What are we up to?

Dr. Andrea Havasi -
“By understanding the mechanism causing kidney cell toxicity we will get closer to finding a therapy which can potentially prevent or cure kidney damage in patients with plasma cell dyscrasia.”
Letter from the Director

Vaishali Sanchorawala, MD

Dear Friends,

Best wishes from the Amyloidosis Center at Boston University School of Medicine and Boston Medical Center for 2018. I hope you will join us in celebrating the many accomplishments of our faculty, trainees and staff described in this edition of our newsletter.

Our Amyloid Clinical Program continues to grow. Each week, 25 or more patients are evaluated by a multidisciplinary team of clinical experts and given opportunities to participate in standard and novel therapies for AL, AA, and ATTR amyloidosis. We are able to offer innovative treatments tailored to each patient’s need and disease type. This is truly a new era of expanding our therapeutic landscape for systemic amyloidosis. We welcome several new physicians who have joined our dedicated clinical team this year: Dr. Vina Nguyen and Dr. Pooja Phull (internists), Dr. Deepa Gopal (cardiologist), Dr. Hanni Menn-Josephy (nephrologist) and Lisa Mendelson (nurse practitioner).

We continue to build our basic laboratory research programs in the Alan and Sandra Gerry Amyloid Research Laboratory and to collaborate with investigators across our university and at other medical centers. We are confident that the treatments of the future will be guided by basic research studies. We are pleased to announce several new research awards. Dr. Celia Torres-Arancivia, a post-doctoral fellow with Dr. Connors, has been awarded an Amyloidosis Foundation Research Grant for studies of Clusterin in ATTRwt amyloidosis. Dr. Lawreen H. Connors is the recipient of an NIH High Priority, Short-term Project Award (R56) from the National Institute on Aging which will help fund the continuation of her research project, “Molecular mechanism of ATTRwt cardiac amyloidosis.” Dr. Connors has also been awarded grants from the Wildflower and Carpenter Foundations for studies on AL and ATTR amyloidosis. Congratulations to Dr. Connors and her team extraordinaire! We are so proud of them. Our laboratory research has expanded with two clinician scientists, Drs. Andrea Havasi and Shayna Sarosiek. They are featured in this edition (page 4).

The XVIth International Symposium on Amyloidosis will be held in Kumamoto, Japan this coming March 2018. Many members of our research and clinical teams will attend and present research at this meeting. It will be a wonderful opportunity to meet with investigators from around the world. We firmly believe that collaboration with other amyloid teams will enhance discovery and lead to a cure for amyloid diseases.

I hope you enjoy reading this report and learning more about our past year. During 2018, we will continue to focus on the three pillars of our vision: excellence, innovation and collaboration.

Our hopes for this year are high; progress is only possible with your generous and steadfast support. I take this opportunity to thank you for your support and friendship. We send our best wishes for a happy, healthy and prosperous 2018 to you and yours.

Sincerely yours,

Vaishali Sanchorawala, MD

Vina Nguyen and Dr. Pooja Phull (internists), Dr. Deepa Gopal (cardiologist), Dr. Hanni Menn-Josephy (nephrologist) and Lisa Mendelson (nurse practitioner).

Center Visitors

The David C. Seldin, MD, PhD Amyloidosis Research Training Fund

The purpose of this training fund, established in 2016, is to provide support to investigators in the early stages of their careers who are conducting amyloidosis research.

Roberta Mussinelli, MD

As previously reported, Roberta Mussinelli, MD was the first recipient of this prestigious award. Dr. Mussinelli is a researcher and an Internal Medicine Fellow at the University of Pavia, in Pavia, Italy. She arrived in Boston in January 2017 and returned to the University of Pavia in July. While here at the Amyloidosis Center, her work focused on analyses of serial echocardiograms, to detect the characteristics of abnormalities in wild type amyloidosis. She also studied the effect of treatments on the progression of other amyloid heart disease. Dr. Mussinelli worked very closely with Dr. Frederick Ruberg, who served as her mentor during her time here.

