Welcome to the conference

A great event is planned

Thank you for joining us

On behalf of all of the European Tay-Sachs and Sandhoff Disease Charity Consortium (ETSCC) charity members, I would like to say a big welcome and thank you for attending the 4th European Tay-Sachs and Sandhoff Disease Family Conference! This year we are back at Disneyland Paris where we hope everyone is able to enjoy visiting the theme parks and meeting lots of Disney characters.

As a consortium, we are always looking to improve our conferences so that everyone is able to get as much out of our weekends together as possible. Therefore, we have changed the format and for this year and we have planned for two days of interesting talks.

The first day is based on our conference theme of feeding, where we have some very interesting presentations on this topic. They include the ways in which feeding intervention can be undertaken and various specialist diets.

The second day is our science and research day where we have some very inspiring speakers. We will hear an update on the research for a treatment for the diseases by Professor Cox's team, and there will also be a talk about alternative therapies. To end this day we have invited some families to give a talk about their own experiences with the diseases and how this have driven them on to try and change the world.

Another change for this years conference are the group activities where the “making memories” and “remembrance corner” have been created for everyone to take part in during the breaks at the conference.

We hope these changes can help everyone take more away from our conferences and that the go away feeling inspired and that they learnt something.

Daniel Lewi
Chairman of the ETSCC
The ETSCC members

The Cure & Action for Tay-Sachs Foundation
United Kingdom
The Cure & Action for Tay-Sachs (CATS) Foundation was established in 2011 to provide support and information to families affected by Tay-Sachs and Sandhoff.

Acción y Cura para Tay-Sachs
Spain
Acción y Cura para Tay-Sachs (ACTAYS) was founded in 2014 so families in Spain had access to a support network and access to information about the diseases.

Hand in Hand gegen Tay-Sachs und Sandhoff
Germany
Hand in Hand gegen Tay-Sachs und Sandhoff in Deutschland was set up in 2015 to collect and distribute information, support families and the national and international research.

Hand in Hand gegen Tay-Sachs und Sandhoff
Austria
Hand in Hand gegen Tay-Sachs und Sandhoff in Austria was founded in 2012 to provide information to Germany speaking families about the diseases.

Vaincre les Maladies Lysosomales
France
VML is an association based in France which was established in 1990 and provides support to parents and patients affected by lysosomal diseases.

Introducing the ETSCC and its work as a collective

THE MEMBERS
The European Tay-Sachs and Sandhoff Charity Consortium (ETSCC) was created to enable European charities to come together in the fight against Tay-Sachs and Sandhoff. Members are all recognised charities in their country of origin, and there are currently organisations from the United Kingdom, Spain, Germany, Austria and France.

THE AIMS OF THE ETSCC
The three aims of the ETSCC are to raise awareness of Tay-Sachs and Sandhoff, support the research for a potential treatment and provide a united European voice. The members of the ETSCC meet once a year to discuss the progress of the research into the diseases and the consortiums strategy.

Our goal as a collective is to help find a potential treatment. We are dedicated to reaching this goal by providing research funding and we are always open to charities from other countries joining the consortium and helping us support more families and to beat Tay-Sachs and Sandhoff.

More information:
If you would like more information about the ETSCC or any of the charity members please visit the consortium website at etscc.org.

During the conference you will have the opportunity to meet and speak with representatives from each of the different charities. Please visit their charity stands during the breaks and they will be more than happy to talk about their work and answer any questions you may have.
What is new in 2016

An updated format

The European Tay-Sachs and Sandhoff Disease Family Conferences have continued to develop and this year there are some noticeable changes. There will be a larger focus on all of the participants interacting and talking amongst themselves about the various subjects which the speakers have presented. It is hoped that this will help us deal with the problems we have encountered regarding translations.

The conference will be run according to the schedule and time line shown on the following pages of this document. We have a wide variety of speakers this year and we ask that you are on time for each of the presentations so that the conference does not over run on the schedule which we have in place.

A CONFERENCE THEME
This year we have chosen feeding as a theme for the conference. All of the speakers on the first day will be presenting subjects which are all related to feeding and children affected by Tay-Sachs and Sandhoff disease. By having a focus on the theme on the first day it means we can then explore the science and research about the diseases on the second day of presentations.

MAKING MEMORIES WORKSHOP
As we have a busy schedule this year we are running the making memories part of the conference during the breaks rather than having a dedicated section during the main part of the conference. A group artwork has been prepared and we encourage everyone to take part as it will enable us to make a group memory of this year’s conference.

