CRND celebrates World Rare Disease Day 2014
Our first large gathering in 2014 was celebrating World Rare Disease Day by hosting a symposium on Saturday, Feb. 15 at the Notre Dame Conference Center. The daylong program comprised of six discussion panels guided by lead speakers as well as poster sessions. The symposium was dedicated in memory of our friends Riley Smith and Tylor White-Richardson, who recently passed away from Niemann-Pick Type C (NPC) disease, a rare cholesterol storage disorder that affects approximately one in 100,000 people.

Elizabeth Berry-Kravis ’79, M.D., Ph.D., professor of pediatrics, neurology, and biochemistry at Rush University Medical Center in Chicago, gave the keynote lecture and led the experimental drug panel. She described her FDA-approved experimental treatment for NPC. It is given every two weeks in a daylong clinical visit and more accessible for patients than week-long residence programs.

A wide range of diseases were discussed, including general growth and neurological disorders, bone malformation, hyperkinetic disease, dysmorphisms and amyloidosis. Because of the lack of awareness, all of the patient families had taken ownership of the process to obtain information on diagnosis, treatment and disease management. They stressed the importance of the National Organization of Rare Diseases (NORD; represented by Muriel Finkel) and patient organizations focused on individual rare diseases. ESTEEM students Bianca Fox and Yuan Gao described the Notre Dame RHE program, a collaboration of students and patient families to develop a database of rare disease medical records: two additional diseases were added this year: Marfan and NKH and the database continues to grow.

Mike Hamerlik, CEO of WPS Health Insurance led discussion on the implications of the recent affordable care act for rare diseases. Fortunately care can no longer be denied on the basis of pre-existing genetic condition.
Research Presentation by Dr. Shaun Lee

The Symposium also included posters and panel discussions on laboratory research on new diagnostics and therapeutics in lysosomal disorders and rare cancers.

Shaun Lee, assistant professor of biological sciences, and Tony Serianni, professor of chemistry and biochemistry, described their research collaboration on new therapies in Sanfilippo syndrome, a disease that prevents proper breakdown of sugars.

Dr. Suhail Alam, post doctoral associate, biological sciences who works with Kasturi Haldar, Professor of Biological Sciences described the first plasma biomarker for neurodegeneration to monitor whether NPC patients are responding to therapy. Olaf Wiest, professor of chemistry and biochemistry, discussed how powerful computers can be used to find FDA-approved drugs that can be repurposed for rare diseases such as NPC.

Başar Bilgiçer, assistant professor of chemical & biomolecular engineering described research on nanoparticles to target a rare cancer called multiple myeloma. Laurie Littlepage, Assistant Professor Chemistry and Biochemistry, explained her research on a rare breast cancer that affects Kenyan women. Cassandra Buchheit, a graduate student in biological sciences who works with Zachary Schafer, Assistant Professor described research on a rare inflammatory breast cancer that is often misdiagnosed as an infection.

To conclude the day, all attendees undertook a rare disease quiz prepared by the RareND club, which reminded us of the sobering gap that exists in awareness for rare diseases, even as we rallied around the Notre Dame Rare Disease fight song. We are grateful for comments received and acknowledgment from families.
Letters to CRND: on Rare Disease Day Celebration!

From Family

Thank you for reaching out to us. It is greatly appreciated. We are VERY happy that we attended rare disease day event at Notre Dame.

One of the main reasons we attended the event at Notre Dame was because we felt like we were so in the dark. We received our diagnosis last year on Valentine’s Day. It was wonderful to speak with [other families] and to meet their children.

We know how many parents before us had nothing to hold on to. You are all such wonderful people devoting time and making it your life’s work caring and working towards curing our children.

It is everything ~ Rare Disease Parents

From students

“Rare Disease Day was an exposure to the reality of living with a rare disease, and the personal testimonies really put the patient perspective into focus”

“The family panel offered insight into what it meant to be living with someone with a rare disease”

“It was amazing to see how people were so positive after so much pain and struggle”

“Hearing about rare diseases demonstrated to me what a wide range of symptoms and disorders the umbrella of rare diseases covers”
Dear Dr. Haldar,

I hope the semester is going well for you and for this semester's students in Clinical Research in Rare and Neglected Disease. I just wanted to reach out to you and tell you about an experience I had working as a graduate student in a genetics lab at Avera Hospital (a regional hospital system is South Dakota).

