Summer 2011

HELPING HANDS

FOR FRIENDS, FAMILY, AND SUPPORTERS OF THE CHILDREN'S GAUCHER RESEARCH FUND

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THE ONLY THING INCURABLE IS OUR PASSION

we are waiting for...a big "WOW" moment to arrive as a result of the research...there is a chance of this happening at the end of 2011

The Children's Gaucher Research Fund continues to make great progress. We are keenly aware that progress cannot happen fast enough for those children who currently suffer from neuronopathic Gaucher disease. However, we also understand that it necessary to create the building blocks, the foundation that is essential for the road to a cure. To date research funded by the CGRF has helped to create those building blocks.

After years of dedication we are also waiting for something other than building blocks - a big "WOW" moment to arrive as a result of the research you have supported. We believe there is a chance of this happening at the end of 2011. As referenced in Dr. Tony Futerman's article below, the Inducible Gaucher Mouse that was funded two and a half years ago by the CGRF holds great promise. If successful, this will undoubtedly be a "WOW" moment for the CGRF, in that this mouse will become available to and will stimulate research in laboratories throughout the world.

We are often asked why we continue this quest. There are multiple answers to this question, some of which are too lengthy to discuss in this newsletter. One reason however, is that we know that Gaucher disease is the most prevalent of over 40 Lysosomal Storage Diseases. At least once every half hour a child is born with a lysosomal disease. Most importantly the mortality rate for these children is quite high. Therefore, the children are left unrepresented; only their grieving parents are left to advocate for a cure.

The CGRF is the voice for these children. With the children passed on we have to ask ourselves, if we do not advocate for a cure, who will? The CGRF, with your support, has decided that we will! As always, we appreciate your continued support and we assure you that the CGRF is administered as efficiently as humanly possible; 100% of your donation will continue to fund medical research.

With the children gone we have to ask ourselves, if we do not advocate for a cure, who will?

Deborah Macres R.N.
Founder

Gregory Macres
Chairman/Founder

Inside

SCIENTIFIC RESEARCH UPDATE

By Tony Futerman Ph.D.

PROFESSOR Department of Biological Chemistry
Weizmann Institute of Science, Rehovot, Israel

It is with great pleasure that I am writing this brief article to update readers on research progress in my laboratory over the past couple of years, and to thank all the generous donors who have made the work possible. I can truly say that without the remarkable efforts of the CGRF, my research would not have been possible.

FIRST A LITTLE BACKGROUND.

I have had the honor of being supported by three research grants from the CGRF over the past decade or so. Each time that I have submitted an application for a renewal of my funding, my knees have trembled!

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The Futerman laboratory on a day trip to the North of Israel, visiting a vineyard.

Would I receive an additional award? Do my scientific peers, who independently evaluate my research grant applications, think that progress has been sufficient to merit another award? What would happen to the research on neuronopathic Gaucher disease in my laboratory if the work was not funded? Fortunately, I have been privileged to receive funding, with the most recent round of funding being awarded towards the end of 2010, for a period of three years. And for this I express my thanks, not only to my scientific colleagues who rated my research as worthy of funding, but also to the CGRF and its generous and committed donors.

How much money is needed for research?

Some of you may be wondering why so much money is needed for scientific research (for your information, the grant which I was just awarded is worth $100,000 per year for three years). Well, research is very expensive. A major expense, and perhaps the major expense, is personnel. I currently have two outstanding graduate students, studying towards their PhD degrees, working on the CGRF-funded projects. Another major expense is laboratory supplies – from simple chemicals to the specialized tools needed to perform technically-demanding aspects of the research. And then there is the cost of international collaborations, of which we have a number. So although the sum awarded to my laboratory may sound like a large sum, every cent is needed to push the research forward.

How long does research take?