REMEMBRANCE CEREMONY
During the conference we will not be having a formal remembrance ceremony. Similar to last year, we will have a remembrance corner where everyone who attends the conference can pay their respects to children who have lost their battle to either disease. For those families who have lost their children we have organised a small gathering for these parents to spend some time together.

LANGUAGE TRANSLATIONS AND ROUND TABLES
During previous conferences we have had issues with the different languages and nationalities of everyone as not all our families have been able to fully understand each speaker. For this year, we are introducing round tables which will be all set-up for people to sit at depending on their native language. After each presentation there will be a fifteen minute period where people sat around the tables can speak about the presentation in their native language where the speaker will circulate the room answering any questions.

If you have any questions about the conference or any of the sessions please contact your charity representative and they will be able to help you.
Conference Day

The role of feeding
### Schedule for the Day

**Saturday June 4 - Morning**

**ARRIVAL AND REGISTRATION**
09:30 - 10:00  Grand Central conference room
Registration will take place in the Grand Central conference room at the New York Hotel and there will be signposts to the location of the room.

**INTRODUCTION TO THE CONFERENCE**
10:00 - 10:15  Speaker: Daniel Lewi
The conference will be opened with an introduction to the next two days of talks and the recent work of the European Tay-Sachs Charity Consortium (ETSCC).

**SESSION 1 – THE IMPORTANCE OF FEEDING**
10:15 - 10:45  Speaker: Anita McDonald
This session will explore the importance of feeding in a child’s development and the role this plays for children with degenerative diseases.

10:45 - 11:00  Language round table
A fifteen minute session for translations and a question and answer session about the importance of feeding which will be facilitated by our language experts.

**SESSION 2 - FEEDING INTERVENTION**
11:00 - 11:30  Speaker: Anita McDonald
Why feeding intervention is undertaken and the ways that this may be done will be discussed during this session.

11:30 - 11:45  Language round table
A fifteen minute session for translations and a question and answer session about feeding intervention which will be facilitated by our language experts.

**COFFEE BREAK**
11:45 - 12:15  Grand Central
Tea and coffee served outside the conference room.

**Saturday June 4 - Afternoon**

**SESSION 3 - SPECIALIST FEEDING – KETOGENIC DIET**
12:15 - 12:45  Speaker: Mary-Anne Leung
An introduction to the ketogenic diet and the ways in which this specialist diet can be managed will be presented in this session.

12:45 - 13:00  Language round table
A fifteen minute session for translations and a question and answer session about the ketogenic diet which will be facilitated by our language experts.

**LUNCH**
13:00 - 14:30  Radio City 3
A buffet meal will be served in the Parkside Diner which is in the New York Hotel.

**SESSION 4 - THE IMPORTANCE OF SPEECH THERAPY**
14:30 - 15:00  Speaker: Kim Lewis
How speech therapy can make an impact on a child’s feeding and why this is so important will be explored in this session.

15:00 - 15:15  Language round table
A fifteen minute session for translations and a question and answer session about speech therapy and feeding which will be facilitated by our language experts.

**SESSION 5 - FAMILY LED DISCUSSIONS**
15:15 - 15:45  Symptom management
A family led session about managing various symptoms will be discussed to enable families to compare how others manage them.

15:45 - 16:15  General care
A family led session about various pre-selected general care topics will be discussed amongst all the families who attend the conference.
Conference day two: Science and research
Conference day two:
Science and research

Schedule for the day

Sunday June 5 - Morning

ARRIVAL
09:30 - 10:00 Grand Central conference room
Families are asked to go straight to the Grand Central conference room at the New York Hotel and there will be signposts to the location of the room.

SESSION 6 – GENE THERAPY
10:00 - 10:45 Speaker: Begoña Cachón Gonzalez
An introduction to gene therapy and the role it has played in developing treatments for different diseases will be discussed.

10:45 - 11:00 Language round table
A fifteen minute session for translations and a question and answer session about gene therapy which will be facilitated by our language experts.

SESSION 7- RESEARCH UPDATE
11:00 - 11:30 Speaker: Prof Timothy Cox
An update on the current research into a treatment for Tay-Sachs and Sandhoff disease will be presented in this session and how this treatment will be undertaken.

11:30 - 11:45 Language round table
A fifteen minute session for translations and a question and answer session about the research update which will be facilitated by our language experts.

COFFEE BREAK
11:45 - 12:15 Grand Central
Tea and coffee served outside the conference room.

SESSION 8 - ALTERNATIVE THERAPIES
12:15 - 12:45 Speaker: Dr Mario Cordero
An introduction about a new Inflammasone Complex treatment for Tay-Sachs will be discussed and how this could help children affected by the disease.

