

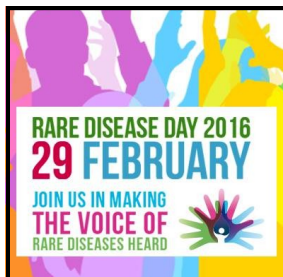


News and Stories - Spring 2016

Indiana Celebrates Rare Disease Day

On Monday, February 29, 2016, citizens living in Indiana gathered at the Parkview Mirro Center for Research and Innovation to celebrate Rare Disease Day in Ft. Wayne. They had over 100 people in attendance, representing various rare diseases, including Amyloidosis.

Rare Disease Day occurs each year on the last day of February, when millions of patients and their families share their stories to focus a spotlight on rare diseases as a global public health concern.

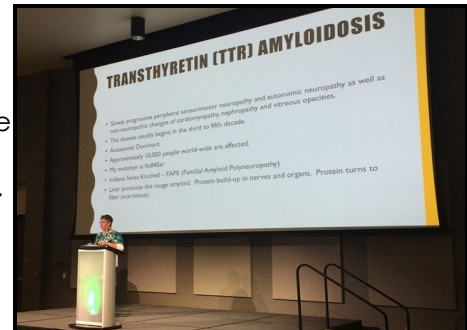


The day was observed in more than 70 nations.

Jennifer Brink, a TTR Amyloidosis patient, gave the patient perspective of living with this rare disease and the effect this hereditary type has had on her entire family.

Patient advocates joined with the National Organization for Rare Disorders (NORD), the national sponsor of the day in the US, to organize these special events in each state. During this event attendees had the opportunity to meet and hear from legislators, patients, caregivers, physicians and members of the media.

Jennifer is currently the Program Director for the Respiratory Care Program at Ivy Tech Community College.



She was tested in 1983 and had an official diagnosis in 1984 when she was 20 years old. Jennifer is now 52, many of her family members have passed from TTR, including her Father at age 61; Brother, 53; Brother, 57; Cousins 57, 55, 62, 61 plus Uncles ages 54 and 61.

Jennifer has provided her DNA in order to 'grow' mice with her amyloid mutation for research studies.

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A Triplet of Monoclonals at Bat Against Amyloid - But Will Any of Them Hit a Home Run?

by Raymond Comenzo, MD

Monoclonal antibodies are proteins that act like "magic bullets" and attack specific targets that are usually molecules on the outside membranes of cells or molecules circulating in the blood. Monoclonal antibodies are made commercially in large vats and the laboratories in which

they are made look for all the world like breweries. The vats contain genetically modified cells that produce the monoclonals. The liquid is drained off and the monoclonals purified and evaluated carefully for use. The whole process is under strict controls.

There are well over 100 mono-

clonal antibodies in current clinical use, many as cancer therapies aimed at molecules that stimulate cancer cells to grow as well as at molecules that are specific for certain types of cancer cells. Monoclonal antibodies can cause cell death in several ways.

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AF Welcomes Two New Members to the Board of Directors

Silva Pregja, Director

Silva graduated from the University of Tirana, Albania and obtained her MBA at the International Business School in Slovenia. She started her career with United Nations Development Program in Albania and eventually joined the Soros Foundation as the General Manager of the Albanian Branch before leaving the country in 1997.

Silva joined the Karmanos Cancer Institute (KCI) as a Project Manager and worked on several research projects. In 2006,



she started working as the Program Coordinator for the myeloma and amyloid program. During her time as Program Coordinator, the Karmanos program has secured membership in the Multiple

Myeloma Research Consortium (MMRC).

Silva helped develop a research infrastructure capable of executing nationwide investigator-initiated clinical trials. The Karmanos program is one of the largest in the state of Michigan, and was recently awarded the MMRC Accelerator Award for contributions to MMRC research in 2015.

Additionally, KCI has an active amyloidosis research program, with six clinical trials currently encompassing both AL and ATTR amyloidosis therapies.

Silva has organized several educational programs for health care professionals, patients, and caregivers. This includes a well-received CME Satellite Symposium titled *Untangling Amyloidosis* prior to the 2015 American Society of Hematology (ASH) meeting.

Dante Burchi, Treasurer

Dante is retired from the financial services industry. He now represents the Detroit Pencil Company for office supplies and furniture, as well as the Absopure company for water, coffee and vending.



Golf is a passion for Dante and he lives with his wife in the Metropolitan Detroit area.