Another question that I am sometimes asked is why it takes so long to discover the causes, and the biochemical mechanisms that cause neuronopathic Gaucher disease. After all, the disease has been known for decades, there is an excellent therapy for type 1 Gaucher disease (that is, the form of Gaucher disease that does not affect the brain), and surely there are hundreds of researchers working on neuronopathic Gaucher disease all over the world? These are all good and relevant questions, but the answers may surprise you. First, even though the genetic cause of Gaucher disease is known, and has been known for decades, the biochemical question of why specific areas of the brain are affected in Children's Gaucher disease, and not others, is simply unknown, as is the reason that some patients develop brain symptoms whereas others do not. As for therapy, I am sure that I have no need to tell any of you that Cerezyme (enzyme replacement), which is used for type 1 Gaucher disease patients, is simply ineffective in the brain since it cannot cross the blood-brain barrier. And finally, and this might be really surprising, but there are actually very few research laboratories working directly on neuronopathic Gaucher disease – one of the reasons for this is that the disease is very rare, and there are limited sources of research funding available from international and federal research funding agencies. This is of course where the CGRF comes in – having recognized the need to support research, the CGRF has pushed ahead and made research possible, at least in my laboratory. Moreover, funding by the CGRF has enabled us to establish a number of important collaborations with leading research laboratories all over the world.

> "…having recognized the need to support research, the CGRF has pushed ahead and made research possible…"

New researchers involved

One other point before I get into the nitty-gritty of my research. I actually foresee a significant increase in the involvement and recruitment of new researchers into the neuronopathic Gaucher research area. In January 2011, I had the honor of chairing the first ever Gordon conference specifically devoted to the study of lysosomal storage diseases – for those of you not in the know, Gaucher disease belongs to a family of genetic diseases known as lysosomal storage diseases, and 180 researchers and students gathered together in Galveston, Texas, to discuss the latest advances. You should also be aware that Gordon conferences are considered the premier research conferences in the world, and the fact that the Gordon conference organization saw fit to sponsor this new conference provided significant new momentum for the field in general. The discussions at the conference were lively, and based on the large numbers of discussions that members of my laboratory had with other participants, I believe that issues related to understanding the pathological mechanisms at play in neuronopathic Gaucher disease will be pushed to the forefront of lysosomal disease research in the coming years. The importance of Gaucher disease research will also be strengthened by the recently-discovered genetic relationship between some forms of Gaucher disease and Parkinson's disease. This is not the place to go into this issue in any more detail, but the neuroscience community is much more aware of neurological aspects of Gaucher disease than they were even five years ago. This has to be good for the research field.

Einat Vitner - whose work is funded by the CGRF – at work in the lab with colleagues.

My research

Let's now get down to some of the details of my research. When I was first funded by the CGRF, we had demonstrated an important connection between changes in calcium levels and the death of nerve cells – this research is all published, and you can find links to the work via the CGRF web page (www.cgrf.org). Suffice to say that all of this work was performed using cultured cells, that is to say, nerve cells which we isolated from mice (or rat) brain, and grew in a culture dish in an incubator. The reason we worked on cultured cells, rather than on more advanced models, was because no advanced models were available. This has changed recently, and our research will now be able to address areas that could not have previously been tackled.

> "When I was first funded by the CGRF, we had demonstrated an important connection between changes in calcium levels and the death of nerve cells…"

A mouse model is generated

A huge breakthrough came in 2007 when Dr. Stefan Karlsson, in Sweden, generated a mouse model of neuronopathic Gaucher disease. A mouse model is basically a genetically-manipulated mouse that resembles, to some extent, a human disease, and allows issues to be examined that could not be studied otherwise. For instance, new therapies are invariably tested first on mouse models of human diseases, before they can be tested on human patients. Dr. Karlsson generously made his mouse available to researchers worldwide, including to my laboratory. Now that we had this mouse, we were able to pursue research directions that had been impossible beforehand. For instance, Einat Vitner, one of the two graduate students currently supported by the CGRF, was able to show changes in levels of a molecule called 'cathepsin' in the brains of the mice. The release of cathepsins from cells in the brain is consistent with a model of brain dysfunction known as neuroinflammation, which interestingly, has been shown to occur in a number of other lysosomal storage diseases. Another research area was to examine which specific areas of the brain were affected in the mouse. This study was performed by the other graduate student, Tamar Farfel-Becker, who defined, for the first time, the progression of some of the neuropathological changes.

> "…CGRF has also funded attempts …to make a new mouse model… I am confident that we will have something exciting to report by the end of 2011."

Remarkably, she found that some areas which are affected might be able to provide an explanation for some of the symptoms found in children. For example, an area known as the substantia nigra reticulata was affected, and this area is known to play an important role in some of the eye movement problems observed in children (for those of you really interested in this work, it was just published in the distinguished journal, Human Molecular Genetics). These examples of some of our results lead me into a discussion of what we are planning to do over the next two and a half years of our funding.

