

Defining Natural History: Notre Dame undergrad students publish their clinical research on a rare disease.

Sixty-four undergraduate students, expertly trained to assess medical records, published their clinical research in the scientific journal *PLoS One*. The manuscript is entitled, “Defining Natural History: Assessment of the Ability of College Students to Aid in Characterizing Clinical Progression of Niemann-Pick Disease, Type C” (<http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0023666>). The work is in collaboration with physician-scientist Dr. Forbes D. Porter, Ms. Nicole Yanjanin, a nurse practitioner, both at the Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health and the Notre Dame Center for Rare and Neglected Diseases. It is also linked to the Clinical Translational Seminar Series, which allows additional expert clinicians and researchers as well as other major stakeholders to interact directly with the students and Notre Dame community (<http://nd.edu/~crnd/CTSSeriesAnnouncements.html>).

Since this type of course has not previously been taught, it was developed in steps over four semesters. The initial incubator stage evolved after consultation with major foundations, families who suffer rare disease as well as Notre Dame’s Center for Social Concern. The first class involved three undergraduate students. It then expanded to 16 students for two consecutive semesters, and then to 30 students in the Spring 2011 class. The 2012 class will accept as many as 50-60 students.



Class of Spring 2009



Class of Fall 2009



Class of Spring 2011



Class of Spring 2010

Students registered for the class “Developing Health Networks in Rare and Neglected Diseases” but gained more than textbook teachings. According to Aaron Patzwahl, a student of the class, “The opportunity to pursue clinical research in Notre Dame’s Center for Rare and Neglected Diseases as an undergraduate pre-medical student is...unique. [It] has exposed me to the need for research and advocacy surrounding these diseases.” Michael Clark added that they had the opportunity, “to think like doctors in a safe environment, which can only serve to make us all better clinicians in the future.” Katrina Epperson, one of the lead authors now in medical school, also appreciates the fact that the course “educate[s] future health care providers about rare diseases.”

Students became clinical experts 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, physicians cannot accurately determine whether a particular drug has any therapeutic effect. This has the consequence of further delaying FDA approval of new drugs to treat a rare disease.

Because diagnosis takes so long, families have a lot of medical records, which can be valuable sources of information to define natural history. When you define natural history, you can define what the disease is. You need to have the natural history of a disease in order 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 undergraduate and biomedical graduate students first received HIPAA certification and learned the rules governing patient privacy and security. Then they learned the clinical disease, symptoms, how to recognize them, diagnosis, and emerging therapies. Using de-identified records from NPC patients, they converted clinical notes into digital information, a disease severity scale. This scale was first developed by Dr. Forbes D. Porter, Ms. Nicole Yanjanin and

colleagues at the National Institutes of Health. Students correctly quantified major and minor symptoms from the previously assessed medical records. Seven clinical records, randomly



Mrs. Eva Luise Koehler, former First Lady of the Federal Republic of Germany and Patroness of the German Alliance for Rare Diseases (ACHSE), visited with students of the class. She and her husband former German President Horst Koehler engaged with students and faculty about the issues facing families with rare diseases. *Top left from left*, Mrs. Koehler and Dr. Kasturi Haldar. *Top right from the top*, Marisa Truong, Natalie Bott, and Brianna McSorley. *Middle left from the left*, Mrs. Koehler, Father James Foster, Wei Lu, Jennifer Van Trieste. *Middle right front*, Michael Clark; *from the left*, Dr. Nitesh Chawla, Dr. Edwin Michael, Dr. Jeff Schorey, Dr. Pamela Tamez. *Bottom right from left*, Dr. Horst Koehler, Brianna McSorley, Michael Clark, Aaron Patzwahl and Natalie Bott. *Bottom left from left*, Dr. Horst Koehler, Aaron Patzwahl and Mrs. Koehler.

selected from a total of thirty-seven previously assessed by Porter and Yanjanin, were also correctly assessed by the students. 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.

According to Mr. John Crowley, Chairman and CEO of Amicus Therapeutics, “This paper confirms the strong contributions that can be made at the undergraduate level toward advancing research into the natural histories of rare diseases. Notre Dame's Center for Rare and Neglected Diseases is at the forefront of this important work.” The Crowley family was the inspiration for the 2010 major motion picture “Extraordinary Measures”.

This study was presented at the National Niemann Pick Disease Foundation, the major patient services organization. Afterwards 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 build natural histories. For families that are interested, please contact Dr. Kasturi Haldar (khaldar@nd.edu), Director, Center for Rare and Neglected Diseases. The students will also provide families with a two page medical summary of the patient records, which helps new doctors to quickly assess the patient history in a standard office visit. For examples of a summary, please contact Marisa Truong (mtruong@nd.edu).

Dr. Haldar, who has taught the class, thinks this an un-plumbed depth in premedical education. “I think that pred-med juniors and seniors offer the perfect combination of skills—smart, driven, enthusiastic to do clinical research, and can devote the time needed for the work.” As one of the reviewer’s of the *PLoS One* paper said, “The study is important...it has potential generalizability. The same approach could be taken for other diseases.” Mrs. Eva Luise Koehler, the former First Lady of the Federal Republic of Germany and Patroness of the German Alliance for Rare Diseases (ACHSE), and her husband Dr. Horst Koehler, (former President of Germany) also a leading advocate for rare diseases, suggested several ideas for disseminating similar models in the EU and US. They met with CRND faculty and students from the class on Friday Set 30th (<http://nd.edu/~crnd/>). Dr. Haldar hopes to export the model, saying, “With 7000 rare diseases, it would be wonderful if we can recruit pre-med programs across the country to leverage their undergraduate strengths to develop natural histories for these diseases.” As one student Natalie Bott put it, “...undergraduate student[s] can make a difference.”

For further information, please visit the Center for Rare and Neglected Diseases website: <http://www.nd.edu/~crnd/>

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