Sunday June 5 - Afternoon

12:45 - 13:00 Language round table
A fifteen minute session for translations and a question and answer session about alternative therapies which will be facilitated by our language experts.

LUNCH
13:00 - 14:30 Radio City 3
A buffet meal will be served in the Parkside Diner which is in the New York Hotel.

SESSION 9 - CTSF AND US RESEARCH
14:30 - 15:00 Speaker: Ken Bihn
A personal story about the Bihn family will be shared with everyone and how their personal journey led to the establishment of the Cure Tay-Sachs Foundation.

15:00 - 15:15 Q & A session with Ken Bihn
A fifteen minute Q & A session facilitated by our language experts.

SESSION 10 - SIBLING LEGACY: WORKING FOR A CURE
15:15 - 15:45 Speaker: Allie Colaço
A personal story about Allie and how losing her brother to Tay-Sachs motivated her from a young age to find a treatment for the disease.

15:45 - 16:00 Q & A session with Allie Colaço
A fifteen minute Q & A session facilitated by our language experts.

CONFERENCE SUMMARY
16:00 - 16:15 Speaker: Daniel Lewi
An overview of what was discussed during the conference, what we hope will have made an impact on everyone who attends the conference and also announcing the location of the 2017 conference.
Group activities:
The daily schedules
Group activities

Friday June 3 - Day time

ARRIVAL AND DISNEYLAND PARIS PARKS
09:00 - 18:00  Disneyland Parks
On the first day families will be arriving to the hotel and will have the opportunity to visit the two Disneyland Parks. On arrival, each family will be provided with a conference welcome pack.

Saturday June 4 - Day time

CONFERENCE DAY ONE
09:30 - 16:15  New York Hotel Grand Central
The first day of talks will be held at the Grand Central conference room which is in the New York hotel where everyone is staying. Please arrive early so registration can be completed and the talks can begin on time.

Sunday June 5 - Day time

CONFERENCE DAY TWO
09:30 - 16:15  New York Hotel Grand Central
The second day of talks will take place in the same conference room called Grand Central. Please arrive on time so that the speakers can start at their allocated time.

Monday June 6 - Day time

DEPARTURE DAY & DISNEYLAND PARIS PARKS
09:00 - 18:00  Disneyland Parks
On the last day families will have the opportunity to visit the Disneyland Parks if they are not heading home until later that day. Both of the parts will be open until the evening.

Friday June 3 - Evening

WELCOME DINNER
18:30 - 22:00  Rainforest Cafe
In the evening of the first day the Welcome Dinner will be held at the Rainforest Café. Everyone will meet at the restaurant from 18:30 where all the families attending can meet one another.

Saturday June 4 - Evening

GROUP DINNER
19:30 - 22:00  New York Hotel - Radio City
After the first day of talks a group dinner will be held in the Radio City room located in the New York Hotel. This meal will give everyone the opportunity to discuss what was talked about during the day and to catch up.

Sunday June 5 - Evening

GOODBYE COFFEE
16:15 - 18:00  New York Hotel Grand Central
After the second day of talks there will be a good bye coffee held in the Grand Central conference room. This will give families and speakers an opportunity to discuss what was talked about during the two days.

Monday June 6 - Evening

DEPARTURE DAY
09:00 - 18:00  Disneyland Parks
Families who visited the Disneyland Parks on the last day will then head home in the evening. Transport to and from the airports and train stations can be arranged in advance if prior notice is given.
Good nutrition and hydration is essential for children with Tay-sachs and Sandoff disease. Feeding is a fundamental process and any children with conditions that affect the ability to feed have a markedly increased risk of malnutrition. Unfortunately, there is no research on the nutritional needs of these children.

There are many adverse consequences associated with poor nutrition. Poor protein intake can lead to reduced muscle mass and strength and cause muscle wasting. Malnutrition may also lead to reduced muscle mass and strength and cause muscle wasting. Malnutrition may also lead to reduced muscle mass and strength and cause muscle wasting. Malnutrition may also lead to reduced muscle mass and strength and cause muscle wasting. Malnutrition may also lead to reduced muscle mass and strength and cause muscle wasting.

