects 1 in 120,000 people, is a fatal, neurodegenerative genetic disorder. Patients can present with a broad range of symptoms, and the age of onset is variable. Because of these

confounding factors, diagnosis can be difficult and delayed by several years. Additionally, since physicians do not have good biomarkers, it is difficult to determine whether a particular drug has any therapeutic effect in NPC. This has the consequence of further delaying FDA approval of new drugs to treat a rare disease.

Families accumulate medical records as they search for a diagnosis. These records can be valuable sources of information to define the natural history of the

undergraduate and biomedical graduate students first received HIPAA certification to understand patient privacy and security. Then students learned about the clinical disease-symptoms, diagnosis, and emerging therapies. Using de-identified records from NPC patients, they converted clinical notes into digital information, a disease severity scale. Dr. Porter, Ms. Yanjanin and colleagues at the National Institutes of Health first developed this scale.



Class of Spring 2009



Class of Fall 2009



Class of Spring 2011

disease. By defining disease manifestations and progression, natural histories allow physicians to determine whether experimental therapies are working.

The class became a model to determine whether students can be trained to accurately assess and define rare disease natural histories from patient records. Upper-class pre-med



Class of Spring 2010

Students correctly quantified major and minor symptoms from seven medical records that had been previously assessed by Porter and Yanjanin. Student assessment of two new records donated by NPC families directly to the study also revealed that the disease was more severe at later stages.

This study was presented at the National Niemann Pick



Dr. Forbes D. Porter from NIH teaches students the clinical severity scale.

Disease Foundation, the major patient services organization. Afterwards Mrs. Karen Quandt, Chair of the National Niemann-Pick Disease Foundation, approved for NPC

families to directly contact CRND to contribute their medical records and further advance the natural history project. The students will provide families with a two page medical summary of the patient records to help new doctors quickly assess the patient history in a standard office visit.

The goal now is to recruit pre-med programs across the country to leverage their undergraduate strengths to develop natural histories for 7000 rare diseases.

As student Natalie Bott put it, "...undergraduate student[s] can make a difference."



Dr. Marc Patterson from the Mayo Clinic talks about experimental therapies for NPC.

Exosomes for use in TB diagnostics and vaccines

Tuberculosis is caused by the pathogen *Mycobacterium tuberculosis*. Although there is a vaccine, it does not protect against pulmonary disease in adults. And because the current diagnostic test is not very sensitive, nearly half of all cases are missed. Consequently, patients go without treatment.

Dr. Jeff Schorey and his team think they have an answer to address these problems. In 2007 through a serendipitous discovery, they detected bio-signatures from the TB pathogen that were released from infected cells as exosomes. Exosomes are vesicles or sacs that contain protein and other cellular material and are released by many different types of cells. Shorey's group in collaboration with two other teams



identified pathogen-associated signatures from TB-infected patients.

They propose using exosomes for diagnostics as well as boosters in vaccines. Exosomes are attractive components of diagnostics because they can be found in many different bodily fluids. They make good vaccines since they contain specific TB proteins that stimulate the human immune system.

Schorey's team is currently testing parameters of sensitivity for a diagnostic, and CRND is happy to contribute to this research. Sensitive tests promise to strengthen TB preventative measures and accelerate drug development.

Congratulations to...

Mr. Nicholas Geraci and Mr. Mike Klemp won Young Investigator Awards for posters presented at the November American Association of Immunologists Conference. Nicholas Geraci is a graduate student in Dr. Mary Ann McDowell's lab, and Mike Kemp is an undergraduate mentored by Geraci.

The V Foundation for Cancer Research named **Dr. Zachary Schafer** a 2011 V Scholar. He is one of only 17 scholars.

The Swedish National Science Council and AstraZeneca

sponsored **Dr. Paul Helquist** for a 14-month scientific visit in Sweden.

The work of **Dr. Souvik Bhattacharjee** was selected for a late-breaker session at the 60th annual meeting of the American Society for Tropical Medicine and Hygiene (ASTMH). It is scheduled for publication in the January issue of the journal *Cell*.

At the request of **Fr. Tom Streit**, CRND was happy to contribute funding for the symposium on Compassion in Global Health held at the annual ASTMH meeting.



Faculty Spotlight on Dr. Patricia Champion



Dr. Patricia Champion has had a long-standing interest in learning how bacteria function. It began when she was a graduate student in Dr. Tom Silhavy's lab at Princeton. Her thesis centered on how bacteria sense and respond to stress. But while at Princeton, she became interested in how bacteria secrete proteins, an important mechanism that allows bacteria to adapt and survive. She decided to study protein secretion in bacteria that cause serious disease in humans, *Mycobacteria*.

As a postdoctoral scientist in Dr. Jeff Cox's lab at the University of California- San Francisco, Champion made a simple but important discovery. She wanted to know how *Mycobacteria* cause diseases such as leprosy and tuberculosis. Bacteria build a biological machine named ESX that secretes a dozen virulence factors into the human host that allow it to survive and thrive. Champion designed a set of experiments to test how these factors are recognized and secreted by the ESX machine. She found,

much to the surprise of scientists in the community, that changing one amino acid in one protein stops the ESX machine altogether. The prevailing thought had been that changing one protein would not interfere with the machine's ability to secrete other virulence factors. She published her findings in the prestigious, peer-reviewed journal *Science*.

Now Champion has assembled a team of 10 scientists at the University of Notre Dame to learn how the ESX machine is built by the pathogen. Her lab has been gaining momentum. Champion was awarded a Career Development Award to fund part of her research. CRND was also happy to contribute by helping fund her proteomics project, a high-tech solution for rapidly identifying the components of the ESX machine. With this funding, the lab optimized the system and generated enough data to be awarded an Exploratory/Developmental R21 grant from the National Institutes of Health. They have also



submitted a manuscript of their rapid identification system to a peer-reviewed journal. Their system is generating enough data to keep the lab busy for several years.

With all the momentum, it is difficult to contain the excitement in the Champion lab. Dr. Champion herself truly enjoys thinking through the problems and cheerleading her group to find the solutions.

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