About a week ago, some of my colleagues and I were approached by a nurse, on behalf of a cardiologist, who was asking about the availability of genetic test for Ehler-Danlos Syndrome. The physician was suspecting this rare disorder in a patient, but was having difficulty finding information related to diagnosis, genetic testing, Ehler-Danlos specialists, and Ehler-Danlos support groups. No one in our lab had heard of Ehler-Danlos, including me, but I suggested the NORD website we had worked with and written for in your class. I helped the nurse search the NORD website and she was able to find a large amount of information related to the disorder and passed it along to the cardiologist.

A few days later, the nurse informed me that with the information from NORD, the cardiologist was able to find the patient a nearby Ehler-Danlos specialist. In addition, the patient was able to join an Ehler-Danlos support group and started receiving information and specialist recommendations from the Ehler-Danlos National Foundation.

Without your class, I would never have been able to make this recommendation to use NORD. Although I am not currently working on any NP-C research, your class continues to serve as a great learning experience and invaluable tool in my current work. Thank you!

Gratefully,

Zach Weber
The RareND club received official SAO status in 2014! Congratulations to Co-Presidents Madison McMenemy and Allison Kress who along with their officers Abraham Yu, Ali (Kareem) Ahmad and a crew of ~30 members have had a busy year. A few events are highlighted below.

March 6th, 2014: Local Middle School Student Visit.
The Lake Shore Middle School student council visited ND and had lunch with Dean Greg Crawford (College of Science). At CRND, the RareND club used a game to show how difficult rare disease diagnosis and expert care can be. The interested and enthusiastic students had lots of great questions for RareND and research presenters.

April 9th, 2014: Staff and Students Discussion on Rare Disease Film.
In 2010 Frances Shavers, Chief of Staff and Special Assistant to Notre Dame’s President Fr. Jenkins was diagnosed with Trigeminal Neuralgia (TN), a rare disease with excruciating pain. To manage her condition, Frances has endured four brain surgeries, requires multiple medications and assistance from her husband George and service dog Hannah. Frances, George and Hannah visited at the screening of an awarding winning movie called ‘The Suicide Disease’ (many TN patients commit suicide) made by ND students on Frances’s heroic life story.

Catholic Tradition Serving Rare Disease Awareness
May 1st, 2014
For his minor in Catholic Tradition Services, Andy McAsey an active member of RHE and RareND researched perceptions of rare disease patients towards their healthcare and presented his findings to the RareND club. He was joined by Stephen Barber a patient representative and Dr. Mary Alice Read, a local pediatrician and ND Alum.
Rare Health Class Tackles Marfan’s Syndrome

Students enrolled in the Clinical Research in Rare and Neglected Disease Class had a new kind of challenge. In previous years, the students reviewed medical records of rare disease patients to determine the severity of the symptoms. This helps develop a natural history of disease progression. This year, starting with the Fall class, the students decided to study Marfan’s Syndrome, a rare disease that affects the heart and eyes of the affected individuals.

What made these classes particularly challenging was over 4,000 pages of medical history! The students had a monumental task but rose to the challenge!

Thank you to the 2013-2014 Class and Congratulations to our Seniors!
Emerging new therapies in Rare and Neglected Diseases

Niemann-Pick Type C: FDA exemption

Professor Paul Helquist and Professor Olaf Wiest (both in Chem and Biochem) were honored for receiving FDA exemption to initiate a new clinical drug exposure study for NPC. The event was organized by the College of Science. Dr. Haldar, Director of CRND presented Drs. Helquist and Wiest with framed copies of the FDA letter on the eve of the Second Annual Parseghian cup (April 5th) where ND and University of Arizona faced off in a friendly rugby match to benefit the Ara Parseghian Medical Research Foundation.

Cindy and Mike Parseghian were honored for their long standing commitment and hope that they bring to NPC.

Malaria: CRND-Lilly-Medicines for Malaria Collaboration Update

The goal is to discover and develop new drugs to combat resistance of malaria parasites to existing drugs, which threatens malaria control and elimination.

In the first phase of this project, over 100,000 compounds from chemical libraries of Eli Lilly & Co were screened for antimalarial activity. In a second phase, the hits re-entered the testing cascade to yield ~45 active compounds that could be clustered in 12 distinct series or (structurally related) families.

