

From: Marylyn House  
AMDA  
Acid Maltase Deficiency Association

To: MDA

Re: "QUEST"

March 12, 2003

In the "early days" the MDA was not as supportive of Pompe research as was suggested in the "Quest" article (*March 2003*). Following is (*past*) correspondence between AMDA and MDA indicating that there was not a great deal of interest by the MDA in the promotion of Pompe endeavors....

.....(*an*) area (*of Pompe research*) overlooked in the "Quest" article (was).... the work done by the researchers in the Netherlands where the **FIRST** clinical trials originated **5-6 months** prior to Duke's trials.....**and they were very successful.**

Dr. Reuser and Dr. van der Ploeg (scientists in The Netherlands) were precursors of research in Pompe's disease, and their work should **not** have been overlooked by the MDA (*or by Genzyme or Duke*). All parties (Duke, Genzyme, MDA) were well aware of the research and the clinical trials that took place in the Netherlands (*MDA contacted Dr. Reuser in regards to his Pompe research in 1998*).

We were aware that Genzyme was arranging a "campaign" with the MDA to publicize their new clinical trial (*for Pompe's disease*). We requested that AMDA and the IPA (International Pompe Association) be included in the meeting because of our prior involvement and contributions to the Pompe "project", but our request was denied.....

**I would like to invite Genzyme and the MDA to respond to the following) correspondence that I have posted here ( posted originally on GSDNET and emailed to both MDA and Genzyme)..... ignoring the issues, will not make them disappear.**

Best Regards,  
Marylyn House  
AMDA

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## LETTER TO AMDA FROM A POMPE PATIENT

2/28/2003

>>I was just wondering if you guys (AMDA) have read the article in this month's Quest Magazine (MDA's magazine) about Pompe disease yielding to modern medicine. I was just wondering what information your organization has received on these trials, and if

you know of any other information. The article was very positive. Dr. Chen's work at Duke University was highlighted, and so was one of the case studies.

**IT IS VERY RARE THAT ACID MALTASE DISEASE IS DISCUSSED IN THIS MAGAZINE.**

Please let us know what you have received on this data. We are very interested in any information your have<<

**A M D A's RESPONSE**

*February 2003*

Genzyme has been collaborating with MDA for months on developing a campaign for Pompe's disease. MDA was not much interested in "us" (the Pompe patients) until Genzyme entered the picture. I think we are going to see a lot more MDA involvement and "credit taken" in the future. The MDA is one of the largest non-profit organizations in the world with "celebrity" recognition. So.....Genzyme wanted their "name" in the game.

Best Regards,  
Marylyn House  
AMDA

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**LETTER FROM A MEMBER OF GSDNET FOLLOWS**

*March 5, 2003*

>>I only know what I read from their (MDA's Quest) publications (March-April 2003), but I thought they paid for a lot of the original research, and some of the more recent also. M.<<

**Reply to Above Letter From GSDnet**

*MARCH 2003*

I'm not aware of them (MDA) paying one cent towards the original ERT research, which was carried out in Rotterdam. Nor did they make the running in taking that original research forward. For that, we have to thank - aside from the researchers themselves - the remarkable achievements of Randall and Marylyn House (AMDA). Make no mistake, they \*made\* things happen. In fact, one of the interesting threads to the Pompe's story (in my view) is the combination of European ideas and US 'can-do' - another example being that other remarkable US couple, John and Eileen Crowley.

FROM MARYLYN HOUSE TO GSDNET

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## Posted on GSDnet March 5, 2003

Thank you, \_\_\_\_\_, but you were the "lead dog" (so to speak), and you (plus the researchers in Rotterdam) **deserve** more recognition for your endeavors. But what you said is **absolutely** correct! AMDA asked the MDA to attend the first, second, and third scientific conferences that we sponsored in 1996, 1997, 1998. These were **very** important meetings attended by 25-30 lead scientists from all over the world that were doing current research in Pompe's disease.

