Behind the scenes at BATCure:

What are some of our roles in the project?

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 666918

"I act as the overall Coordinator for BATCure and I chair the General Assembly and Executive Board. In my role as coordinator of the project, I ensure that it proceeds as planned to achieve its aims of understanding more about Batten disease and particularly developing new therapies for CLN3, CLN6 and CLN7 diseases. I organise and host regular meeting with all partners to share and discuss progress. I also direct the work of my own lab within UCL that contributes to specific BATCure work packages."

Professor Sara E. Mole, Professor in Molecular Cell Biology and BATCure Coordinator

" I work as a European Project Manager at the UCL European Research and Innovation Office. I am in charge of the financial, contractual and administrative matters directly associated with BATCure. In collaboration with the project Coordinator, I monitor the work progress against the plan and liaise with our dedicated EU Project Officer in Brussels."

Cristina Soriano, European Project Manager

"As part of BATCure we are aiming to develop gene therapies for CLN3, CLN6 and CLN7 disease. Here at UCL Institute of Ophthalmology we are particularly interested in treating the eye as preventing the visual failure of Batten disease would significantly increase quality of life of patients.

During Sophia's PhD project that was generously funded by BDFA we already obtained promising preliminary data showing that we can treat the loss of vision in a mouse model of CLN6 disease. We are continuing this and also now planning to use similar strategies for models of CLN3 and CLN7 disease. In addition, we are working closely with Dr Ahad Rahim at UCL School of Pharmacy to develop gene therapies targeting the brain. Eventually we would aim to combine brain and eye treatments in the individual animal models of the disease."

Dr Sander Smith, UCL Institute of Ophthalmology

Dr Sander Smith and Dr Sophia-Martha kleine Holthaus at UCL

"My expertise is in the use of zebrafish for disease modelling and drug discovery. This tropical freshwater fish that many people keep at home is widely used in laboratories to study human disease, as it has a remarkable amount of shared features with humans. The embryos are particularly useful for doing lots of experiments quickly, such as screening compounds, because they are easily produced in large numbers, are very small, and develop very fast.

One of the first steps in the BATCure project is the generation of zebrafish which exhibit the hallmarks of Batten disease. Concurrently, compounds will be screened in cellular models to identify those with therapeutic potential. The zebrafish models will then be used to select a few of the most promising compounds to test in a mouse model of Batten disease."

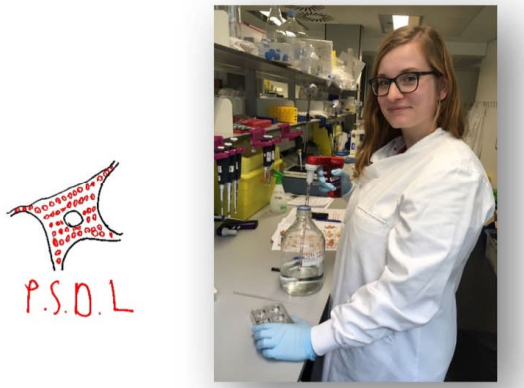
Dr Claire Russell, The Royal Veterinary College

Dr Clinton Monfries in the aquaria at the RVC, which houses many zebrafish.

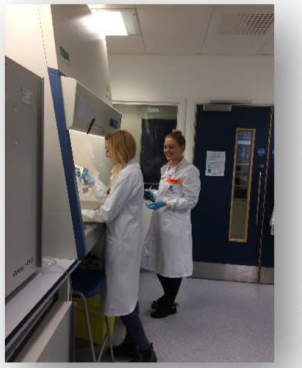
The supervisory team consists of Prof Robert Harvey and Dr Jason Rihel from UCL, plus Dr Claire Russell from RVC. Dr Clinton Monfries is the Researcher employed to complete the lab work.

"Under the supervision of Prof. Jon Cooper and Prof. Liz Bradbury, I'm working to identify new therapeutic targets for the NCLs by analysing the spinal cord and peripheral tissues from mouse models of Cln3, Cln6 and Cln7. This work is done together with our BATCure collaborators at UCL London and UKE Hamburg in order to investigate these transmembrane protein-deficient NCLs. Pinpointing where pathology occurs outside the brain and how it progresses will help us to target therapies to where they are needed."