Changes in gastrointestinal function. In severe cases of malnutrition, there may be villous atrophy (gut villi are finger like tentacles responsible for absorbing nutrients), reduced disaccharides activity, an enzyme responsible for breaking down milk sugar, and altered gut bacteria. These problems may in turn lead to nutrient malabsorption, diarrhoea and faltering growth. Infections are more frequent in children with malnutrition due to immunological abnormalities. These in turn can exacerbate the effects of poor nutrition with further loss of appetite, but increasing metabolic rate and nutritional requirements. In children there is correlation between nutritional status, body weight and rate of wound healing. Also associated with chronic undernutrition is rickets and poor bone mineral density (due to Vitamin D deficiency and low calcium intake), zinc deficiency, which causes skin rashes and decreased ability to fight infections and anaemia associated with iron deficiency. Puree ready prepared baby milk and high intake of unmodified cow’s milk are commonly responsible for poor intake of iron. Vitamin deficiency may be associated with limited variety of foods eaten, vitamin losses through liquidising food or long cooking methods. Sodium and potassium intakes tend to be low. Micronutrient supplementation is commonly required.

**GROWING CHILDREN**

Growing children have relatively low energy reserves and the younger the child, the shorter the time before energy reserves become depleted if energy/calories intake is inadequate. However, energy requirements may be lower in children with Tay-sachs and Sandoff disease associated with low mobility but energy requirements must be determined on an individual basis with regular monitoring of weight changes, length/height and energy intake being essential. Changes in clinical symptoms such as seizure activity or infections may affect energy requirements.

Constipation is a further common problem which may be painful, decrease appetite, cause irritability and may compromise urinary continence. It may be due to a number of factors but poor fibre and low fluid intake are important contributing factors such as immobility, dysmobility of the lower bowel and medication. Fibre requirements are relatively high but difficult to achieve on a puree or blenderised diet or even with tube feeding. For healthy children, fluid requirements ranges from 150 ml/kg/day in infants aged 0-3 months to 50 ml/kg.day in teenagers. Water must be provided in sufficient quantities to replace fluid losses for normal metabolism, but requirements depend on variables such as urine output, vomiting, fever and stool output. Constant drooling also contributes to fluid losses although excess fluids can lead to increased secretions. For some children, thickened fluids can enable more successful drinking other children may need the support of tube feeds. It is important that nutritional intake of children is regularly assessed preferably by a dietitian to ensure that children are supported in obtaining optimal nutrition.
Attention to good nutritional care has the potential to improve quality of life for both the child and family, and should be a priority within a child's assessments, reviews and care planning. Assisted feeding, also called hand feeding or oral feeding is the action of a person feeding another person who could not otherwise feed themselves. A feeding tube is a medical device used to provide nutrition to patients who cannot obtain nutrition by mouth, are unable to swallow safely, or need nutritional supplementation. Every effort should be made to optimise oral food intake before embarking on tube feeding. This may involve many measures including change of posture, special seating, specialist bottles or teats, oral desensitisation, food texture changes, thickening of liquids, increasing energy density of food, use of energy and nutritional supplements, and treatment of reflux or oesophagitis. Tube feeding should be considered when one or more of the following factors are identified:

1. Unsafe swallow and aspiration
2. Inability to consume at least 60% of energy needs by mouth
3. Total feeding time more than four hours per day
4. Unpleasant feeding

Before initiation of enteral tube feeding, assessment is needed to 1) to ensure there are no contraindications for enteral feeding; 2) to assess any possible gastrointestinal problems (e.g. gastro-oesophageal reflux, risk of aspiration); and 3) to determine the optimal delivery site for feeding (i.e., choosing either a nasogastric tube inserted into the nose and going down to the stomach; a gastrostomy tube/button- a surgically placed device directly into the stomach and is used for long-term enteral nutrition; or a naso-jejunal- a tube inserted into nose and going down to the small intestine). Hopefully, some children receiving enteral feeds may continue to receive oral food and drink (providing they have a safe swallow) and this should be actively encouraged so they can enjoy the pleasurable aspects of eating.

Tube feedings of infants and children can be administered by continuous feed, regulated by an enteral feeding infusion pump, periodic bolus, or combination of the two methods. When oral feeding is also possible, the best combination is a regular schedule of normal and tube feeding that fits the needs and routines of the child and the family. For periodic bolus feeding, the enteral formula is delivered at regular times each day, with each feeding lasting up to half an hour. Bolus refers to the discrete volume of nutrient material moving through the gastrointestinal tract. Advantages of bolus feeding include freedom of movement between feeds, and similarity to a normal eating schedule. Disadvantages can include an increased possibility of aspiration compared to continuous drip feeding, and in some cases diarrhoea, bloating, and cramp particularly when the feed volume is too large. For continuous drip feeding, an electronic pump is used to control and measure the intake without any interruption, and may be administered during the night. Typically, continuous drip is administered for several hours during the night so that smaller regular bolus or oral feedings can be administered during the day. The choice of an enteral formula is specific to the patient, and a range of prepared formulas are available commercially.
Hippocrates in 5th century BC described that a man’s seizures were cured by fasting. In 1911 and in 1921 there were scientific papers describing the benefits of fasting in those who had seizures. During starvation the body’s metabolism changes and there is increased production of ketones and these can be used by the brain as a fuel and energy source. It was found that having a very high fat and low carbohydrate diet (sugars and starchy foods) this mimics what happens in starvation. Since the 1990’s the Ketogenic diet has been recommended at many centres around the World and several studies have shown that this dietary approach in the treatment of seizures has often been successful when previously individuals had been resistant to medication.