He is currently the Treasurer for the 21st Century Club, a non-partisan PAC.

Dante is also a board member of the Detroit Regional Dollars for Scholars, a 501c3 organization that helps local students prepare for life after high school, through scholarships and academic support, to enable post-secondary success. **AF**

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Patient Resources

The foundation has several programs that benefit patients and their families. All of these are provided free of charge.

- Webinar recordings posted on our website
- Accurate informational pamphlets
- New & comprehensive website with information for patients, caregivers and physicians
- Toll Free Number **1-877-AMYLOID**
- Listing of experienced physicians that specialize in amyloidosis, it's diagnosis and treatment. Email us anytime with questions: info@amyloidosis.org



President's Corner

Spring is in the air!

This special time of year brings exciting news from the foundation. We are honored to introduce our two new board members, Silva Pregja and Dante Burchi. Both share a commitment and passion for the mission of the Amyloidosis Foundation. *Welcome aboard!*

We are proud to announce the 2015 Research Grant recipients in this newsletter. We have two new memorial research grants to honor Donald Brockman, founder of the AF and David Seldin, MD, PhD, valued friend and physician from Boston University Medical Center.

We thank the many of you who participated in 2016 Rare Disease Day events, telling your story and spreading amyloidosis awareness. If you didn't get a chance this year, think about it for 2017—it's very empowering to see the rare disease community come together on a global scale.

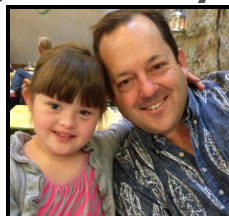
As always, thank you for your support. Your donations are used to continue our initiatives for education, awareness, support and research for amyloidosis patients and families.

Enjoy the warmer days and nights of this season in your community, take care.

- Mary O'Donnell

4Tres - Amyloidosis Orange County Marathon Team

Terry Loughran and Kevin Hauri lost their good friend, Tres Heald, in 2015 after his battle with Amyloidosis. They are running in the Orange County, CA Half Marathon on May 1st to honor Tres and to raise money to support those still fighting the disease. All proceeds will be donated to the Amyloidosis Foundation.



Please consider a donation in honor of Tres and those that passed away last year, we sincerely thank you.

<https://www.crowdrise.com/amyloidosis/fundraiser/terryandkevin>



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Our newsletter is published quarterly (Spring, Summer, Fall and Winter) by the **Amyloidosis Foundation**. We welcome letters, articles and suggestions.

Please contact us anytime at: **info@amyloidosis.org**, **1-877-AMYLOID** (877-269-5643) or **7151 North Main Street, Ste. 2, Clarkston, MI 48346**

If you no longer wish to receive this newsletter OR if you wish to receive a printed version, please send us an email:

info@amyloidosis.org

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Amyloidosis Foundation Awards 2015 Research Grants

The Amyloidosis Foundation awarded four research grants in December 2015. Since 2005, the AF has funded over \$1 million to promising clinical amyloidosis investigators from around the world. We applaud their efforts and look forward to the success this work will bring to patients.

Heather Landau, MD



Gene Expression Changes in AL amyloidosis

Amyloidosis Foundation
Donald C. Brockman
Memorial Research Grant,
2015

Memorial Sloan Kettering
Cancer Center, Medicine
Division: Hematology

Amyloidosis is caused by the expansion of abnormal plasma cells that produce abnormal proteins that accumulate in tissues to cause end-organ damage. To date, mutations in amyloid-forming plasma cells and their resulting consequences on the genes expressed have been poorly characterized.

perform the first large-scale characterization of the mutations and gene expression changes in AL amyloidosis by evaluating patient's plasma cells at diagnosis and following treatment. We expect such studies to allow us to identify genes that contribute to the development of disease, predict treatment responses, and identify new therapeutic targets. This study will play an important role in future development of a cure for amyloidosis.

Michael Rosenzweig, MD



Cell Therapy for AL amyloidosis

Amyloidosis Foundation
David Seldin, MD, PhD Memorial
Research Grant, 2015

City of Hope, Medicine Division:
Hematology & Hematopoietic
Cell Transplantation

Amyloid light-chain (AL) amyloidosis is a rare blood disease that is treatable but often fatal. With the help of the Amyloidosis Foundation, we plan to develop a new treatment for AL amyloidosis by genetically engineering a patient's own immune system to recognize and kill the abnormal blood cells when rein-

roduced into the body. We will evaluate blood cells in patients with AL for expression of a specific protein that could be targeted by this approach. Once the target is identified, genetically engineered cells will be generated and tested in the laboratory. The ultimate goal is developing this therapy for clinical trials in patients with AL amyloidosis.