Charlott Repschlager, PhD student in the PSDL at King's College London



Charlott Repschlager analyses the spinal cord and peripheral tissues from NCL mouse models to identify new treatment targets for Batten Disease.



"I have just started my PhD where I am studying the role of a process called "autophagy" in Batten disease. Batten disease results from the build up of lipofuscin inside many cells but particularly neurons in the brain and this results in the cells eventually dying. Within the cell lipofuscin builds up in vesicles called lysosomes which are the cell's recycling centres for old or unwanted proteins and cellular structures. Some are broken down and discarded but some are recycled; when this system goes wrong the neurons die. It is not entirely clear why things go wrong in the different forms of Batten disease and I am using stem cell models of CLN6 and CLN7 to look at autophagy, one of the main processes that delivers recycling materials to the lysosome."

Louise Bullen, PhD Student

The BATCure team at Professor Tristan McKay's Lab at MMU (Professor in Stem Cell Biology)

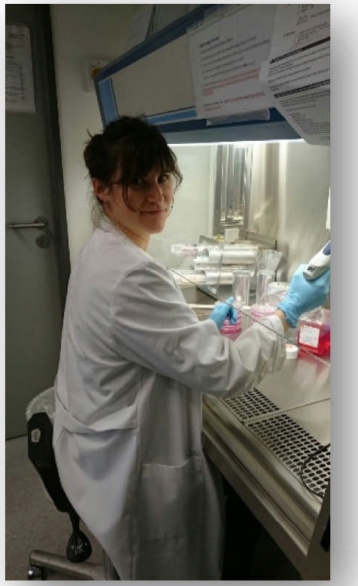
"I am in the first year on my post-doctoral research career working as part of the BATCure consortium. My project is based on generating new stem cell models from Batten patient skin biopsies to aid the testing of new drugs by the consortium. Often, a skin biopsy is taken from patients after informed consent at the time of diagnosis to confirm disease using lab tests. If the family agree, cells grown out from this biopsy can be "reprogrammed", using a special technique, to become stem cells. These stem cells can then subsequently be differentiated into any cell type that is affected by Batten disease meaning we are able to understand the disease better at the molecular level. Crucially, these cells can also be used to test new potential drugs and I am currently carrying this out using skin cells archived from patients with CLN3, CLN6 and CLN7 diseases."

Dr. Lorna FitzPatrick, Post-Doc Researcher

Manchester Metropolitan University

"The objective of our task is to find out how the most common 1 kb mutation in the CLN3 protein harms important functioning processes in cells and thereby causes CLN3 disease. In order to understand these mechanisms, we use two human cell lines expressing either the healthy or defective CLN3 proteins. The proteins as labelled so that we can determine their localization in the cell structures, their half-lives and degradative pathways. A second approach is to analyse neuronal cells from a mouse model of CLN3 disease. We use proteomics and lipidomics which allow us to investigate how and which protein and lipid pathways are affected by the disease in these cells. In addition, we will evaluate how healthy CLN3 protein and specific transcription factors might be able to rescue the defect in CLN3 disease."

Dr Georgia Makrypidi, Researcher at the NCL Research Group at UKE Children's Hospital

