



Deutsche Duchenne Stiftung

eine Stiftung der
aktion benni & co e.V.

*Your task is not to foresee the future,
but to enable it.*

(Saint-Exupéry)



Deutsche Duchenne Stiftung (German Duchenne Foundation)
of „aktion benni & co e. V.“ Aktion benni & co e. V -
Association for promoting research in Duchenne muscular
- Aid for kids with muscular diseases -

Donations: Sparkasse Bochum | IBAN DE67 4305 0001 0000 4277 24, BIC WELADED1BOC
Volksbank Ruhr Mitte | IBAN DE44 4226 0001 0603 1297 00, BIC GENODEM1GBU

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Facts and figures

- 1996 The Over family founds the support group "aktion benni" (campaign benni)
- 1998 "aktion benni & co e. V." is registered as association ("e.V.")
- 2010 The "Deutsche Duchenne Stiftung" (German Duchenne Foundation) is recognized, patron is Ms Hannelore Kraft, minister-president of North Rhine-Westphalia, Germany

Members: about 900

Membership fees: 50 Euros

Teenage patients do not have to pay any fees, neither do families with low income nor single parents.

Scientific advisory board: 1 member in the foundation – 5 members in the "aktion benni & co e. V." association

The committee of „aktion benni & co e. V.“ and the "Deutsche Duchenne Stiftung" board of trustees are serving in an honorary capacity.

What is muscular dystrophy?

Muscular dystrophy is a genetic disorder inherited in an X-linked recessive mode. It is characterized by the absence or mutation of the structural protein dystrophin in the genetic blueprint, leading to slow muscle wasting. The Duchenne muscular dystrophy (DMD) is the most common hereditary muscular dystrophy and affects almost solely boys, since girls are normally able to compensate the defect through their second X-chromosome. In most cases, the first abnormality is the delayed motor development. Symptoms are a delay in walking, the children's having little pleasure in moving around, frequent falls and "clumsy" work movements. The affected children already have to cope with severe muscle wasting in early infancy. In the final stages of the disease, the respiratory and cardiac muscles are affected. The patients – about 2,500 boys today in Germany – mostly die in early adult life.

The diagnosis not only changes the family's life abruptly but also permanently. Their daily life is marked by worries about dealing with the beloved child, adapting to society, his further development, for instance regarding his school career, and many others. By the age of about 8, the boys affected by the muscular weakness are confined to a wheelchair. The Deutsche Duchenne Stiftung of the "aktion benni & co e.V." association is committed to push research on therapy development and to improve the patients' life conditions. The foundation's work also includes informing the public about DMD and implementing social and psychological projects for DMD families. Thanks to donations and gifts, the Deutsche Duchenne Stiftung may enable the future for children and teenagers with the muscular disease.

Our projects

■ Twice a year we hold our **mother workshops**, financially made possible by the Techniker Krankenkasse health insurance. In these workshops, we aim to help the mothers awaken and boost their inner strengths so that they may carry on a healthy family life every day and are able ensure the continuous care of the sick children.

■ Since 2012, we have been producing our magazine **Duchenne Magazin** once a year. We aim to share important information about our work, findings about Duchenne muscular dystrophy, research developments and a lot of commitment with our Duchenne families, interested persons and benefactors.



■ We arrange **father and son weekends** and try to highlight them with organized leisure time activities. We offer e-wheelchair hockey, swimming and trips in a relaxed atmosphere. There is also time for getting to know the other participants!

■ With our **project “Ü16“** (older than 16), we want to specifically strengthen our young Duchenne adults. Once a year, an interesting supporting program and offers for talks aim to help the Duchenne men getting to know each other.

■ Once a year in an official setting, we award **prize money to researchers** or research groups. By doing so, we aim to push research projects with doctors and scientists in Germany to find therapies for people with Duchenne muscular dystrophy.

■ Our **Duchenne Symposium** addresses key subjects such as symptoms, diagnosis, psychological aspects, improvement of health care structures, social pedagogy, orthopedic treatments and physical therapy. Target groups are pediatricians, public authorities, health insurances, therapists and educationalists. We hold the symposium because of their questions and insecurities when dealing with Duchenne children and their families. By sharing this information, we also try to improve the sick children's and their family's care and provision, and promote integration, inclusion and acceptance. The Techniker Krankenkasse health insurance sponsors the symposium once a year.

■ Thanks to the good cooperation with our therapists, doctors and affected families, we are able to summarize the findings in information brochures such as the “Psychologischer Leitfaden” (Psychological Guideline), symposium, several guides, “Informationsbroschüre für Teenager” (information brochure for teenagers), “Hilfsmittelbroschüre” (Resource for everyday life and loss of function) and much more.