Lorena Saelices, PhD



New Strategy for TTR amyloidosis

Amyloidosis Foundation
Research Grant, 2015

Regents of the University of
California

Treatments for systemic transthyretin amyloidosis have been held back by lack of information on the structures and causes of aggregation of the amyloid fibers formed by transthyretin (TTR). In previous work, we identified two protein segments involved in TTR aggregation, and developed a novel strategy to inhibit the process by small non-natural peptides. Based on the amyloid structure of the aggregation-

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Research Grants

driving segments, we designed two peptide inhibitors that hindered TTR aggregation. With the support of the Amyloidosis Foundation in our research, these peptide inhibitors will be tested for their ability to halt fibril formation in the disease model of fruit flies. This new strategy will assist in providing successful therapies for TTR patients.

**Clare-Louise Towse,
MChem, MPhil, PhD**



Trying to Inhibit Amyloid Formation

Amyloidosis Foundation
Research Grant, 2015

University of Washington,
Medicine Division: Office of
Research

The proteins involved in amyloid diseases share an intermediate state that forms before the insoluble fibril form found in diseased tissue. This intermediate can be prevented from forming the fibrils by adding peptides, designed by the Daggett lab, in vitro.

Rare Disease Day-Indiana

Continued from page 1

There are two ongoing TTR clinical trials but she does not meet the criteria. Her lower extremity polyneuropathy is not severe enough to grant her admission.

Jennifer is a passionate and outspoken advocate for Amyloidosis. She spoke at the Patient Meeting with the FDA in Silver Spring, MD in November 2015 coordinated by the Amyloid Research Consortium (ARC). Indiana has a "Right to Try" law, which she gave a presentation to her Legislators in favor of this Law. Marlin Stutzman is planning to move forward with a Federal "Right to Try" law. She is working with his office to promote the passing of this law.

In her immediate family, there is a potential for 33 members to have Amyloidosis. This does not include her "shirt-tail" relations. Her Grandma, Elma Dubach Kaehr, had seven children, four

Our grant from the Amyloidosis Foundation will help us build on these designs by placing them inside a larger protein to increase their structural stability, which in turn is linked to their ability to prevent fibril formation.

We will be optimizing the designed peptides within the protein using computational methods and, once optimized, these molecules will be chemically synthesized and tested for the potential to inhibit amyloid formation. Results from this study will hopefully prevent amyloid formation in the future and give hope to amyloidosis patients. **AF**



Jennifer Brink, 2016 Rare Disease Day speaker and TTR Amyloidosis patient.

were affected (all are deceased). There were 24 grandchildren, nine are or were affected (three deceased, six living with disease). Total of 71 great-grandchildren, two confirmed positive, one confirmed negative. Plus there are 65 great-great-grandchildren – none tested.

Current trials will not be complete for at least three years. Realistically, it will take five to seven years for the drugs that are currently in trial to actually get to market.

Jennifer continues to work with Legislators, the Amyloidosis Research Consortium and the Amyloidosis Foundation to support laws for drug research and availability. **AF**



A Triplet of Monoclonals at Bat Against Amyloid

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Cells that are covered by monoclonal antibodies can become prime targets for certain immune cells such as 'natural killer' cells, for example. When monoclonal antibodies attach to a cell, they can also disrupt a growth circuit and when they attach to a molecule in circulation they can clear that molecule, diverting it from its intended function.

There are currently three monoclonal antibody-based approaches to amyloidosis in clinical trials. The targets for 2 of the monoclonals (11-1F4 and NEOD001) are AL amyloid fibrils while the target for the remaining 1 is serum amyloid P protein (SAP), a molecule found in all amyloid deposits that protects the fibrils from being degraded. All three of these monoclonals have been produced for clinical testing in patients. We do not know if any of them will provide a benefit to patients by reversing or preventing organ amyloid damage or extending patient survival.