**MDA WAS NOT, AT ALL, INTERESTED AND WOULD NOT SEND ANY REPRESENTATIVES!!!!** The NIH must have thought that the AMDA conferences were worthwhile events because in 1999 the largest scientific conference for Pompe's disease (50-60 attendees) was sponsored and hosted by the NIH (in conjunction with AMDA).

And, on a personal note: **MDA was absolutely no help to us in dealing with Tiffany. We couldn't even get an appointment at the MDA for 3 months when Tiffany was first diagnosed....**

**In addition, Dr. Reuser's group in the Netherlands** was not mentioned in this article (nor the lead work on enzyme replacement therapy that was done in The Netherlands).

The transgenic therapy has **never** received the acclaim that it deserves. I know, first hand, that Tiffany (and others) did better on the transgenic enzyme than on the CHO enzyme that she is now receiving (granted the dosage was decreased).....**but** Genzyme claimed that this CHO product was **AT LEAST** twice as effective as the transgenic product (*that they discontinued*). The Novazyme product was touted as being the BEST yet, but where has it .....gone????????.....

Marylyn House  
AMDA

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## Letter from Patient Posted on GSDnet

*March 7, 2003*

>>On the other hand if MDA gives money towards the project to build more bioreactors would that not improve the time problem towards ERT becoming available to all patients around the world<<

## Reply to the Above Letter

I do not think that MDA will fund bioreactors----this is the corporation's (**Genzyme**) role--they (MDA) are research oriented. I do not have any objection to MDA's involvement--

we (AMDA) requested their involvement early on, but we were rebuffed!

What I do resent is their claim that they took the lead and that MDA (and Duke University) are the keys to the development of the whole Pompe project....

No doubt that it will take an institution like the MDA to get the coverage necessary to educate and inform the medical community (*and insurance carriers and the government!*) about Pompe's disease. This is good!

BUT.....

It is, once again, an example of how things are slanted. With all of their financial resources and influence, the MDA **should** be a **leader** in research initiatives not a usurper of credit!!!! (*and the same goes for other entities as well*).

Marylyn House  
AMDA

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## MESSAGE TO AMDA from a PATIENT

MARCH 12, 2003

>>Dear Marylyn, Thanks for sending all these letters to GSDNET. I think it's important that people know how things go..... My conclusion is that **without Dr. Reuser we wouldn't have come this far as we are now.....<<**

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## LETTER FROM MDA

MARCH 17, 2003

**To:** Marylyn House  
Acid Maltase Deficiency Association  
San Antonio, Texas

**From:** Carol Sowell  
Director of Publications  
MDA  
National Headquarters  
Tucson, AZ

Dear Ms. House:

I'm writing in response to your emails of March 12, in which you take issue with our recent articles in Quest (March-April 2003) describing the success of enzyme replacement therapy (ERT) for Pompe's disease.

Your imply that the main article exaggerates MDA's commitment to research on Pompe's disease/acid maltase deficiency, and that it omits important facts about the history of this research. Both of these accusations are unfair and unwarranted. Judging from documents attached to your letter, they stem from a long-held resentment over MDA's decision not to participate in an AMDA-sponsored meeting in 1996. **(see response below)**

- "In the early days," you say, "MDA was not as supportive of Pompe research as was suggested in the Quest article."

I'm not sure what you consider early days, but Pompe's disease became part of our research and health care services program in 1976. Since that time, we've spent more than \$1.5 million on Pompe's disease research. Much of that sum has gone to Yuan-Tsong Chen at Duke University in Durham, N. C., to support the pre-clinical development of ERT. **(see response below)**

You claim that the article "overlooked...work done by the researchers in the Netherlands where the first clinical trials originated six months prior to Duke's trials."