Stefano Perlini, MD

During Dr. Mussinelli’s stay, we were visited by her mentor and our friend, Dr. Stefano Perlini. Dr. Perlini is a highly respected amyloidologist from Italy. He is a Consultant Cardiologist of the Center for Research and Treatment of Systemic Amyloidosis at the University of Pavia, Italy. He is the Head of the Metabolism and Cellular Pathology Laboratory of the Internal Medicine Department at the university. Dr. Perlini’s main research areas are studies of the mechanisms underlying systolic and diastolic dysfunction evident in myocardial hypertrophy and in different cardiomyopathies, in both clinical and experimental setting. While here he also presented to the Amyloidosis Center Research Group. His talk was entitled “Cardiac TTR-Amyloidosis: new insights on genotype/phenotype correlations”.

Christopher Mueller, MD

Dr. Mueller visited the Amyloidosis Center in early May of this year. Dr. Mueller is an Assistant Professor within the Department of Cardiology, Medical College of Wisconsin, in Milwaukee, WI. Dr. Mueller is a board certified cardiologist interested in amyloid diseases that affect the heart. He plans to start an amyloid clinic in Milwaukee and visited to learn more about how we function here at the Amyloidosis Center. He worked closely with our cardiologists, Drs. Frederick Ruberg and Omar Siddiqi, during his visit.

Analiese Fernandes

This summer Dr. Lawreen Connors and the Gerry Amyloid Research Laboratory hosted Analiese Fernandes, a sophomore from the University of Pennsylvania. Analiese is double majoring in Biology, with a concentration in Neurobiology and Economics from the Wharton School. She is very interested in learning more about research while developing new skills and more details about how drug therapy is discovered for specific diseases.

On her final day she presented to our amyloidosis research group. Her presentation was entitled “Studying AL Amyloidosis” in which she highlighted her achievements during this internship. She learned the disease process of AL (Light Chain) Amyloidosis, how the diagnosis is made and the possible treatments. She was fascinated by the various processes used to identify amyloid deposits.
New Research Initiatives

Andrea Havasi, MD

I am a nephrologist and have worked in the Center since 2010. My research in the Gerry Amyloid Research Laboratory focuses on the toxic effects of light chains in the kidney. Light chains are components of antibodies and are secreted in excess from plasma cells (antibody-producing cells) in a group of malignant diseases called plasma cell dyscrasia. These circulating light chains are deposited in different organs in the body, including the kidneys, causing organ damage by both architectural destruction and direct cell toxicity. We aim to determine the mechanisms involved in direct kidney cell toxicity focusing on autophagy, the main recycling process in the cells. We hypothesize that autophagy is impaired in renal cells exposed to excess light chains.

We will expose primary mouse and human kidney cells in culture to light chains obtained from urine of patients with renal involvement, and test which steps in the autophagic process are affected. We will use pharmacologic and molecular biological techniques, including an innovative method based on nanoparticles to increase autophagy, and examine if this ameliorates cell toxicity.

By understanding the mechanism causing kidney cell toxicity we will get closer to finding a therapy which can potentially prevent or cure kidney damage in patients with plasma cell dyscrasia.

Shayna Sarosiek, MD

As a hematologist at our Center, I enjoy being involved in the clinical care of our patients. I also take great pride in conducting research that will improve the care of AL amyloidosis patients.

Most recently, I have had the opportunity to lead three research projects that are studying different aspects of AL amyloidosis. The first project uses a sample of bone marrow to perform a detailed genetic test to detect very small amounts of disease which might persist after treatment and would not be detected on a standard bone marrow test. I am hopeful that this type of testing will be a better way to assess if a patient’s disease is in remission and allow us to make more informed decisions about treatment.

The second research study uses the clonal plasma cells in the bone marrow (the cells that produce the abnormal protein which leads to organ damage) to study the specific mechanisms that cause death in those cells when they are exposed to traditional or new innovative therapies.

The third research project is a clinical trial studying propylene glycol-free melphalan, a newer and potentially less toxic formulation of the high-dose chemotherapy that is typically given prior to a stem cell transplant. This trial will determine if patients have fewer side effects to already damaged organs (such as the kidneys) when this new drug is used prior to stem cell transplantation. These results could potentially lead to the development of new treatment strategies.

I look forward to completing enrollment in these trials and I am very hopeful that the results from these studies with improve care for patients with AL amyloidosis.