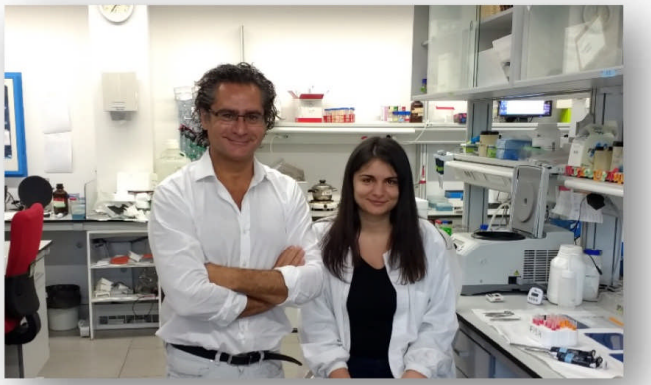


Carolin Schmidtke at work in the lab

Universitätsklinikum Hamburg-Eppendorf

"My group is interested in understanding the molecular bases responsible for the bioenergetics-redox coupling in the central nervous system, both under normal and disease-related conditions. The typical experimental approaches of the group involve neural cell primary cultures from genetically modified mice, *in vivo* behavioral tests in mice, molecular biology techniques, cell signaling, biochemistry and immunocytochemistry. In the context of the BATCure consortium, we are investigating the molecular bases underlying the metabolic re-programming occurring in neural cells in Batten disease."

Professor Juan Bolaños , Research Leader based at the Institute of Functional Biology and Genomics



Professor Juan Bolanos and Dr. Costantina Buondelmonte (BatCure PostDoc) in Juan's laboratory at the Institute of Functional Biology and Genomics (IBFG), a joint research centre between the University of Salamanca and the CSIC.

Marc at work in Barcelona

Guillermo Quintás at work in Valencia

"LEITAT is non-for-profit private technological center based in the Barcelona. Our activities on BATCure are in three different areas:
1) We are developing monoclonal antibodies against CLN3, CLN6, CLN7 and SCMAS to be used by other consortium partners as research tools. These monoclonal antibodies will contribute to the research progress towards the discovery of a therapy as well as to gain more knowledge on the Batten disease pathophysiology.
2) Using urine from those affected by Batten disease, we will analyze the content of exosomes present in the urine. The exosomes are small vesicles which contain proteins and nucleic acids. These small vesicles come from cells from different body compartments so these exosomes are small pieces of cellular information. The analysis of exosomes is aimed to find a exosome composition different from healthy vs affected to be able to improve diagnosis, monitor disease progression and eventually assess the response to treatment.
3) The metabolic components of the urine will be also analyzed. These activities are being done in collaboration with Torbjörn Lundstedt from company AcureOmics and Angela Schulz from University Medical Center Hamburg-Eppendorf. The discoveries will extend our understanding of CLN3, CLN6 and CLN7 diseases, reveal biomarkers for these diseases, provide insight into how to treat these diseases and so normalize their disturbed metabolome, and tools to monitor the efficacy of treatment."

Marc Masa, Diagnostic Working Group Manager, LEITAT

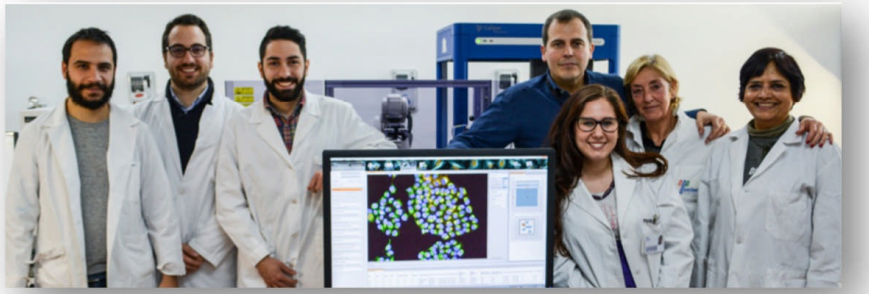
"Our core competences here are medicinal chemistry and innovative drug discovery with outstanding expertise in molecular modelling, organic synthesis, medicinal chemistry and preclinical drug development. Together with other BATCure project partners, chemists from the Latvian Institute of Organic Synthesis plan to design and synthesise novel compounds for testing in a variety of model systems relevant for Batten disease treatment."

Dr Maija Dambrova, Head of the Laboratory of Pharmaceutical Pharmacology of the Latvian Institute of Organic Synthesis (OSI)

Researcher Anastasija Ture synthesizes new molecules to be tested for biological activity in preclinical screening tests.

"Our laboratory is focused in the study of the pathogenesis of lysosomal storage disorders (LSDs) and in the development of innovative therapeutics using cell-based high content imaging approaches for drug discovery. Together with other BATCure project partners, our laboratory will develop assays in a variety of cellular models of Batten disease to identify compounds for Batten disease treatment."