Research projects, e.g.

■ Exon skipping combinations

Description: Preclinical studies on exon skipping are carried out on GRMD dogs. The dogs are treated with systemically applied AAV U7 in order to reach long-term and ubiquitous exon skipping. The first results are very promising. We are developing combined therapies in order to reverse muscular fibrosis and muscle loss. Moreover, in many cases exon skipping changes a DMD phenotype for the better into a Becker phenotype without completely curing the patient. The aim is a complete reconstitution of the dystrophic muscles. For instance, we are currently combining dystrophin exon skipping and myostatin blockade in the Duchenne mouse model with very positive results.

Institution: Helge Amthor, Dr. med., PhD & Professor Dr. Thomas Voit, Institut de Myologie (Institute of Myologie) Paris, France

■ Gene therapy of cardiomyopathy to improve cardiac output

Description: Our therapeutic approach is the gene transfer of a shortened Dystrophin via Adeno-associated viral (AAV) vectors. These vectors enable a very efficient and also low-risk gene transfer. Long-term studies with mdx mice were able to show that cardiac functioning was maintained with systemic transfer. Successful trials on retroinfusion in coronary pig veins were also carried out. In the long term, the transfer via AAV vectors can be seen as a promising method to maintain cardiac muscles.

Institution: Team Dr. Bauer & Dr. Müller, Universitaetsklinikum (teaching hospital) Heidelberg, Germany

■ Inflammatory response suppression by immunoglobuline therapy

Description: Immunoglobulines are antibodies that are already commonly used with different medical conditions. The therapy treats inflammations in tissue that are aftereffects of DMD and additionally weaken the muscles. By administering immunoglobulines intravenously, we aim to reduce the inflammation. We test the therapeutic procedure on mdx mice in exercise wheels and prove it via the CK value. In summary, a long-term treatment with immunoglobulines is well tolerated and improves muscle strength. Transferring the therapy onto humans is basically possible, corresponding pilot studies are being planned.

Institution: Team Dr. Liebetanz, Dr. Klinge & Dr. Schmidt, Universitaetsklinikum (teaching hospital) Goettingen, Germany

■ Treatment via intravenous application of muscle-specific peptide-coupled adenoviruses to transfer exon skipping constructs

Description: Above all, the project deals with the problem of spreading agents throughout the whole body, especially with overcoming the blood-brain-barrier. In cell cultures, we were able to successfully use anchoring proteins in the transfer. For a DMD therapy, we focus on improving the effect of exon skipping. As a perspective to the project, we aim for a holistic, specific DMD therapy that also influences brain activity.

Institution: Prof. Dr. Pahnke, Universitaetsklinikum (teaching hospital) Rostock, Germany

■ Sunphenon, Green tea study

Description: In cell cultures and animal research, EGCG (hard capsule, partly with green tea extract) showed a positive effect that is probably due to its antioxidant properties. In mdx-mice, EGCG was able to reduce the histological changes in the muscle and achieve a functional improvement. This project aims to test whether EGCG has a positive effect on the course of the disease in Duchenne patients.

Institution: Charité - Universitaetsmedizin (teaching hospital) Berlin, Germany, Dr. Paul, Dr. Grieben

■ Selection of vectors from AAV libraries for efficient gene transfer in healthy and dystrophic skeletal muscle

Description: Based on the successful research activities as of today, now we aim to optimize the gene transfer of viral vectors. By doing research in large animal models, we are getting closer to human models, which is of interest to us. Though only being an aspect of the larger picture, it would be the way for a gene therapy of Duchenne muscular dystrophy.

Institution: Universitaetsklinikum (teaching hospital) Heidelberg, Medizinische Klinik (Medical Clinic) III, Germany, Dr. Müller, Dr. Bauer

■ Treatment of cardiac insufficiency in Duchenne muscular dystrophy - development of test procedures in cell culture

Description: The project aims at a cell biological-technical improvement, among others to produce "Duchenne myocardial cells" out of dermal fibroblasts. Observations based on cardiomyocytes point to a lack of dystrophin in early childhood. The examination consequences lead to timely and appropriate measures, having positive effects on cardiac involvement and strongly improving quality of life and life span.

Institution: Institute of Genetic Medicine, Newcastle University, UK, Professor Hanns Lochmüller

■ Molecular basics of inflammation and fibrosis in Duchenne muscular dystrophy

Description: We aim to characterize macrophage populations from DMD and control muscle biopsies and then compare the data with mice models regarding inflammatory infiltrates and processes. In order to follow treatment approaches, we need to clarify the complex connection between inflammation, regeneration and fibrosis.