Three major research areas

We are working on three major research areas. First, we want to understand why certain areas of the brain are affected in the disease, and of no less importance, why certain areas are not affected. If we could understand this, we might be able to make predictions about the kind of therapies that are needed. Second, we want to understand the process that I mentioned above, namely neuroinflammation, in disease progression. As I also mentioned, neuroinflammation has been observed in a number of other brain diseases, and also in other lysosomal storage diseases, meaning that lessons learned, and tools available from some of these other studies might be applicable to neuronopathic Gaucher disease. Finally, we want to take advantage of the two goals above to try to discover new therapeutic options. For instance, there are many common drugs that can be used to treat neuroinflammation – might these be useful to ameliorate disease symptoms in the mouse, and then possibly in humans? I should say that so far this approach has not been successful in the mouse that we received from Dr. Karlsson – however, there is a caveat in the use of the Karlsson mouse inasmuch as it only lives in the laboratory for a relatively short period (2-3 weeks), meaning that the window of opportunity for treatment is fairly limited.

A mouse is a mouse – not really

This is one of the reasons that the CGRF has also funded attempts by myself and two colleagues in the Weizmann Institute, who are experts in mouse genetics, to make a new mouse model. I am unable to go into detail at this stage, but I am confident that we will have something exciting to report by the end of 2011.

Is there cause for optimism?

So this is where we are in the middle of 2011. Is there cause for optimism? Yes. New researchers are being attracted to the field. One mouse model is available and others are on the way. Neuroscientists are becoming interested in Gaucher disease research. Links are being found between Gaucher disease and other lysosomal storage diseases, and also Parkinson's disease. Are we close to finding a cure? Well, certainly nearer a cure than a few years ago, but much more basic research is still required before therapies will be available. How long will this take? And to that question, I must honestly say that we have no idea. Scientific discoveries normally occur due to the right environment being established for ideas to develop and come to fruition, and due to funding being available to put these ideas into practice. I can only say that my laboratory is doing its utmost to understand what is going on in the disease, and to take these findings along the path that will lead to a cure. And none of this would be possible without the wonderful support of the CGRF, and for this I express my deep gratitude.

In Loving Memory

In Loving Memory of

Sofia Jaramillo Rios

"BeBa always in Mommy and Daddy's heart"

March 31, 2010 to February 11, 2011

Toronto, Canada

In Loving Memory of

Ella Marie Hood

"To our sweet angel baby Ella, you will always and forever be in our hearts"

January 27, 2010 to November 25, 2010

Guilford, Maine

In Loving Memory of

Willow Ansley Jaynes

"We miss our sweet Willow and cannot wait to be reunited with her one day!"

August 10, 2009 to August 10, 2010

Jackson, Tennessee

In Loving Memory of

Dezmond Moore

"Our first son out of three girls, we loved you so much and we also miss you so much"

May 8, 2010 to January 16, 2011

Montgomery Village, Maryland

In Loving Memory of

Demiyah Moore

Our beautiful daughter you paved the way for your brother and you are missed and loved as well.

January 18, 2009 to April 29, 2010

Montgomery Village, Maryland

First Annual "Macres Heaven Birthday Ride"

April 13th, 2011 marked the fourteenth Heaven Birthday of our precious son, Gregory. We have chosen to honor his legacy through the efforts of the CGRF. On April 13th of this year we chose to celebrate his life through a Memorial Ride visiting significant locations in his journey as he battled Gaucher Type 3.

I (Greg Macres) along with my daughter Ashley and my son Matthew rode a 31-mile memorial bike ride around the South Bay area beginning in Palo Alto on the steps of my boyhood home. We then rode to Kaiser Hospital in Santa Clara, where over a four year period Gregory received treatment for Gaucher disease. From the hospital we rode to Saratoga Presbyterian Church where, in 1997, over 400 friends and family gathered at Gregory's memorial service to honor his life. The last stop was in San Jose, to the site where Gregory was laid to rest.