Dr Diego L. Medina, Head of the high content screening facility at the Telethon Institute of Genetics and Medicine (TIGEM, Pozzuoli-Italy)



The High content screening team at the TIGEM facility.

"We are based in Copenhagen Denmark and develop novel therapies for rare degenerative diseases. As part of the BATCure project we will characterize various stress responses in patient cells from a wide spectrum of clinical presentations of Batten disease. In addition, the patient cell lines will be used for evaluation of efficacy of potential new treatments of Batten disease, focusing on known treatment candidates, as well as potential new classes of compounds suggested from the work in the BATCure project.

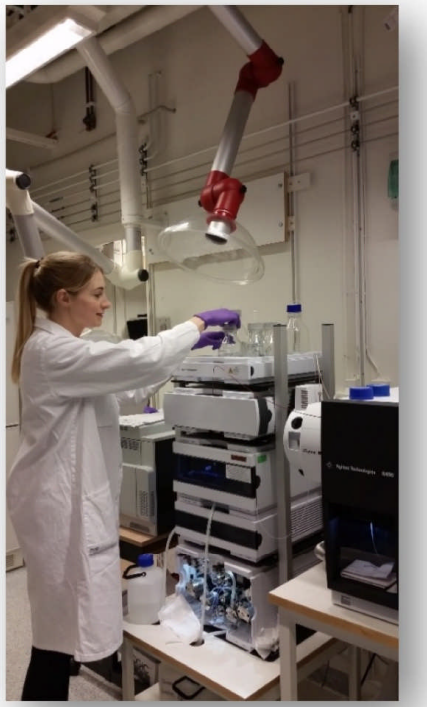
Our approach is based on augmentation of the naturally occurring cellular stress responses, to prevent the protein misfolding, degradation and/or aggregation commonly seen in degenerative diseases. We develop small molecule inducers of the stress responses and are currently running a clinical trial in Niemann-Pick Disease Type C, another very rare lysosomal storage disease."

Nikolaj H.T. Petersen, Sr. Science Manager, Orphazyme

Senior Scientist Raffaella Magnoni has been hired specifically to work full time on the BATCure project, and the work will be coordinated by Sr. Science Manager Nikolaj H. T. Petersen.

"As part of BATCure, AcureOmics will use metabolomics to identify disturbed biochemical pathways in CLN3, CLN6 and CLN7 diseases. This knowledge will be used to help design novel treatments that act to normalise the disturbed biochemical pathway. Evaluation of the efficacy of selected test compounds in the disease models will also be made."

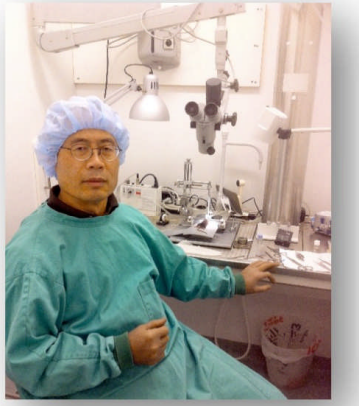
Dr Kate Bennett, AcureOmics



"We are a preclinical contract research organization (CRO) offering advanced services and collaborative projects in CNS pharmacology, neurochemistry and bioanalysis. Our mission is to serve pharmaceutical companies and research organizations aiming to accelerate the process of drug discovery, evaluate mechanisms of drug actions and strengthen the functional validation of candidate drugs.
Pronexus core expertise is focused on PK/PD studies using *in vivo* microdialysis in experimental models of CNS and metabolic disorders.

The bioanalytical services include UHPLC-MS/MS, UPLC-TOF, high-sensitive HPLC methods and immunoassays for quantification of neurotransmitters, metabolites, drugs, neuropeptides and proteins in biological samples including microdialysates, cell lysates, CSF, plasma, urine and tissue extracts."

Dr Jan Kehr, Pronexus Analytical



Senior scientist Fu-Hua Wang, MD, PhD in the surgery room.