How the Ketogenic diet works is still not really understood and there are several hypotheses. It has been shown that the Ketogenic diet can not only improve seizure control, but often children have improved alertness. It is often possible for children who respond to the diet for the Neurologist to reduce the medications. The Ketogenic diet should be very carefully calculated for each individual child by an experienced dietitian so that ketosis can be achieved. It is also important that the diet provides adequate protein for the child to grow and the necessary minerals and vitamins for health so as to avoid malnutrition. Any child following a Ketogenic diet should be assessed and monitored by a Paediatric Neurologist who is a specialist in this therapy as there are side effects and sometimes complications from following this diet. However, there are fewer side effects with the Ketogenic diet than with medications.

There are now 3 main types of Ketogenic diets and the aim with all is to produce ketosis and to improve both seizure control and also quality of life. It is important that the dietitian makes a careful assessment for each individual child considering their medical, physical and social needs so that they are prescribed the most suitable diet.

**THE CLASSICAL KETOGENIC DIET**
This diet is calculated so that there is a ratio of fat to carbohydrate and protein with the aim to produce ketosis. This might be a 3:1 ratio which means there is 3g fat to 1g carbohydrate and protein. This type of diet can also be given to children who receive their nutrition partially or fully by either nasogastric or gastrostomy tubes.

**THE MCT DIET**
Slightly more carbohydrate can be included into the diet if there is an energy source from MCT – Medium chain triglycerides fat. Again this diet has to be carefully calculated and administered.

**THE MODIFIED KETOGENIC DIET**
It was developed in 2003 by the John Hopkins Centre in Baltimore, and is less restrictive and easier to implement than the traditional Ketogenic diets. Most centres teach it using household measures and exchange lists for carbohydrate and fat. The aim is still to achieve ketosis and the carbohydrate is low but there are not the protein and calorie restrictions. It is now offered by most Ketogenic diet centres and is helpful when planning the diet for older children and those who eat more selective diets. It is not used for children fed by either nasogastric or gastrostomy tube.
I am a Speech and Language Therapist working with children with complex feeding and communication needs in London since 2005. This talk will include information about the Speech and Language Therapist's role relating to feeding and how we work with families and other professionals. I will also take a practical look at signs that your child may be having difficulties eating, drinking or swallowing and how everyone can support children at different stages of the condition.

THE DEVELOPMENT OF SWALLOWING
We will briefly cover typical swallowing development and the role of the nervous system for swallowing. We will explore some of the difficulties that may present in Tay Sachs and Sandhoff including the signs to look for that your child needs more support, signs that their swallow skills have changed and signs of aspiration (when food or drink enters the lungs). I will briefly discuss gastro-oesophageal reflux, when the stomach contents escape upwards into the oesophagus and the impact this may have for you and your child.

We will go over the reasons why it is important to support children with their swallow safety including the risks of aspiration and the different ways your child’s needs may be assessed. This will usually start with discussion with parents/carers and observations of your child eating and drinking. Assessment may also include instrumental assessments such as a videofluoroscopy, a moving x-ray of the swallow. Often there are not clear answers about a child's needs at first and it is vital to review information regularly and have regular discussions with family and the rest of the medical and therapy team. We need to pay close attention to how each child responds when they are eating and drinking to try to get their view.

MAKING A PLAN FOR YOUR CHILD
We will then discuss the factors to consider when making an individualised plan, including different approaches to intervention, balancing a child's nutrition and hydration needs and quality of life for the whole family. There are many non-invasive ways to support children and I will try to cover a range of these in a visual way, for example:

- Positioning and use of seating.
- Choosing cups and spoons to control the flow of liquid or ability of the child to take food from the spoon.
- Adapting the texture and/or temperature of the food and drink offered to maximise the child's ability to swallow at the right time.
- Adapting the cues we give a child and how much time children are given between mouthfuls.
- Use of specific techniques when offering food and drink, such as physical prompts to help a child maintain control over their jaw.