In the third phase, over the last nine months, Dr. Guille Estiu (CAMD Core), Dr. Rui Liu (Chem-Biochem) and Dr. Trupti Pandharkar (Biological Sciences) took a leading series through structure-activity relationship (SAR) studies to determine the relationship between the 3D structures of compounds and the biological target. This resulted in a library of over 60 chemical entities tested with multiple potent on-target compounds ready to be moved into pre-clinical development. The studies were in close consultation with Lilly to mirror industrial processes but in an academic context. The partnership with MMV progresses leads into drugs in the pipeline for malaria elimination. *Dedicated to the memory of Dr. Estiu who sadly passed away on May 9, 2014.*
Professor Schorey’s group has pioneered the study of exosomes produced by immune cells infected with the *Mycobacterium* bacteria that causes tuberculosis (TB). These exosomes are vesicles of defined size (30 to 100 nm) that bud from infected cells. They contain *M. tuberculosis* proteins (or antigens) that can elicit an immune response. The Schorey lab recently reported that these exosomes when injected into mice can protect the animals from TB as well as the current BCG vaccine (Cheng, Y. & Schorey, J.S. (2013) *European Journal of Immunology,* 43 (12) 3279). The exosomes are likely to be simpler and better defined than BCG, which is an attenuated form of live bovine tuberculosis (*M. bovis*). The next steps will be making exosomes of defined antigens (anywhere from 2-5) and in sufficient quantity. The goal will be to develop exosome vaccines that target bacteria which are in an actively replicating phase as well as in the latent phase with the outcome of reducing total pathogen burden and killing the latent reservoirs that underlie persistence and resistant to treatment by drugs.

**Faculty Spotlight: Dr. Miguel Morales**

Leishmania is a mosquito-borne parasite that affects more than 12 million people worldwide with over 2 million cases each year. The disease caused by Leishmania results in disfigurement or life-threatening visceral complications. There is no vaccine for leishmaniasis and the most common drugs used to treat infection are old, toxic and expensive.

Research in the Morales lab (ND Biology) aims to shed light on this neglected tropical disease by examining how the molecular pathways within the parasite function. Already, the Morales lab has identified a number of “drug targets”. These are important parasite proteins that can be targeted by new drugs. Dr. Morales is using this knowledge to search for new molecules that can inhibit the function of these proteins. Dr. Morales, who grew up in Madrid, Spain, draws on his experience working with some of the world’s top leading Leishmania researchers, including his doctoral mentor Dr. Jorge Alvar, the former Leishmaniasis director at the World Health Organization (WHO). With his experience and the commitment at Notre Dame to impact the lives of the poor, the research aims to advance the health standards of people affected by this neglected disease.

Outside the lab, Dr. Morales enjoys spending time with his wife and son, playing soccer and building basic robots. In addition to being a movie lover, he is an aviation enthusiast, currently preparing for private pilot license test.
Using bacteria to fight bacteria

The research of Dr. Shaun Lee (Biology) focuses on a type of molecules known as bacteriocins. These molecules, which are produced by almost all bacteria, can be sent out as communication messages or to fight against other bacteria. Dr. Lee’s group recently had a paper accepted for publication in *PLOS Pathogens*, a leading journal in microbial pathogenesis. The work describes how bacteriocins can be used to develop new ways to fight bacteria. This is particularly important, since antibiotic resistance has become a major problem. *Congratulations to Dr. Lee and his research group! Look out for the article.*

A new publication from the Haldar lab in *Malaria Journal* describes work that looks at the prevalence of malaria infections in Cameroon. The vast majority of infections are caused by the parasite *P. falciparum*. A second parasite species *P. vivax* which causes significant disease in Asia is thought to be largely absent from sub-Saharan Africa, where humans lacks a receptor needed for *P. vivax* to cause infection. The study, carried out by Jerome Fru-Chou, a visiting doctoral student from the University of Buea, found that almost 25% of malaria cases were caused by *P. vivax*. This stresses the importance of developing detection methods and multiple therapeutics for malaria elimination programs. *Congratulations to Dr. Fru-Chou who received his Ph.D. in 2014. Find the Article here.*

**The Michael, Marcia & Christa Parseghian Scientific Conference for Niemann Pick Type C Research** was held at Jordan Hall June 12th - 14th 2014. A wide range of presentations covered the most recent work in basic, translational and clinical research in NPC.
The 4th Annual Midwest Neglected Infectious Diseases Meeting

August 15-16, 2014
University of Notre Dame

Keynote Lecture:
Dale J. Kempf, Ph.D.
AbbVie Inc.

Neglected Tropical Diseases Research:
A new Model for Corporate Responsibility