Institution: Institut fuer Neuropathologie (Institute for Neopathology), Charité, Berlin, Germany, Team Dr. med. Werner Stenzel

■ Mechanisms of fibrosis in muscular dystrophy and characterization of the role of a key enzyme in fibrosis regulation

Description: In this project, we aim to look into an aspect of fibrosis development. There are indications that the so-called serum- and glucocorticoid-dependent kinase 1 may stimulate myocardial fibrosis. We aim to use this knowledge for the question of fibrosis development in dystrophic muscles.

Institution: Institut für Pathophysiologie (Institute for Pathophysiology), Greifswald University, Germany, Prof. Brinkmeier, Dr. Landsberger

■ **Extended project: Mechanisms of fibrosis in muscular dystrophy and characterization of the role of a key enzyme in fibrosis regulation**

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■ **New antisense oligonucleotide linkages for molecular DMD therapy (exon skipping)**

Description: The group of researchers has developed a gene therapeutic treatment strategy in which they were able to synthesize DMD-RNA antisense sequences via AAV vectors. Compared to synthetic AON chemistry, this so-called AAV-U7 gene therapeutic strategy has the advantage of reaching a long lasting and very effective expression of dystrophin in the whole organism by only one treatment. This is a crucial aspect for developing these strategies into therapeutic options for Duchenne patients. As a logic conclusion of the present research, we will name clear and explicit project goals with works on a landmark study on toxicity, on a systemic pharmacokinetic study and on a systemic study in pharmacodynamics.

Institution: Université (university) Versailles Saint-Quentin-en-Yvelines, France, Dr. Amthor

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Institution: Université Versailles Saint-Quentin-en-Yvelines, France, Dr. Amthor

■ **Morphologic characteristics of skeletal muscles in female conductors of Duchenne muscular dystrophy**

Description: Female conductors show symptoms that lead to severe impairments as well. As of today, there is no treatment concept intended. The project is based on current studies concerning inflammation and fibrosis mechanisms, and interactions. On the basis of the findings, we aim to find treatment options but also to diagnose the health problems.

Institution: Charité Berlin, Institut für Neuropathologie (Institute for Neuropathology), Germany, Prof. Stenzel, co-applicant: Uniklinik (teaching hospital) Essen, Germany, Prof. Schara

■ **Identification of cardiomyopathies in “female Duchenne conductors”**

Description: This is a clinical cross-sectional study. It aims to describe in detail the clinical symptoms and instrumental diagnostics in order to learn more about the risks of cardiac involvement in female Duchenne conductors.

Institution: Uniklinik (teaching hospital) Essen, Germany, Dr. Neudorf

■ **Strategy for treating muscular dystrophy by normalizing the muscular Ca²⁺ level: Importance of TRPV₄ ion channel and effect of GsMTx₄ spider venom**

Description: Description: Fundamental research titled „Strategy for treating muscular dystrophy by normalizing the muscular Ca²⁺ level: Importance of TRPV₄ ion channel and effect of GsMTx₄ spider venom”. The tests are carried out on cell cultures and mice models. For a long time, there has been good evidence that calcium influx into muscle cells through cell membrane channels contributes to the Duchenne pathogenesis. However, it has not been achieved yet to explicitly name these channels. This is important since channels are generally well accessible and may be used in therapy.

Institution: Institut für Pathophysiologie (Institute for Pathophysiology), Greifswald University, Germany, Prof. Brinkmeier, Dr. Landsberger

■ **Anti-inflammatory gene therapy approaches for Duchenne cardiomyopathy**

Description: In patients with Duchenne muscular dystrophy (DMD), the absence of dystrophin leads to unstable myocardial cell membranes, leading to progressive cardiomyopathy due to contraction-induced cell injury (1). By migrating into dystrophic myocardial tissue, immune cells cause an inflammatory reaction, thus substantially contributing to the progress of cardiomyopathy (2,3). Especially tissue macrophages and circulating cytokines such as tumor necrosis factor alpha (TNF α) play a central part in this (4). TNF α activates nuclear factor- κ B (NF- κ B) and c-Jun N-terminal kinase (JNK) associated signaling pathways (5-8). It is yet to be identified if a cardiac AAV induced IL-10 gene therapy could be suitable for treating cardiomyopathy in DMD as well.

Institution: Heidelberg University, Germany, Dr. Müller, Dr. Bauer

■ **Therapy testing with Eplerenon in patients with Duchenne muscular dystrophy**

Description: Pilot study trying to clear if Eplerenon has protective effects on muscle fibers and slows muscle fibrosis. The participants are examined closely.

Institution: Universitaetsklinikum (teaching hospital) Ulm, Germany, Prof. Dr. Lehmann-Horn, Dr. Jurkat-Rott