

## *Spotlight on...*

### *Interview*

#### **The NCL-Foundation ... promoting cooperative research for Neuronal Ceroid Lipofuscinosis**

Neuronal Ceroid Lipofuscinosis (NCL) is a metabolic disorder involving the abnormal intracellular accumulation of autofluorescent wax-like lipid materials within neurons of the brain as well as other tissues of the body. It is characterised by progressive loss of sight and motor skills, personality and behavioral changes and worsening seizures. There are distinct subtypes that differ primarily in two main points: age of onset and the speed of disease progression. Batten disease, named after British paediatrician Frederick Batten who first described the disorder in 1903, refers to the juvenile form of NCL, although professionals commonly use the same term to describe all forms of NCL. Unfortunately, all forms of the disease share the trait that they are not curable at present.



The [NCL-Foundation](#) is a non-profit organisation located in Hamburg, Germany that is dedicated to Batten disease. The foundation lists its principal goals as:

- Increasing public awareness of NCL in order to promote the early diagnosis of the disease
- Building an NCL network of medical specialists and basic science researchers of different disciplines, in order to coordinate national and international expertise
- Initiating research to develop possible cures

The NCL-Foundation is committed to cooperative research funding. To initiate important NCL research projects, the Foundation is continuously on the lookout for suitable cooperation partners from both the profit and non-profit sectors.

*OrphaNews Europe* recently had the opportunity to interview Dr. Frank Stehr, in charge of research for the NCL-Foundation:

***OrphaNews Europe:*** How has the NCL-Foundation developed since its debut?

***Dr. Frank Stehr:*** The NCL-Foundation was established in August, 2002 by Dr. Frank Husemann, an economist whose son Tim is suffering from Batten disease. The first years of the foundation were devoted to scientific market analysis in order to determine who was working on what and what research was missing. We then started co-financing NCL-projects, and are now focusing on PhD scholarships, which are potentially available to promising candidates from any country. We are interested in seeding new projects and encourage groups to send in proposals for new research activities. We award an NCL research prize (worldwide) each year to the most promising project. The NCL-Foundation has evolved from national to international funding, and has participation from the USA, Great Britain and Israel.

We also organise scientific NCL workshops on a regular basis; offer medical training to relevant groups, such as ophthalmologists and (neuro)paediatricians; have a school project (biology up-to-date) that is intended to raise awareness for rare diseases in young people (high school age); organise, host and support a variety of charity events; interact with ACHSE (the German national alliance of patient groups for rare diseases); and present on various NCL-related topics at relevant conferences (such as the recent meeting of lysosomal storage disease consortium Brains for Brain).

We are interested in collaborating in EU-level projects and would be open to any interesting proposals on this level. We would also be interested in collaborating with any relevant biopharmaceutical industry initiatives.



***OrphaNews Europe:*** How is the Foundation funded?

***Dr. Frank Stehr:*** The foundation is funded through a variety of sources including private and company donations, sponsoring, charity events that we

organise, and collaborations with other foundations. We also apply for grants.

***OrphaNews Europe:*** Promoting research initiatives is one major goal of the NCL-Foundation. What kind of research projects is NCL-Foundation funding?

***Dr. Frank Stehr:*** We are funding initiatives that cover various research needs:

- Therapy oriented initiatives
- Projects that address research gaps
- Collaborations

***OrphaNews Europe:*** How do you encourage and establish collaboration between different disciplines and different countries?

***Dr. Frank Stehr:*** Our scientific board is very helpful with this. We try to bring different researchers together by organising direct contact (visits); via scientific marketing; offering co-funding; and through working with pharmaceutical companies. The NCL-Foundation is interested in collaborating more with industry.

***OrphaNews Europe:*** Can you discuss further the Foundation's doctoral fellowship programme?

***Dr. Frank Stehr:*** Usually we try to match funds; collaborative research funding meaning that the group itself is a partner by providing the "consumables", overhead costs, laboratory space, supervision etc. and we offer, sometimes together with other partners, a fellowship.

We want to encourage NCL researchers - and non-NCL researchers - to submit an outline of their proposed project which would first be reviewed to determine whether it makes sense to send in a full proposal (this process saves time for both sides). In some cases we make recommendations to modify a proposal.

Each proposal is peer-reviewed by two or three external experts in the relevant field and/or the scientific board. The final decision on funding is made by the board of the foundation. After this we create a research contract. We request interim reports from funded projects on a regular basis. We also visit the group punctually to review progress made and to see if we can be of any further help or if additional methods, partners, or patient tissue are needed.

***OrphaNews Europe:*** Which of the various strands of research for Batten disease is currently proving most promising?

***Dr. Frank Stehr:*** Gene therapy as a causative treatment for monogenic diseases is showing promise. Alzheimer studies on small molecule neuroprotection could be interesting for the NCL disorders. Furthermore, there is interest as to whether anti-inflammatory medicines could be beneficial in treating NCL diseases.

***OrphaNews Europe:*** Can you comment on stem cell treatments for Batten disease, such as the Stem Cells Inc trials that took place at the HSU Doernbecher Children's Hospital in Portland, Oregon?

