



# UNIVERSITY OF ROCHESTER BATTEN CENTER (URBC)

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University of Rochester Medical Center

601 Elmwood Ave., Rochester, NY 14642

Phone: (585) 275-4762

## New CLN3 Studies

The URBC will be carrying out a new research study in collaboration with Batten disease experts, Dr. Angela Shultz and Dr. Miriam Nickel in Hamburg, Germany. The overarching goal of this study is to prepare for future clinical trials focused on CLN3 disease. This will be done in three main ways.

1) Testing clinical outcome assessments: Clinical outcome assessments are tools (e.g., questionnaires) used to measure a patient's symptoms and functioning. For clinical trials, carefully measuring symptoms and symptom changes allows us to recognize the potential impact of an experimental therapy. Therefore, clinical outcome assessments help us determine whether or not a new treatment has noticeable effect or benefit. As part of this study, we will be examining potential clinical outcome assessments to make sure that they are useful, reliable, and practical for use in future CLN3 clinical trials.

2) Confirming a neuroimaging biomarker: Biomarkers are objective, measurable characteristics of *biological processes*. Biomarkers are important for many reasons. Like clinical outcome assessments, biomarkers can help researchers test the effectiveness of a new treatment. There are currently no known disease-specific biomarkers that are sensitive or appropriate for use in CLN3 disease. However, brain imaging may reveal a biomarker for CLN3 disease progression. In this study, we will examine brain-imaging data with symptom progression to look for a biomarker for CLN3 disease.

3) Developing training materials and resources for use in multi-site trials: The URBC has spent years developing and refining the Unified Batten Disease Rating Scale (UBDRS) to use as a clinical assessment tool for NCL disorders. As part of this new study, we will develop materials to train other Batten disease researchers on administering the UBDRS. These training materials will be useful resources for future multi-site clinical trials and will ensure standardized use of the UBDRS within and across studies.

We plan to enroll 35 individuals with genetically confirmed CLN3 disease and 35 age- and sex- matched controls (i.e., individuals without CLN3 disease) across the Rochester and Hamburg sites. Six study visits will happen across three years. The first five visits will take place every six months, and the final visit will happen one year later. There are seven general procedures that will happen at each study visit:

1) Medical History and Medications Review: At the first study visit, information about demographics, diagnostic testing, medical history, and medications will be collected. At each subsequent study visit, medication changes will be reviewed.

2) The Unified Batten Disease Rating Scale (UBDRS): Videotaped UBDRS evaluations focused on motor features, seizures, behavior, cognition, and functioning will take place. A UBDRS-trained neurologist will ask questions about symptoms, and the individual with CLN3 disease will undergo a brief physical exam.

3) Eye Exam: A thorough eye exam will be conducted to assess vision and retinal thickness .

4) Cognitive Assessment: Cognitive testing involves an individualized assessment of cognitive abilities, using tests of attention, memory, and other skills. This assessment is adapted to each child's abilities.

5) Seizure Assessment: In addition to information about seizures collected as part of the UBDRS, at each study visit, participants will complete a video-EEG. Parents will also be asked to maintain a real-time seizure log between study visits.

6) Adaptive Function Assessment: Parents will be asked to complete the Vineland Adaptive Behavior Scales, a questionnaire that assesses functioning in four domains: communication, daily living skills, socialization, and motor skills.

7) Brain Imaging: A non-sedated magnetic resonance imaging (MRI) scan will take place at each visit. Multiple strategies will be used to prepare children for the MRI and ensure their comfort during the procedure.



## International NCL Conference

URBC members attended NCL2018, the 16<sup>th</sup> International Conference on Neuronal Ceroid Lipofuscinoses (NCLs, also called Batten disease) in September 2018 at Royal Holloway, University of London. The meeting brings together basic scientists, clinicians, industry representatives, and patient advocacy leaders to share recent discoveries and advances related to NCL disorders. NCL2018 featured a number of talks and presentations by members of the URBC and our collaborators at the Foxe Lab. URBC Members (Vierhile, Mink, Adams) also participated in the DEM-Child Satellite session (a multinational Batten disease research collaboration) and the NCL2018 “Market Place”, an opportunity for parents, advocates, and others to meet one-on-one with scientists for informal Q&A. Finally, Dr. Shannon Dean, a URBC Fellow in Experimental Therapeutics, received a travel award to attend NCL2018.