At his resting place, I joined my wife Deborah and Gregory's brother and three sisters along with Richard Spencer (the minister at Gregory's memorial service) to share stories and reflect on Gregory's humor, his resilience, and his courage. It was a celebration of his life, knowing that the legacy of his fingerprints are paving the way toward a cure for children with Gaucher disease.

We thank those who sponsored the ride, helping us to raise over $4,800 for medical research.

The CGRF encourages all families who have lost a child to create one annual fund raising event that honors their child's life, their struggle, and their memory.

Wheatley's Honor Their Son

On July 13, 2009, Zachary and Kelly Wheatley lost their 8 month old son Lincoln Lewis Wheatley to Gaucher disease. In march of 2010 they organized the first in a series of Annual Memorial Charity Poker Events (www.playforgaucher.org) to honor his son's life. Recently the Wheatley's held the second annual Play for Gaucher tournament and raised $2,700 for medical research.

The Wheatley's have taken their grief and pointed it in a direction that honor's their son's battle with Gaucher disease. The CGRF encourages all families who have lost a child to create one annual fund raising event that honors their child's life, their struggle, and their memory.

Additional Information call 614-439-7369

2012 Play for Gaucher Event Information

Date: **March 31, 2012**
Location: **430 Walnut Avenue**
Canton, Ohio 44702
Start Time: **6:00 p.m.**
Entry Fee **$65.00 Pre-pay / $75.00 at door**

Pleasant Grove KEY Clubbers Raise $6,100 for CGRF

The KEY Club students at Florin High School and Pleasant Grove High School have been tremendous supporters of the CGRF over the past 8 years. The prime mover of the Awake-A-Thon project is educator Robert Tabares of Pleasant Grove High School. In the words of Robert Tabares, here is an inside story of how it began.

"I got the idea from a news report of students staying awake all night to raise funds for their fundraiser. Ten years ago we started the Awake-A-Thon because the Key Clubbers at FlorinHigh School wanted to help the Make-A-Wish Foundation. After the first two Awake-A-Thons, our Vice Principal Mr. Mark Macres told me about another needy group: the Children's Gaucher Research Fund. He knew of this group, because his nephew died from Gaucher disease at the age of four. Mark Macres' brother Greg Macres (who spoke at the Awake-A-Thon) started gathering funds to support research to find a cure for the Gaucher disease. So I suggested that our Key Clubbers at Florin High take on the Awake-A-Thon that would allow kids to help kids. After completing five Awake-AThons at Florin High School, I also added the Awake-A-Thon to Pleasant Grove High School for the past five years. By completing the Awake-A-Thons it shows that teenagers can do positive acts in this world while we hear negatives acts by other teenagers."

New CGRF Website

www.childrensgaucher.org
www.cgrf.org

With the help of our volunteers, the CGRF has invested considerable time and effort in creating our new state-of-the-art website. Visit our new website keeping in mind the following:

1. **Donations** – can now be given via credit card on our website
2. **Subscribe** – you can subscribe to receive email notification of the latest articles pertaining to fund-raising – research progress – and recent news.
3. **Research** – publications in scientific journals resulting from CGRF funding can be accessed on the website.
4. **Scientific Conferences** – abstracts from presentations at past conferences can be accessed on the website.
5. **100% to Research** – learn in detail how we maintain this commitment.
6. **Family Stories** – all family stories are posted on the website.
7. **How You Can Help** – if you have a passion to help, on the top menu click "How To Help" and then select "Become a Champion". Here you will find examples of simple fund-raising ideas. Many are simple, easy, and will not consume your time.

ONLINE DONATIONS

can be made by visiting
www.childrensgaucher.org
OR
www.cgrf.org
All family stories can be read on the web site.

100% TO RESEARCH

You need to know:

1. The CCRF is a *legitimate* IRS approved 501 c3 non-profit organization.
2. *100% of every donation* goes to medical research.
3. We *do not* hire professional fundraising companies who keep 50% of donated funds.
4. We have talented volunteers who *donate* their time and talent for a variety of our needs.
5. All administrative costs are paid for by the *founders.*

Simply put: if you send your hard earned dollars - *It ALL goes to medical research.*

Visit our web site at:
www.childrensgaucher.org
All family stories can be
read on the website.

Contributions Payable To:
Children's Gaucher Research Fund
P.O. Box 2123
Granite Bay, California 95746-2123

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