Research Funding
£112 000 to support 3 projects for 2012-3

The BDFA has great pleasure in announcing our research Funding for 2012-13. Each year the BDFA has sought to provide more funds to support Batten disease researchers in their vital work towards finding therapies & ultimately a cure. This year is no exception and the BDFA is pleased to announce that £112 000 has been awarded to support 3 projects, one in the UK, and for the first time internationally in the USA and Israel. These projects were chosen not only for their exceptional potential, but to reflect the BDFA's commitment to support research into all forms of the disease.

This funding is also ground breaking in that it is part of a wider initiative by the BDSRA to enable collaborative funding of research by many different Batten disease charities & foundations. The BDFA would like to thank Dr. Danielle Kerkovich, (Principle Scientist for Beyond Batten disease foundation) for all her dedication & hard work in bringing this complex project together.

BDFA Research Funding 2012-13

New Projects:

1) Prof. Sandra Hofmann, Professor of Internal Medicine and Molecular Genetics, UT Southwestern Medical Center (with Prof. Jon Cooper, Kings College) will receive funds to continue her excellent work on Infantile Batten disease looking at Enzyme Replacement Therapy for PPT1-Related NCL.

Batten disease is a serious progressive neurological disorder of children caused by inherited deficiencies of one of several lysosomal enzymes or proteins. In the CLN1 form of the disorder, the enzyme palmitoyl-protein thioesterase (PPT1) is missing. The function of this enzyme is to remove fatty acids that are covalently attached to proteins so that the fat and protein can be recycled. In the absence of the enzyme, these fats and protein built up in neurons, eventually killing them.

The purpose of the proposed research is to determine optimal methods to provide the missing enzyme to the brain, using a mouse model of the disease. Various methods will be compared, including continuous administration of high-dose enzyme to the cerebrospinal fluid via an external device, intermittent spinal fluid injections, and

intravenous delivery using carrier beads (nanoparticles). Two different cellular routes for uptake will be exploited (called the mannose 6-phosphate receptor pathway and the lipoprotein-related receptor pathway). These preclinical studies will set the stage for direct translation to improve the lives of children with PPT1-related Batten Disease.

2) Professor Jon Cooper & Dr. Brenda Williams Kings College London, UK have been awarded funds for their work on Cell based systems for drug discovery in JNCL. The work will be undertaken by Greg Anderson,(NCL-Stiftung funded PostDoc) and Jenny Lange (Kings College funded MRC-PhD student).

The aim of this research is to use human neural stem cell lines that carry the JNCL mutation to generate different brain cell types. These can then be used to screen for drugs that can correct or improve their functional defects.

3) Prof. Jeffrey Gerst, Weizmann Institute of Science, Israel on the development of a cell-based assay for identifying down-stream effectors of CLN3 and use in drug screening. NCL-Stiftung is providing the funds for the Stipend (salary) for a PhD student, the BDFA is supporting the consumables needed to complete this 3-year project.

Targeting proteins to their correct intracellular site of action is essential for cells to grow and to function normally. Correspondingly, protein mislocalization can lead to cellular defects and disease onset. As the function of CLN3 Batten disease gene in humans remains unknown, we employed a simple genetic model (e.g. yeast cells) to better understand the localization and functions of the CLN3 protein and its yeast ortholog, Btn1. Through this work we identified a cellular signaling pathway that functions downstream of CLN3/Btn1 and is involved in the intracellular targeting of a specific subset of proteins.

Importantly, we also identified the downstream effector of CLN3/Btn1, called a kinase, that is likely to represent an ideal drug target - given its known cellular function and the fact that small molecule libraries tailored to regulate kinase function already exist.

We are currently recapitulating our yeast studies using instead mouse cells that lack a functional copy of CLN3, in the hopes of validating our earlier work and to generate a mammalian cell-based model for drug screening. Through the screening of high-content small molecule libraries we hope to find potential drug candidates for the treatment of Batten disease/JNCL.

We are continuing to provide funds for our existing projects from 2011-12.
On-going Projects:

PhD studentship
Dr. Sara Mole & Prof. Robin Ali

"Gene therapy to treat the visual failure of Batten Disease"
Award, £80 000 over 3 years
Studies performed by Sophia kleine Holthaus

Higher, JNCL Grants
Dr. Sara Mole
"Identification of new therapeutic targets for JNCL using yeast genetics"
Award, £9500
Studies performed by Mariana Vieira, UCL-NCL Stiftung PhD studentship,

Dr. Claire Russell
"Enabling high throughput *in vivo* drug discovery for JNCL"
Award, £9761
Studies performed by Kim Wager, Royal Veterinary College studentship

Dr. Brenda Williams & Dr. Jon Cooper
"The role of astrocyte in the pathogenesis of JNCL"
Award, £14800
Studies performed by Lotta Parviainen, Kings College studentship
PhD thesis due for submission, December 2012.

Dr.Sara Mole
1) "Investigation of Golgi morphology"
Award £5000
Studies performed by Davide Marrotta, joint UCL-NCL Stiftung PhD studentship

Prof. Jon Cooper
Tuition Fees for PhD student "Pathogenic impact of immune-related cells in two models of NCL"
Award £4738 (£14 738 in total over 3 years)
Studies performed by Tomas Kuhl, NCL Stiftung/ BDSRA PhD studentship,
PhD thesis due for submission, Sept. 2012