On the contrary, beginning on page 17, the article states "...Chen began his first trial of enzyme replacement therapy for Pompe's disease in 1999...(Genzyme) began testing enzyme replacement therapy for Pompe's disease in 1998, through a joint venture with Pharming, a Dutch biotech company..." The article goes on to explain that Genzyme and Pharming were testing a form of the acid maltase enzyme that was different from Chen's version, and that Genzyme eventually acquired the rights to the enzyme from Pharming. **(see response below)**

Finally, I'd like to point out that the feedback to the quest article has been overwhelmingly positive. In fact, Dr. Chen, who we note is a member of your scientific advisory board, reviewed and approved the article before it was published. Also, the Unite Pompe Foundation has, with MDA's permission, placed a link to the Quest article on its Web site. I hope that this letter clears up any misunderstanding, and that both our organizations can continue to focus on what's really important—helping people with Pompe's disease. **(see response below)**

Sincerely,  
Carol Sowell  
Director of Publications  
MDA

cc: Daniel T. Stimson, Ph.D., Senior Science Writer (MDA)  
Ronald J. Schenkenberger, Director of Research Administration (MDA)

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## LETTER TO MDA FROM A M D A

MARCH 23, 2003 (posted on GSDnet)

Dear Ms. Sowell:  
Director of Publications (MDA)

***The following addresses your letter of March 17, 2003:***

I do not dispute that Pompe's disease became part of the MDA's health care services program in 1976 as you stated in your letter. After all, it is a muscle disease and thereby, rightfully should have received the attention of such a vast philanthropic organization as the MDA.

**>>You stated, "Since that time (27 years), we've spent more than \$1.5 million on Pompe's disease research." <<**

Our interest in Pompe's disease started only eight years ago when our eleven year old daughter was diagnosed with this rare life-threatening disease. During the last eight years, we, too, have spent more than \$1.5 (**Over 4.9 Million!!**) million funding research for Pompe's disease. This is vastly disproportionate funding between the MDA and AMDA (Randall and Marylyn House) considering the size of our two organizations and the number of years of our respective involvement. (**AMDA-8 years; MDA-27 years**)

**>>You stated, " Much of that sum has gone to Yuan-Tsong Chen at Duke University in Durham, N.C., to support the pre-clinical development of ERT."<<**

We, also, supported Y.T. Chen's efforts during pre-clinical development of ERT. In 1996, in addition to other funding at Duke, we financed the patent of Dr. Y.T. Chen's....invention entitled: "Tissue Specific Recombinant Human Lysosomal Acid Alpha-Glucosidase." ..... we did not retain royalties in this endeavor as is customary with some organizations.

**>>You stated, "You (*Marylyn House*) claim that the article 'overlooked...work done by the researchers in the Netherlands where the first clinical trials originated six months prior to Duke's trials.' <<**

**>>You (*Marylyn House*) stated, "On the contrary, beginning on page 17, the article states "...Chen began his first trial of enzyme replacement therapy for Pompe's disease in 1999...(Genzyme) began testing enzyme replacement therapy for Pompe's disease in 1998, through a joint venture with Pharming, a Dutch biotech company..." The article goes on to explain that Genzyme and Pharming were testing a form of the acid maltase enzyme that was different from Chen's version, and that Genzyme eventually acquired the rights to the enzyme from Pharming."<<**

Pardon me if I have misinterpreted this attempt to recognize the research efforts of the

investigators in the Netherlands, but I feel that their contributions to enzyme replacement therapy for Pompe's disease deserves more than this succinct reference.

**>>You state, "Finally, I'd like to point out that feedback to the Quest article has been overwhelmingly positive."<<**

..... this is not a point of contention with us. I only wish that the MDA had been more responsive to the needs of the Pompe community in the past seven years. We, also, have had overwhelming response to initiatives that we have undertaken to spur a treatment for Pompe's disease. Our most recent initiative was the publication of "**The Physician's Guide to Pompe's Disease**" (<http://www.rarediseases.org/nord/programs/freebooklets> ) that we funded and distributed to over 15,000 physicians in the US. This pamphlet is part of a series of NORD publications made available to physicians free of cost.