**Jonathan Mink:** [Oral Presentations](#) - Natural History Studies in Batten Disease: A Picture of CLN3 Disease (JNCL)

[Poster Presentations](#) – a) The Unified Batten Disease Rating Scale (UBDRS): Validation and Reliability in an Independent Sample; b) A Proposed Staging System for CLN3 Disease (Juvenile Batten disease)

**Eric Nicholas:** [Oral Presentation and Poster Presentation](#) - High Density Electrophysiological Measures of Auditory Sensory Processing as Potential Biomarkers of CLN3 disease

**Heather Adams:** [Oral Presentations](#) - a) Evaluating adaptive function measures in NCL disorders; b) The arc of time: Changes in cognitive function over 15 years in CLN3 disease

[Poster Presentations:](#) a) Using PEDI-CAT to assess functional capabilities in CLN3 (Batten) disease; b) Monitoring neuropsychological function in CLN2 Disease. [AT to Assess Functional Capabilities in CLN3 \(Batten\) Disease.](#) [Satellite session: The JNCL and Education Project](#)

## Did You Know?

Did you know there are a number of restrictions, based in federal law, related to sharing research data? These restrictions are in place to protect the privacy and confidentiality of those who take part in research studies.

For every research study conducted at the URBC, a protocol is developed. This protocol outlines exactly why and how the study is conducted, who can participate, and how data collected are stored and protected. All research protocols are carefully reviewed and approved by an *Institutional Review Board* (IRB), established to protect the rights and welfare of people who participate in research. As researchers, we must follow exactly what is described in study protocols, including how we will collect, use, and protect participants' data. We also go through an *informed consent* process with participants, to explain the study and seek their permission to participate.

The IRB-approved study protocol and informed consent form will list the organizations and individuals outside of the study team (if any) who are authorized to view or access the data, including personally identifying information. Participants or parents of participants must review and sign the consent form, before participating in the research study. This also ensures that they know who might view their data. We can never release research data to individuals or organizations that are not included in our IRB-approved protocol and consent form.

This rule even applies within the University of Rochester. For example, the URBC collaborates with the Cognitive Neurophysiology Laboratory (aka “Foxe Lab”), which conducts EEG and MRI studies at the University of Rochester. Although the URBC and Foxe Lab collaborate closely, our respective groups work under separate research protocols. Therefore, we must obtain consent from participants (or parents) and have IRB-approval in order to share data between the URBC and the Foxe Lab.

To summarize, any data sharing must be outlined in an IRB-approved study protocol and consent form, *and* agreed upon by study participants or their parents. Although these rules may seem complicated, they are in place to protect the rights and welfare of study participants. At any time during or after the informed consent process, participants/parents are welcome and encouraged to ask questions about data sharing and all other aspects of the research.



## Understanding CLN1 Disease

*Have you ever been frustrated by how little is known about CLN1 Batten disease? As we prepare for future treatment trials, we want to change this.*



The University of Rochester Batten Center is looking for parents of living or deceased children with CLN1 Batten disease to share their child's healthcare and school records with us. If you choose to participate, you will not be asked to collect these records on your own unless they are easily available to you. Your participation will take up to 1 hour and can happen by phone. Findings will be shared with the Batten community.

Please call (585) 276-5966 or email [batten@urmc.rochester.edu](mailto:batten@urmc.rochester.edu) to learn more.

## URBC Contact Registry

Do you want to be informed about future Batten disease research? The URBC Contact Registry asks your permission to keep your contact information on file, so that we can send you updates about the URBC and related research. Individuals with **all forms of Batten disease** and their parents/legal guardians are eligible to participate. Sign up to be in our contact registry by visiting our website: [www.rochesterbatten.urmc.edu](http://www.rochesterbatten.urmc.edu)



## Natural History Research

***We invite families with children who have all forms of NCL disorders to participate in our ongoing natural history study.*** The focus of this study is to better understand how NCL disorders progress. This study helps us learn about which symptoms may lead to disability and which factors may be related to fewer symptoms and/or less disability. Many families participate year after year, which helps us track symptoms over time. Understanding the progression of NCL disorders is important for measuring the effects of future therapies. This study has multiple parts:

Medical History Interview: You will be asked questions about your child's medical history and medications.