The anti-amyloid 11-1F4 monoclonal binds to AL fibrils and causes amyloid fibrils to be labelled for degradation by 'pacman' like cells called phagocytes or macrophages. In an early phase trial, a radioactive molecule was linked to 11-1F4 that allowed visualization of amyloid deposits in certain organs such as the liver and spleen but not in the kidneys and heart. In a subsequent and on-going early phase trial in AL patients with relapsed refractory disease (NCT02245867), 11-1F4 has been safely given as therapy to a small number of patients, and cardiac and GI

organ responses were reported in 3 of the first 6 patients.

NEOD001 also attaches to AL amyloid fibrils and amyloid aggregates and elicits the 'pacman' response by macrophages. In an early phase clinical trial (NCT01707264), 27 patients with AL amyloidosis in hematologic remission but with persistent organ dysfunction received NEOD001 once a month with no treatment-related toxicities. Sixty percent of patients with heart or kidney involvement achieved organ responses by standard biomarker criteria such as NT-proBNP and urine protein levels. Several patients who were years out from any chemotherapy had organ responses. A phase 3 registration trial, seeking approval of NEOD001, is in progress for newly diagnosed AL patients with heart involvement. Patients are randomized, like the flip of a coin, to receive NEOD001 or a placebo at the same time they receive bortezomib (Velcade) based chemotherapy (NCT02312206). Other trials are in the process of being opened across the country for NEOD001.

The anti-SAP monoclonal attacks serum amyloid P component (SAP) in amyloid deposits and in the blood. In the Amyloid Centre in London, full-body scans for amyloid using the SAP protein linked to a radioactive tracer have been used for many years. In the early phase clinical trial (NCT01777243), patients received one treatment with anti-SAP after a drug was used to clear SAP from their blood. They also had SAP scans performed before and 6 weeks after receiving anti-SAP. There were no serious adverse events in the 16 patients who were treated.

Four patients had a significant decrease in amyloid in their livers. Patients with heart involvement were not allowed to participate in this early phase trial.

These monoclonal antibodies may be an important part of the future for amyloid patients. It will take many years, though, to learn if they work by helping patients to achieve improved organ function or to live longer. We hope that the use of biomarkers, such as the cardiac biomarker NT-proBNP, will help to shorten the clinical trial timelines and get answers faster. Both the Amyloidosis Foundation and the Amyloidosis Research Consortium continue to work with the biotech industry and with regulatory authorities in the USA and in the EU to get well designed monoclonal antibody studies underway. We really need to learn if anyone or if the triplet of monoclonal antibodies is a home run for patients.

For more information on the clinical trials, go to clinicaltrials.gov. Use the names of the monoclonals or the NCT numbers to find out about the current active trials and how to contact the centers in which the trials are being conducted. **AF**



Raymond L. Comenzo, MD
Director
The John C Davis Myeloma and Amyloid Program
Tufts Medical Center
Professor of Pathology & Medicine
Tufts University School of Medicine
Boston, MA



A Conversation with Amyloidosis Patient, Cyclist and Heart Transplant Recipient, Paul Langlois *by Lawrence Creswell, MD. Reprinted with permission.*

Thinking back to before your heart transplant, can you tell us a little about your interest in cycling? When did you get started? Were you involved in team cycling? Or competitions, of various sorts?

Yes, I had been actively involved in competitive Masters cycling since the age of 30, attaining Category 2 status on the Road, Track, and Cyclocross. Before I became a cyclist, I competed in collegiate rowing at the Coast Guard Academy, winning three national titles. After college, I got hooked on the running boom and completed four marathons (qualified for Boston), ran many shorter events, and did some medium distance triathlons. Problems with my right knee resulted in two surgeries when I was 30, when I switched my competitive focus entirely to cycling, which became part of a long rehab process for the knee. Only a few years later at age 34, I won the All-Military National Cycling Championships stage race in Colorado Springs. Over the years, I had competed at over 20 various Masters National Championship events for road, track, and cyclocross. Somewhat surprisingly, some of my best performances on the bike were attained in my early 50s, when I won two consecutive years as Best All Around Rider 50+ in the Mid-Atlantic District, and

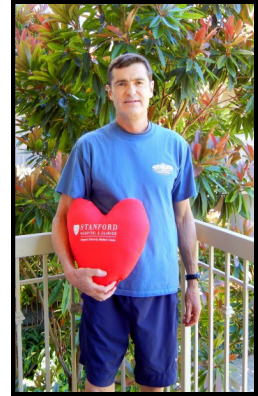
rode a Personal Best 40K Time Trial in 54 minutes.