**>>As you also stated in your letter, "Judging from the document attached to your letter, they stem from a long-held resentment over MDA's decision not to participate in an AMDA-sponsored meeting in 1996." << (And two others!)**

You are absolutely right. I am resentful that the MDA rebuffed us. I am also resentful of the physician/scientist at the Mayo Clinic that diagnosed Tiffany but would not even discuss her diagnosis with me (although, I was told, that there were less than 100 cases of this disease ever diagnosed). I am also resentful of the pediatrician that told me that he hoped that I would find something wrong with Tiffany because I was so intensely concerned about her. I am also resentful of the orthopedic surgeon that so coldly addressed Tiffany about her prognosis for the future. I am also resentful of a neurologist, urologist, proctologist, and pulmonary doctor that were all inept. There are more incidents that I could add to this list!

**>>In closing you stated," I hope this letter clears up any misunderstanding, and that both our organizations can continue to focus on what's really important- helping people with Pompe's disease."<<**

This is certainly the motivation of AMDA, and that is why we started this organization. In 1995 there was little interest in this disease, and because of this lack of interest, we had little hope for Tiffany's future. We are more than thankful for the events that have transpired in the last 7-8 years. We only wish that things could have happened faster, so that Tiffany could still walk; so that Tiffany had more than 12-14% breathing capacity, so that Tiffany could have gone to high school and had friends and dated and enjoyed her teenage years. We wish that things had happened faster not only for Tiffany's sake but for the sake of the many patients and families that we have had contact with over the past eight years. We would have welcomed MDA's involvement eight years ago, and we still do today.

**Better late than never!**

Marylyn House (AMDA)

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## **Letter From MDA to AMDA**

*March 26, 2003 (Posted on Gsdnet)*

Dear Marylyn House:

Thanks for your response to my letter about Quest's story on Pompe's disease. Both of our organizations can be proud of having a part in advancing the research to the very promising level it has reached.

I don't have a relative with a neuromuscular disease but I've come to know many families who are affected by the diseases in our program. So my heart truly goes out to your family when I hear about the terrible treatment you received from medical professionals. I've heard many such accounts from people whose children have very rare diseases, and it's distressing to know that families who are simply trying to help their kids still sometimes run into such insensitivity.

At this point, I think the future is what matters. MDA is committed to helping advance the research that offers new hope for a Pompe's treatment.

Our efforts -- and yours -- will someday deliver lifesaving results.

Sincerely,  
Carol Sowell  
Director of Publications  
Muscular Dystrophy Association

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## **Letter To MDA From AMDA**

*March 27, 2003 (Posted on the GSDnet)*

Dear Ms. Sowell:

Thank you for your nice letter. We, as a family, have been through some very trying times, but this is not really why I forwarded information concerning Pompe's research to you.

I feel that vital developments involving the clinical trials and a treatment for Pompe's disease were overlooked in your recent article (March-April 2003) in Quest. Whether this be an unfortunate oversight or not, the situation needs to be rectified. The MDA (Genzyme or Duke) should have given credit to the accomplishments of:

Arnold J.J. Reuser, Ph.D.  
Department of Genetics  
Erasmus University  
Rotterdam, The Netherlands

and

Ans T. van der Ploeg, M.D., Ph.D.  
Department of Pediatrics  
Sophia Children's Hospital  
Rotterdam, The Netherlands

They headed the team that initiated the first clinical trials with ERT for Pompe's disease which started in the Netherlands--months before Duke University started a clinical trial. The trial in the Netherlands started in January 1999 with four infantile patients. Six months later in June 1999, a second trial was initiated there with three juvenile patients (AND both of these trials were successful). In addition, the Netherland's team published their data on the infantile trial in "The Lancet" before Dr. Chen published.

The enzyme used in the two trials in the Netherlands was derived from the milk of transgenic animals (rabbits). This is a novel (and probably a forthcoming) approach to producing enzyme as well as other drugs.