Unified Batten Disease Rating Scale (UBDRS): The UBDRS is a disease-specific assessment tool that was developed at the University of Rochester to help us learn about how NCL disorders progress. A Neurologist will ask you questions about your child's symptoms. This also includes a brief 5-10 minute physical exam with your child.

Cognitive Testing: Cognitive testing helps us learn about thinking skills (such as attention and memory) and how thinking skills change due to NCL disorders. Cognitive testing involves an assessment of your child's thinking skills in a quiet room, which usually takes about 30 minutes.

If you choose to enroll in the Batten Natural History Study, you and your child may be asked to take part in additional study activities, such as an eye exam or a interviews/questionnaires.

Study visits take place in Rochester, NY at the URBC and/or at annual BDSRA meetings. For more information about participating, contact Amy Vierhile at (585) 275-4762 or email us at: [batten@urmc.rochester.edu](mailto:batten@urmc.rochester.edu)





## Heather Adams – Research Sabbatical

Heather Adams, Neuropsychologist for the URBC, recently completed a 6-month research sabbatical at Cardiff University (Wales, United Kingdom) where she built a collaboration with Dr. Dougal Hare, PhD, Reader in Clinical Psychology at Cardiff University. Dr. Adams and Dr. Hare are conducting an in-depth online survey to perform neurobehavioral phenotyping of a variety of pediatric rare diseases that impact learning and behavior. The goals of the project are to determine the feasibility of obtaining detailed information about rare diseases through an online survey, and to identify any unique cultural differences in how symptoms are described or experienced in the USA versus the United Kingdom. Dr. Adams' sabbatical in Wales also provided her with an opportunity to meet with families of children with Batten disease who live in the UK and to visit schools where they attend classes. Some students attend their local community schools but many attend "specialist schools" that serve children who are blind/visually impaired and/or have learning challenges. Last year, Dr. Adams consulted on a European-Union funded project to develop an educational assessment tool for children with juvenile Batten disease. The tool guides parents and teachers through a set of topics and questions relevant to educational support needs of children with JNCL. It is currently being piloted in schools in the UK and Europe. During Dr. Adams' sabbatical, she met with staff at several schools in the UK, to learn about how the assessment tool is being used there, and receive feedback that will help inform revisions to the tool in the future.

## New Collaborator- Ruchira Singh, PhD

Ruchira Singh, PhD, is an Assistant Professor in the Departments of Ophthalmology, Biomedical Genetics, and the Center for Visual Sciences at the University of Rochester Medical Center. Her project is entitled: Determining the Role of CLN3 in the Eye.

Dr. Ruchira Singh has her PhD in Cell Physiology and completed postdoctoral training in pharmacology and stem cell biology. She studies how specific diseases affect the eye. The major goal of her research lab is to find treatments for retinal and neurodegenerative diseases. Dr. Singh's research with juvenile Batten disease (JNCL; CLN3 disease) includes questions such as...

*How does the retina and other parts of the eye change over time with disease progression?*

*How do the changes in the eye relate to the vision loss experienced by individuals with CLN3 disease?*

With this research, the aim is to gain a better understanding of what causes the vision loss in JNCL, why vision loss occurs early in the course of the disease, and whether there are treatments that can target the causes of vision loss, and preserve vision, in affected individuals. Dr. Singh's collaborators for this project include the URBC team in Rochester, and Jill Weimer, PhD a developmental neuroscientist at Sanford Research in Sioux Falls, South Dakota. If families are interested in learning more about Dr. Singh's research they are welcome to contact her at her email:

[Ruchira\\_Singh@URMC.Rochester.edu](mailto:Ruchira_Singh@URMC.Rochester.edu)

**We thank all of the children and families who participate in our research – you make it possible for us to do this work!**

*We love to hear from you! Please contact us with your questions and comments. With your permission, we may post answers to your question on our Facebook page and in upcoming issues of our newsletter.*

Phone: (585) 275-4762

E-mail: [batten@urmc.rochester.edu](mailto:batten@urmc.rochester.edu)

Web: [www.rochesterbatten.urmc.edu](http://www.rochesterbatten.urmc.edu)

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