I raced with numerous amateur teams in different parts of the country, as the Coast Guard typically relocated me to a new duty station every three years. I served for 30 years in the Coast Guard, primarily as a helicopter rescue pilot, and retired as a Captain in 2006. After retirement, and settling in Santa Rosa, California, I continued non-stop racing, until a year before my diagnosis at age 56, mentioned below.

I understand that you were diagnosed with Cardiac Amyloidosis, a rare cause of heart failure. How did you and your doctors discover this problem?

It took me a bit more than one year of frustration before I was properly diagnosed. I attribute my eventual diagnosis in large part through my own keen awareness of my slow, but steady deterioration in fitness level. Initially, I noticed that I was having trouble keeping up with my teammates on training rides, especially when climbing. And then, soon thereafter, I had to pull out of a criterium race after two laps, experiencing almost no aerobic capacity, in the same race I had nearly won the year prior. I first checked with my primary care physician, who commented "I was simply getting older", which I refused to believe was the problem.

I was later referred to a cardiologist and a pulmonologist for stress tests and neither test came back with any abnormality.



Over the next six months, I progressed into becoming short of breath when climbing one flight of stairs, and nearly fainting when I quickly rose out of a chair. I noticed my legs and ankles were swelling in a way which I had never seen. Finally, I checked myself into my local ER, and by a stroke of luck, a talented cardiologist was on duty who performed an Echocardiogram, an EKG, a chest x-ray, and did some lab work. He noticed I had very high protein in my urine, and suspected I might have Amyloidosis.

The following week, I had a heart biopsy, and a special test revealed I was positive for Amyloidosis. This was the cause of my heart failing, and it readily became apparent to me that it was a life and death situation. I was referred to Stanford Hospital for further evaluation, as they have one of the few clinics in the USA with significant experience treating this rare blood disease.

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A Conversation with Amyloidosis Patient Paul Langlois

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Once heart transplantation was recommended, how long did you spend on the waiting list? And during the waiting period, were you able to exercise? What was your fitness level right before the transplant operation?

My first consultation at Stanford was with their Cardiology Dept, which recommended heart transplant, as no other option was available to keep me alive. I went through the pre-qualifying tests successfully over a period of six weeks, until I was allowed to be listed for transplant. I have Blood Type AB, and was listed as Priority 1B, and I was extremely fortunate to only have to wait for eight days until a good match was found for me. Leading up to the transplant, my fitness level had diminished considerably over the past year due to the onset of heart failure, although I still attempted to get exercise, primarily through cycling.

As an example, in the months just before transplant, I was not able to get my heart rate

over 130, when giving it my hardest effort, whereas the previous year before I became ill, I could easily exceed 165 during a hard effort.

Tell us a little bit about your early recovery after the transplant operation. How long were you in the hospital? When did you begin walking, afterwards? How long did it take to get healed up?

Heart Transplant is obviously a very traumatic surgery, including the need to separate the center of the rib cage to perform the transplant. And so the body needs many weeks to heal and rest afterward. I spent only one week in the hospital. I was up and walking slowly around the ward within three days. After discharge, I was required to live nearby Stanford for many weeks with a Caregiver (my wife Linda), to allow for frequent clinical check-ups at Stanford, including many heart biopsies, Echos, and lab work, with a focus on ensuring no organ rejection might be taking place. I began exercising very gently at first, and then with steadily increasing intensity and distance as the weeks

went by. Within one month and much to my surprise, I completed a six mile hilly walk around the Stanford Campus. I had to wear a protective mask whenever I was outside or around people to minimize any chance of catching an infection or virus. I finally got to go home at almost two months after the transplant which was a wonderful day.

I understand that you're back to cycling now. What's your routine? Are you still competing?

Yes, I have been able to get back into cycling, but have not been able to develop the required fitness to race competitively. As I approach the five year mark, I have endured almost nonstop chemotherapy treatments, and clinical trial drugs. Amyloidosis has no known cause, and still has no proven cure. Having said that, I still have the mental mindset to someday be competitive, and so I keep training with the belief that I may attain that level again. **AF**

The Amyloidosis Foundation appreciates your continued support.

If you would like to become more involved in the foundation, interested in starting a fundraiser or becoming an amyloidosis ambassador—we would enjoy speaking with you and helping in anyway we can.

Please call our office today **1-877-AMYLOID** (877-269-5643) or send us an email at **info@amyloidosis.org**.

Thank you!