It is still not too late to rectify this oversight, and I sincerely hope that the MDA and Quest will do so prominently in the upcoming issue of Quest. This would be the proper thing to do!

Best Regards,  
Marylyn House  
AMDA

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***FOLLOWING IS PAST CORRESPONDENCE WITH THE MDA***

**CORRESPONDENCE REGARDING THE MDA'S PARTICIPATION IN THE FIRST  
AMDA SPONSORED POMPE SYMPOSIUM**

To: Dr. Norine Stirpe  
Director of Research Development  
MDA  
January 9, 1996

Dear Dr. Stirpe,  
I spoke with you by phone yesterday about a conference planned in late March (1996) by the Acid Maltase Deficiency Association. Dr. Y.T. Chen of Duke University suggested that I contact you and discuss the possibility of the MDA co-sponsoring this conference. I am sending you preliminary information about the conference and will forward the MDA forms to you as soon as I receive them.

I would also like to extend an invitation to you to speak at this conference. If this is not possible, perhaps you could recommend another representative of the MDA to make a presentation.

Please contact me if further information is needed.

Sincerely,  
Randall H. House  
President, AMDA

**From:** Dr. Y. T. Chen  
Duke University

**To:** Norine Stirpe, Ph.D.  
Director of Research Development  
National Headquarters 3300 East Sunrise Drive  
Tucson, AZ 85718-3208

**Conference Objectives:**

To gather the principal investigators worldwide to discuss and share information on Pompe disease and to plan a collaborative effort to find a cure for Pompe disease.

Dear Dr. Stirpe:

Enclosed you will find my official application requesting the funding for the Pompe Disease Meeting to be held in March (1996). I am sending this per your advice and upon the request of Mr. Randall House who is the President of the Acid Maltase Deficiency Association.

I hope this is the information you will need but if there are any further questions or concerns please do not hesitate to contact me.... Thank you very much for your time and consideration.

Sincerely,  
Y.T. Chen, M.D., Ph.D.  
Professor of Pediatrics and Genetics,  
Chief, Division of Medical Genetics  
Duke University Medical Center

**FROM MDA to Dr. Y. T. Chen—DUKE UNIVERSITY**

*February 9, 1996*

Dear Dr. Chen,

Thank you for your January 24 letter and the grant request it transmitted seeking support for the March symposium on acid maltase deficiency being held under the aegis of the **Acid Maltase Deficiency Association**. Through its Special Grants Program,

MDA does consider requests for supplemental support of meetings. However, as a result of current fiscal imperatives, our budget for support of such meetings is severely limited and all requests for supplemental meeting support must necessarily be closely evaluated. For this reason we regret that we are not able to respond positively to the request for supplemental support the March Acid Maltase Deficiency Meeting.....

Ronald J. Schenkenberger  
Director of Research & Patient Services Administration  
cc: Karen Mashburn-Grants Coordinator

## **To the MDA from the AMDA**

*February 13, 1996*

**To:** Karen Mashburn  
Grants Coordinator  
Muscular Dystrophy Association  
National Headquarters  
Tucson, Arizona

Dear Ms. Mashburn,

I received your response of February 9, 1996, responding to the request for funding for the conference of March 21-22, 1996, in San Antonio, Texas, sponsored by the Acid Maltase Deficiency Association, a non-profit organization. **This request was made on behalf of the Association by Dr. Y. T. Chen at Duke University.** I am disappointed that the MDA will not be able to co-sponsor the meeting with the Association, but I would like to request that the MDA have a representative present at the meeting.

This is the first time that the key investigators, worldwide, will be gathered together to focus on this devastating disease. We have received enthusiastic response from the investigators in this field and representation by the MDA would certainly be in order since this falls under your genetic disease program.