It is common for a child's swallowing to vary in relation to their general health and seizure activity/medication and we will consider ways to manage this. I will talk about other people who can help us to support your child with their feeding, for example the physiotherapist, dietician or respiratory doctor. Finally we will discuss the importance of good oral hygiene for all children who have swallowing difficulties.
Session five: Family led discussions

Charity leaders
The ETSCC charity members will lead the discussion

There will be two family led discussions during the conference that will cover various topics relating to general care and symptom management. These sessions will enable families to discuss these topics in depth and to share any useful advice they may have for other families. Each session will have pre-defined subjects and they will be facilitated by the ETSCC charity representatives who are attending the conference. All the printed materials used during the sessions will be available via email after the event.

SYMPTOM MANAGEMENT SESSION
The symptom management session will focus on various techniques that parents have developed to help manage their child's symptoms. Some of the subjects that will be discussed are:

- Talking about epilepsy with a focus on the medication parents have used, their experience of specialist diets and how they comfort their child when they have a seizure.
- A focus on secretions with a discussion about the medications and interventions which parents have used, including techniques and equipment which have made a child more comfortable
- A discussion on helping a child's breathing and the equipment, physiotherapy and medication that can be used.
- Discussing ataxia and the useful pieces of equipment parents have used to help their child with mobility.

GENERAL CARE SESSION
Parents are encouraged to actively take part in this session as the experience they have at looking after their child may help another family who is attending the conference.

- The general care session will focus on ways in which families can help their children to have as high a quality of life as possible. Some of the subjects which will be discussed are:
- Talking about dental care and how good oral hygiene can have a dramatic impact on a child's comfort levels.
- A discussion focusing on bathing and grooming, where families will share special techniques and how they have overcome issues, as their child has grown larger.
- Mobility is a subject that will be discussed in detail and how wheels chairs have been obtained from National Health Service.
- Generic equipment which parents have used at home will be shared so that other families can find out what they can use to impact on their child's well being.

General care is an important subject as there may be some useful advice that can be shared between families. Families are encouraged to talk freely during this session and share their knowledge.

AFTER THE SESSION
Once the session has finished families can continue discussing these topics in greater depth as the opportunity to learn from one another should not be restricted to one afternoon.
Gene therapy attempts to treat genetic diseases at the molecular level by correcting what is wrong with defective genes. Clinical research into gene therapy’s safety and effectiveness has just begun. No one knows if gene therapy will work, or for what diseases. If gene therapy is successful, it could work by preventing a protein from doing something that causes harm, restoring the normal function of a protein, giving proteins new functions, or enhancing the existing functions of proteins.

**HOW DO THEY DO IT?**

Gene therapy relies on finding a dependable delivery system to carry the correct gene to the affected cells. The gene must be delivered inside the target cells and work properly without causing adverse effects. Delivering genes that will work correctly for the long term is the greatest challenge of gene therapy.

Viruses (adenowirus) are often used by researchers to deliver the correct gene to cells. Viruses deposit their own genetic material into host cells to instruct those cells to make more viruses. In gene therapy, the DNA for the desired gene is inserted into the genetic material of the virus. The virus is engineered so that it cannot reproduce, but it does deliver its new genetic material which contains the desired DNA. Gene therapy researchers are investigating ways other than viruses to deliver the correct gene to cells. Fatty molecules known as liposomes may also be used as can micropipettes, sometimes called „gene guns“ to insert genes into cells physically.

**THE FIRST GENE THERAPY TRIAL**

A four-year old girl became the first gene therapy patient on September 14, 1990 at the NIH Clinical Center. She has adenosine deaminase (ADA) deficiency, a genetic disease which leaves her defenseless against infections. White blood cells were taken from her, and the normal genes for making adenosine deaminase were inserted into them. The corrected cells were reinjected into her. Dr. W. French Anderson helped develop this landmark clinical trial when he worked at the National Heart, Lung, and Blood Institute.

**ADVANCES IN UNDERSTANDING HUMAN GENETICS**

Thanks to dramatic advances in our understanding of human genetics, we can now pinpoint many of the faulty genes that are responsible for particular childhood diseases. This has opened up the potential for this lifesaving technique called ‘gene therapy’ – the precise insertion of a working gene into a patient’s DNA to replace or correct a faulty, disease-causing gene.