***Dr. Frank Stehr:*** I was not involved with these trials. The researchers were treating children with the classical late infantile NCL-form (CLN2) which has one major difference from CLN3 in that a lysosomal enzyme is affected (rather than a lysosomal membrane protein). The idea behind the process of stem cell treatment is to introduce cells into the brains of affected children that would act as enzyme producers, allowing the secreted enzyme to be taken up by the surrounding cells (cross-correction).

***OrphaNews Europe:*** There have been instances of parents seeking treatment in China for their children with Batten disease. What would be your comment on this?

***Dr. Frank Stehr:*** I would advise parents, patient organisations and health professionals to be very cautious and to not raise false hopes. While this could be an effective approach, there is no official study as far as I know. Nor have I seen any publication in peer-reviewed journals telling us what kinds of cells are being used (safety profile). Treated CLN2-children that I know of have not been cured and furthermore it is not possible to determine if there is significant improvement because there has been no clinical study (natural history studies would be necessary.)

***OrphaNews Europe:*** In terms of patient care, what can the medical community currently offer patients and their parents?

***Dr. Frank Stehr:*** The medical and scientific community can offer hope that through research this disease can be cured with the help of the patients and families. Doctors cannot solve the problem on their own - interaction is critical and it reminds the researchers of why and for whom they are making an effort.

***OrphaNews Europe:*** Can early diagnosis affect the progression of the disease?

***Dr. Frank Stehr:*** Yes and no. With early diagnosis we can avoid administration of the wrong medication (anti-seizure drugs must be selected carefully, for example; some can cause parkinsonian like symptoms). Early diagnosis saves parents from having to go from doctor to doctor. Certain tools that have become available might also be better optimised if introduced early. For example, there is a computerised tool named Struktur, which was developed in Sweden and has modules to aid patients communicate. With Batten disease, besides losing vision in a period of one to three years, patients experience a parallel intellectual decline which affects skills such as reading and calculating. There is also loss of speech and echolalia. The frustration this creates can lead to psychological problems. The Struktur software addresses this via modules that aid patients to communicate during school. The NCL-Foundation created a grant proposal to use Struktur in Germany. We presently have 20 computers available in 9 different schools. We would like an official study proving the efficacy of these computers, which cost about 2000 euros each, and could be used for other rare diseases that have similar symptoms.

Another good reason for early diagnosis would be for any future therapy that becomes available and for which it would be better to start treatment as early as possible. Finally, early diagnosis allows palliative options to be better planned and thought out. All of this said, currently the disease is still lethal despite early diagnosis.

***OrphaNews Europe:*** What is the current trend in diagnostics for this disease? Does the disease tend to be recognised by physicians who may not have any specific training on Batten disease?

***Dr. Frank Stehr:*** There is usually a false diagnosis, most often that of retinitis pigmentosa. I do not know the specific numbers (as no study has been done) but I have heard that a correct diagnosis is made anywhere from 3 months to 15 years from the time the first symptoms appear. This is why we also focus on raising awareness. Our next step on this front is to include Batten disease in relevant text books. We would like to have a collaborative project to develop differential diagnostics with Pro Retina, a German self-help association for problems with retina degeneration. It is important for ophthalmologists to keep in mind when coming across an anomaly suspected as retinitis pigmentosa that it could be something different, such as Batten disease and to furnish the names and contact details of experts that the examining physician could consult with.

***OrphaNews Europe:*** How does the NCL-Foundation increase public awareness?

***Dr. Frank Stehr:*** We achieve this through a variety of tools including scientific marketing, talks and lectures, school projects, participating in rare disease day, media outreach including television, newspapers, and radio, our website, publicity spots and non-profit advertisements, and engaging VIPs to speak for us.

***OrphaNews Europe:*** Does Germany have a registry for Batten disease?

***Dr. Frank Stehr:*** There is a registry in Hamburg, which is trying to become international.

***OrphaNews Europe:*** With which other national and international organisations are you collaborating? What do these collaborations consist of?

***Dr. Frank Stehr:*** As mentioned, we hope to collaborate with Pro retina to work on raising medical awareness. A project has been proposed to work on differential diagnosis between retinitis pigmentosa and juvenile NCL. Other collaborations on the national level include McDonald's Kinderhilfe (for the speech computers); R+W-Stiftung; Hamburg Marriott Hotel; Griebel-Stiftung; German Mouse Clinic; ACHSE; Ein Herz für Kinder; Auerbach Stiftung; and E.W. Kuhlmann Stiftung.

On the international level we collaborate with Batten disease organisations BDSRA, BDFa, Beat Batten, and Beyond Batten Disease. We match funds or write a proposal to apply for money, or we match researchers with other organisations, thus forming a knowledge exchange. I would like to reiterate here one last time that we are always on the look-out for funding partners and would like to get involved in EU-level projects and also partner with members of the biopharmacy industry.

**Contact Dr. Frank Stehr:**

Phone: +49 (0) 40 - 69 666 74 - 10

Mobile: +49 (0) 178 - 3416057

Email: [frank.stehr@ncl-stiftung.de](mailto:frank.stehr@ncl-stiftung.de)