Celia Torres Arancivia, PhD, Post-Doctoral Fellow

CLUs to a possible role for clusterin in ATTRwt amyloidosis

Acquired wild-type transthyretin (ATTRwt) amyloidosis is an underappreciated cause of heart failure in older adults. With symptoms that can manifest as early as 60 years of age, this fatal disease features infiltration of the heart by amyloid fibrils composed of the plasma protein, transthyretin (TTR).

In familial TTR amyloidosis, mutations in TTR are responsible for destabilization of the protein’s native state. However, in acquired ATTRwt amyloidosis, TTR lacks destabilizing alterations and it is plausible that other factors may be responsible for the onset and progression of the disease. Thus, I believe that clusterin (CLU), a plasma circulating glycoprotein known to exhibit chaperone-like activity, may play a role in wild-type TTR amyloid fibrilization.

I plan to define such a role with the generous support of the 2018 Amyloidosis Foundation David Seldin, MD, PhD Memorial Research Grant that I was awarded in November of this year. I will compare the structure of CLU derived from patient and healthy control sera, and characterize disease-specific structural elements that may be responsible for limited chaperone capacity towards non-native forms of TTR. In addition, will evaluate whether serum levels of CLU have utility in monitoring disease progression and their response to treatment.

These studies are novel and could potentially advance a previously unexplored therapeutic approach that considers CLU as a key component in this pathologic process.

Information Corner

Genetic Counseling

Familial amyloidosis patients might notice some new faces at our Center. We are joined this year by genetic counseling students, who are learning more about how best to help patients navigate their genetic health. The students are in their first year of a two-year program at Boston University School of Medicine. In cooperation with Boston Medical Center, they rotate through different clinics such as the Amyloidosis Center, prenatal clinic, pediatric clinic, Down syndrome clinic, and Cancer Center, so they can gain exposure to different areas of clinical medicine and learn the full scope of what hereditary disease means for patients and their families.

Genetic counselors are healthcare professionals, trained in both medical genetics and counseling. They interpret the complicated system of genetic testing for patients by helping determine which genetic tests they should take, and make informed decisions about their healthcare, and they explain the implications of genetic testing. They provide emotional support, while educating patients and their families on inherited diseases and the genetic risks. Genetic counselors can be found at work in hospitals and clinics, government agencies, public health organizations, biotechnology companies, and in research. Through their observations with the Amyloidosis Center, the students prepare for their future careers by learning the clinical application of genetic counseling, to best be able to support the affected patient population.

If you and your family would like to speak with a genetic counselor as part of your amyloid evaluation, please let us know!
Family Fundraisers

“Bill’s Race to Beat Amyloid”

Bill Cunningham loved to ski. “Any day skiing is a great day,” he was often known to say. He was a certified ski instructor and spent more than 30 years at Cannon Mountain in New Hampshire, as instructor, director, technical director, and of course skier. After being ill for some time, Bill was diagnosed with AL amyloidosis and succumbed in 2007 at age 58. He is survived by his wife Carol, and their children, Will and Cait.

Bill’s loss was devastating to his family. Bill and Carol were best friends, soul mates, and partners in everything they did. They were active in their life together, and spent their free time fishing, skiing (on snow and on water), playing tennis and golf, or just cruising out on the boat together. Bill’s presence loomed large in the community. Carol knew that she could do something extraordinary to honor his memory.

In March 2008, Carol organized the first, of what would become the annual, “Bill’s Race to Beat Amyloid.” It is a ski race, along with an entire day of celebration, complete with raffles, silent auction, and prizes for winners. Carol wanted to honor Bill, and also to raise money for research while drawing attention and awareness to a rare disease. She continues working to spread the word, so that people who are affected can be diagnosed sooner and get earlier treatment.

In the years since his passing, Will and Cait have grown up. Now they help their mom organize the race. Many of the items in the silent auction are ski related. This year featured lift tickets to Bretton Woods, a “gold tune” ski tune-up from The Race Room, and a season pass to Cannon Mountain, where the race takes place. There are also items donated from area businesses, such as a cut and split cord of firewood, an Adirondack chair, a membership to the local Colonial Theatre, and stays at area hotels and resorts.

“Bill’s Race” has grown over the past ten years. People attend from far and wide: many participants remember Bill, and there are many newcomers who come for the festivities. We are astonished at what the Cunningham family have accomplished for the Amyloid Research Fund! To support the effort and join the fun, participate in the 11th annual “Bill’s Race” on Saturday, March 3, 2018.