By resolving the root cause of genetic diseases, gene therapy offers the prospect of effective and lasting treatment for children with conditions that were previously difficult or even impossible to manage. Despite early success, more needs to be done and many medical institutions are refining and developing their gene therapy techniques so that they can be used to help children with a wider range of life-threatening and life-limiting genetic diseases. These include some metabolic disorders and certain blood diseases.
Extensive work has been undertaken at Addenbrooke’s Hospital and the University of Cambridge to explore Tay-Sachs and Sandhoff disease. The research team, led by Professor Tim Cox, has spent more than eighteen years gaining a deeper understanding about the diseases and this has culminated in them being able to develop the full use of gene therapy in animal models of Tay-Sachs and Sandhoff disease. This work has the potential to have a huge impact on those people who are currently affected by the diseases.

**GROUNDBREAKING WORK**
In this groundbreaking work, it was found that when mice that were an authentic model of these diseases were given a single treatment in early adult life there was a greatly increased life quality and survival. In addition, it was found that the treatment prevented the onset of the devastating neurological disease that mimics the acute illness occurring in babies and young children. Further work in the laboratory has perfected this approach: given at the right time, long-term cures or near-cures are the rule.

**SECURING A GRANT FROM THE MEDICAL RESEARCH COUNCIL**
In October 2013 the team received a £2.84 million grant from the UK Medical Research Council to develop and fund the clinical trial for a treatment for Tay-Sachs and Sandhoff diseases. Already several planning meetings have taken place and more will be needed with a variety of regulatory bodies as required to approve all the work so that the trial can start. One of the main milestones of this complex work involves developing the best clinical vectors for delivering the corrective genes safely and effectively in the brains of the patients with the disease.

Although the team encountered a set back in 2015 when issues with the vectors not having the desired effects were reported, they were able to examine and why this unexpected effect occurred. The project is now back on track, although it has been subject to a delay.

**THE FUTURE FOR THE TRIAL**
With the expected support of the Medical Research Council, the research team should be able to continue with its work to make this trial of gene therapy a reality and one that could enter the phase of more prolonged testing across the board (phase 3 studies).

**PROMOTING THE TRIAL**
With the support of The CATS Foundation, Professor Cox and his team have been able to update the Tay-Sachs and Sandhoff community with the progress of the trial. Through this partnership it has allowed them to focus on developing the trial so it can begin as soon as possible.

The team in Cambridge were involved with The CATS Foundation and ACTAYS as they developed the European Registry for Tay-Sachs and Sandhoff disease and this project will enable them to gain access to patients when the trial is ready to start.
Mario D. Cordero, PhD, is a research associate in the University of Sevilla, Spain. He has a degree in Human Nutrition Sciences and a Master’s degree in Molecular biology of Rare Diseases from the Universidad Pablo de Olavide in Sevilla, Spain. In the last few years, his work has shown the implication of autophagy process in mitochondrial diseases.

Actually, his research interests include the molecular implication of mitochondria, AMPK and inflammasome complex in inflammatory and rare diseases and the study of new therapeutic targets.

**ALTERNATIVE THERAPIES: INTRODUCTION OF A NEW INFLAMMASOME COMPLEX TREATMENT FOR TAY-SACHS**

We are a basic research laboratory and our principal work is related to biochemistry and molecular biology of rare diseases and aging. In this sense, our lab usually works with skin fibroblasts from patients to evaluate the molecular bases of the disease. In this section, we will talk about a very interesting process in the cell, the autophagy. In this process different parts from the cell are sequestered within double membrane vesicles that deliver the contents to the lysosome/vacuole for degradation and recycling of the resulting macromolecules. Autophagy is typically activated by different events to generate amino acids and metabolic intermediates to maintain energy (ATP) production. Both insufficient and excess autophagy can promote cell injury. Appropriate regulation of autophagy is thus essential for cellular homeostasis. After a defective autophagy process the cell suffers an “accumulation of trash”. Increased levels of this “cellular trash” induce activation of inflammatory events.

**STUDYING THE MOLECULAR PROCESS OF TAY-SACHS**

We will show the principal topics which will be evaluated in our project in order to study the molecular process of Tay-Sachs disease. Into these topics, autophagy will be accompanied by a new interesting concept, the inflammasome complex. Inflammasome is a new molecular platform, considered a sensor for metabolic danger and stress. Indeed, it has been implicated in the development of major diseases such as gout, type 2 diabetes, and is increasingly suspected of playing a major role in several major neurodegenerative diseases. Of all the inflammasomes, NLRP3 is activated by the most diverse array of danger signals. Our studies have shown an over activation of NLRP3-inflammasome complex under different stressful situations in cells. In this sense, autophagy has been involved in inflammasome control. So, in this project we will evaluate the role of both events, autophagy as a cleaning mechanism and NLRP3-inflammasome as a mechanism involved in neuro-inflammation and cell death. Furthermore, we will propose a screening platform of different compounds to find drugs to modulate the correct degradation of cellular waste and inhibition of NLRP3-inflammasome activation.