Following is a list of the investigators that will be attending and making presentations:

Andrew Balbar, Ph. D.	Duke University
Arthur Beaudet, M. D.	Baylor College of Medicine, Houston
Richard Bertin, Ph.D.	FDA, Orphan Products Development
Ned Bodamer, M.D.	Institute of Child Health, England
Y. T. Chen, M.D., Ph.D.	Duke University
Janice Chow, M.D.	National Institutes of Health
Blythe Devlin, Ph.D.	Duke University
Robert Eanes, M.D., Ph.D.	Stephen F. Austin University
Peter Healy, Ph.D.	Mac Arthur Agricultural Institute, Australia
Rochelle Hirschhorn, M.D.	New York University
Maryann Hui, M.D., Ph. D.	New York University

Tateki Kikuchi, Ph. D.	National Institute of Neuroscience, Japan
Frank Martiniuk, Ph.D.	New York University
Ralph Nichols, Ph.D.	National Institutes of Health
Paul Plotz, M.D.	National Institutes of Health
Nina Raben, M.D., Ph.D.	National Institutes of Health
Arnold J.J. Reuser, Ph.D.	Erasmus University, The Netherlands
James Sidbury, M.D.	National Institutes of Health
Alfred E. Slonim, M.D.	North Shore University Hospital, New York
Seiichi Tsujino, Ph.D.	National Institute of Neuroscience, Japan
Ans van der Ploeg, M.D., Ph.D.	Erasmus University, The Netherlands
Johan Van Hove, M.D., Ph.D.	Duke University
Joseph Zaretsky, M.D., Ph.D.	National Institutes of Health

This will be a very informative gathering dealing with developments in enzyme and gene replacement therapy in Pompe Disease. **The MDA should be present for this meeting .....**

Sincerely,  
 Randall H. House  
 President  
 AMDA

### Reply from MDA National Headquarters

*February 14, 1996*

**To:** Y. T. Chen, M.D., Ph. D.  
 Duke University Medical Center

Dear Dr. Chen:

Thank you for your February 13 fax transmission to MDA Grants Coordinator Karen Mashburn acknowledging receipt of our February 9 response to your request for MDA support of your (AMDA's) March 21-22 (1996) symposium. Again, we regret that MDA is not able to respond positively to your request for financial support (**\$10,000!**).

Also, an Association Board meeting scheduled for the same period as your meeting in March in which key members of MDA will participate precluded their attendance at your meeting (**as per AMDA's and Dr. Chen's requests**). We do extend best wishes for a successful conference and would appreciate receiving any summary of the event that may be made available.

Very truly yours,  
 Ronald J. Schenkenberger  
 Director of Research & Patient Services Administration

cc: Karen Mashburn-Grants Coordinator



**Letter from Bill Moore**  
**MDA--Research Program Coordinator**

*Dec. 23, 1998*

Dear Randall House,

I greatly appreciate your response to our inquiry forwarded to you from Dr. Reuser. We are certainly very interested in the information about the clinical trial. As Dr. Reuser suggested, I visited your web site and was very pleased with what you have done with your web site and the important information about your organization. I apologize for not knowing more about your effort before this time.

I wish I could do something in relation to your past experiences with MDA to assist your efforts but I am afraid that policy has not changed.

What I do wish to do is at least increase a communication line between ourselves. We both have an interest in AMD patients **and I totally agree with you that AMDA, and other such organizations..... can and does fill a gap that MDA may not be best at.** MDA covers a considerable range of research in different disorders which has allowed the utilization of discoveries from one area being applied to another.....We believe that what we learn from these efforts will have application not only to the other diseases covered by MDA ....but to those diseases.....as well. **Your efforts to target AMDA patients and families with information to assist them is of great value and I am sure that your information is more focused for them.**

I hope that we can assist each other in information to our AMDA people. We would like to work with you in getting the information about the clinical trial on our website and in "Quest" when the information is available.....

I guess I was expecting, Dr. Martiniuk or Dr Chen's group to be ready for a clinical trial soon. **I was not expecting the Netherlands work and was surprised by it.... (BUT at this point they were aware of it!)**

Sincerely,  
Bill Moore