Bob and Floris Palmer were married for 43 years. They were friends and constant companions. Floris knew there would have to be a very special event to honor his memory. After all, while a devoted husband, father to Megan and Kevin and grandfather to Reed and Willa, he also had a considerable impact on the community. Bob held degrees in psychology, special education and school psychology, and was dedicated in his 30 years as a school psychologist. Inspired by this, Floris and Megan began planning “Fit to Be Tied: Race for Amyloidosis Awareness”. Participants are invited to wear their craziest ties, in honor of the crazy ties that Bob wore to make his students laugh.

Fit to Be Tied has a 5k run and a 3k walk in the Onondaga Lake Park that Bob loved so much. Awards are given to the top finishers of both races, and all participants receive a “Fit to Be Tied” t-shirt and raffle ticket for varying prizes. There is also a prize for the craziest tie! Racers are encouraged to bring their most outlandish and creative best.

In the two years since its beginning, “Fit to Be Tied” has grown. Racers attend from all across the region. The Palmer family are joined by their family, their friends, people who knew and loved Bob, and people who love running. The Palmers have organized “Fit to Be Tied” for two years running, and they are not stopping there! Join them for the 3rd Annual “Fit to Be Tied” event on Sunday, May 20, 2018.

We are so grateful that the Cunningham family and the Palmer family have chosen the Amyloidosis Center as the recipient of their fundraising efforts.

Here’s how you can help!

Are you interested in participating in these fundraisers? You can find out more here:

- [http://billsrace.com](http://billsrace.com)
- [http://www.fittobetied.org](http://www.fittobetied.org)

Are you interested in planning a fundraiser? Please contact us by phone or by email at amyloid@bu.edu or 617-638-4317 to find out how we can help!
We are pleased to announce that the Amyloidosis Center is now on social media! This past spring, we launched our official Facebook and Twitter pages. Follow us here:

Facebook ► BU Amyloidosis Center  
Twitter ► @Amyloidosis_BU

By establishing a social media presence we hope to keep patients, doctors and colleagues informed on the latest Amyloidosis Center news and updates, while continuing to spread awareness on Amyloidosis. We also hope that our social media platforms can serve as a resource for visitors who would like to know more about Amyloidosis and the Amyloidosis Center. In particular, our website has information on the following aspects:

- Amyloidosis Types: Signs and Symptoms
- Our evaluation process: How initial evaluation works and arrangement
- Research: Our Laboratory and Publications
- Diagnostics and Genetic Testing

SAVE THE DATE: Thursday, January 18, 2018 | #AskBUAmyloid

What is the difference between AL and AA Amyloidosis? What are the symptoms of ATTRwt Amyloidosis? Where in my body can Amyloidosis occur? If you have general questions about Amyloidosis and would like to hear from a doctor, this is the event for you! We are excited to announce our first-ever Live Tweet event happening on Thursday, January 18, 2018 from 9:00am–4:00pm ET.

Here’s how it works:

1. Log into your Twitter account, or start a Twitter account if you do not have one already.
2. Follow us at: @Amyloidosis_BU
3. Press the “Tweet” button on the upper right hand corner and enter your question in 280 characters or less. Be sure to include #AskBUAmyloid in your tweet, as this is how we track and reply to your tweet!
4. Press the “Tweet” button to submit your Tweet!

Dr. Vaishali Sanchorawala, our director, will be personally replying to your tweets. Dr. Sanchorawala is a hematologist, and is also the Director of the Stem Cell Transplantation Program. She has been affiliated with the Amyloidosis Center since 1994 and is one of the pioneers in the field of clinical research in AL Amyloidosis.

Please submit tweets within the allotted time period, as we will not be able to reply to tweets outside of the event period. If you have any unanswered questions, please refer to our website or our social media pages. Please do not include any personal information, as tweets are publicly posted. We look forward to tweeting with you!
We hope you will consider a charitable donation and support our research on amyloid diseases, as together we work toward a cure.

Donations can be made through our website or by mail. For more information on bequests and other planned giving options, contact us at the address listed above or by phone 617.638.4317.

bu.edu/amyloid/donate

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