Finally, we will show a preliminary data about this Project. In this preliminary approach we have corroborated an increased NLRP3-inflammasome activation in fibroblasts from Tay-Sachs patients. This observation was accompanied by several interesting observations such as bio-energetic dysregulation and accelerated aging biomarkers in these fibroblasts. We will discuss the implication of these preliminary data.
I was married to my wife Julie in September 1993 and have two daughters - Bailey born in October 1996 and Dakota born in May 1999. In September 2005 Dakota was diagnosed with Juvenile On-Set Tay-Sachs disease. Dakota had a cord blood transplant at Duke Medical Center in January 2006. We founded the Cure Tay-Sachs Foundation (CTSF) in June 2007. The CTSF mission is to support research that shows promise to treat or cure Tay-Sachs disease. We do not provide family support or sponsor screening events – we are singularly focused on Tay-Sachs disease research.

Since June 2007 the CTSF has raised $3.9 million dollars for Tay-Sachs disease research. We have received donation from all 50 US states, two US provinces and 15 other countries. We are the single largest private funder of Tay-Sachs research in the US and the largest private funder of the Tay-Sachs Gene Therapy Consortium (TSGT) in the US. We have issued $1.9 million in research grants ($1.3 to the TSGT) and have committed another $500,000 to on-going research projects.

Dakota passed away in April 2014 at the age of 14. She was the light of my life and the strength I needed to fight his horrible disease. We continue to work hard to find treatments and a cure for Tay-Sachs disease in her memory and in the memory of all the kids who fought so bravely.

REMARKABLE KIDS MAKE REMARKABLE PARENTS
I have always maintained that Tay-Sachs children are not born to remarkable parents, but Tay-Sachs kids make parents remarkable if you let them. The greatest honor of my life was to be the father of Bailey and Dakota – they have changed my life for the better in every way. While I admittedly now struggle with finding the strength Dakota once provided each night as we cuddled on the sofa – I know that as parents of a Tay-Sachs child we must lead the fight to eliminate this disease. Why would others prioritize Tay-Sachs over the many other disease that kill hundreds if not thousands or people. We are the ones motivated and educated to tell our stories, to lead this fight. If we don't do it – it won't get done.

THE GOAL OF THE CTSF
The goal is not to get donation from the parents of Tay-Sachs kids, the goal is to get donations from the friends and family that know and care about that child. The goal is to tell our story anyway possible to motivate people to action. When a kid falls down a well the whole world stops to get that child home safely. We have dozens of kids stuck in well – but if no one knows there is no rush to help. Find the strength to tell your story!
Having a sibling with a disease such as Tay-Sachs was such a monumental part of my life, yet besides my close friends, most people don’t know this about me. It’s not a secret by any means, it is an integral part of who I am and has shaped where I am today, but for most of my life I didn’t know anyone else who had a sick brother - and felt less comfortable telling people about it. Growing up my parents weren’t in touch with any Tay-Sachs communities or support groups, and it wasn’t until much later I even realized they existed, as my parents mainly relied on family for support.

**STUDYING BIOLOGY**

And while I knew that I wanted to study biology and work on Tay-Sachs or other related disorders, putting that into action turned out to be more difficult than I expected. It wasn’t until my second year of university while searching for scholarships that I learned about one of the charities in the US - NTSAD (National Tay-Sachs and Allied Diseases), and started to get a little more involved and connected with other families, as well as researchers in the field.

**BEGINNING MY WORK IN LYSOSOMAL STORAGE DISEASES**

I think I really started pursuing this while spending the summer working in a lysosomal storage disease research lab in Boston, and as NTSAD is headquartered there, getting to hear more about things from their perspective and beginning to form an idea of what I wanted to do once I finished at university. That took me, much to my amazement, to Oxford University where I have been ever since. Here, I worked initially on the validation of a biomarker study for GM2 gangliosidosis and now am finishing with my PhD looking at therapies for the lysosomal storage disease Niemann-Pick type C. I know its not over yet, but my journey so far has played out better than I could have imagined when I sent in an essay for the sibling scholarship to NTSAD all those years ago.

**THE AMAZING COMMUNITY**

I am constantly amazed by the community of families and researchers committed to furthering knowledge and care for this disease, and am happy to be a part of it both as a sister and as a scientist working for a cure.
Make **notes** at the event

Use this **space yourself**

Things to remember

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“Which way you ought to go depends on where you want to get to...”