



# NEWSLETTER

The official publication of the Shwachman-Diamond Syndrome Registry.



## INAUGURAL ISSUE

- Welcome from the Directors
- SDS Registry Family Day report
- Hello from the Registry staff

## WELCOME!

By Dr. Akiko Shimamura  
and Dr. Kasiani Myers  
Directors of the SDSR

This year, we celebrate the **10th anniversary of the SDS Registry!**

Centered at Boston Children's Hospital and Cincinnati Children's Hospital, the SDS Registry team works tirelessly to accelerate SDS research and treatment development. This work critically depends on clinical information and samples provided by patients and families like you. We use them to facilitate high-impact research and collaborations, and provide

education to patients, families, and healthcare providers. At the SDS Family Day in Boston this fall, we were delighted to celebrate this 10 year anniversary and to share with you the progress and current research from the SDS Registry.

We are fortunate to work with the SDS Registry family representatives, Eszter Hars and Nicole Shen. Eszter and Nicole are working with us to launch the SDS Registry Newsletter to keep you in the loop on upcoming events, breakthroughs, publications, studies, reminders, and more, throughout the year. We hope you will find it beneficial!

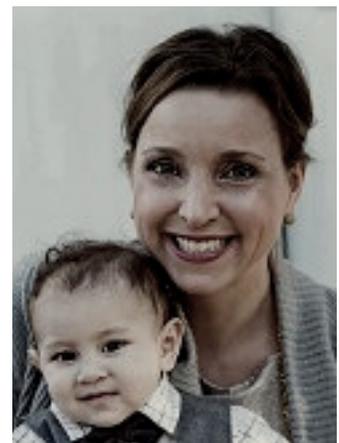


**Read the report about the SDS Family day, below!**



Dr. Akiko Shimamura and Dr. Kasiani Myers  
Directors of the SDSR

Eszter Hars (left) and Nicole Shen (right)  
Family Representatives of the SDSR





## SDS REGISTRY FAMILY DAY

### Summary

September 15th, 2019

Boston, MA

## A REPORT OF FAMILY DAY

By Eszter Hars, Ph.D.  
Family Rep, SDSR

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**We benefited so much from the cutting-edge contents and all the opportunities to network with families, doctors, and researchers.**

On September 15th 2019, a beautiful fall day, the SDS Registry celebrated its **10 Year Anniversary** by giving back to the patient community through the **SDS Registry Family Day**.

There were 33 families, 85 family members, and numerous scientist, doctors, and speakers in attendance, from 17 states across the country. While the adults received an update on the cutting edge science and progress in medicine from the top SDS experts in the field, the children got to enjoy a day full of fun, crafts, and friendship.

After a warm welcome by Dr. Shimamura and Dr. Myers and grateful acknowledgments of past and current financial supporters, the attendees were invited to introduce themselves to break the ice and facilitate networking.

The first lecture was by **Dr. Akiko Shimamura**, co-director of the SDS Registry. She provided an overview of the registry's accomplishments, and highlighted several ongoing projects and collaborations.



**As of the meeting, 254 participants were enrolled in the registry.**

Dr. Shimamura highlighted some recent results and publications and collaborations that were made possible by the registry and collaborations with researchers worldwide.

- SDS can present in various ways even in genetically confirmed patients helps. Publication of these results raises awareness in the medical community, so that doctors are willing to test more patients, and patients are more likely to get insurance coverage for testing.  
<https://www.ncbi.nlm.nih.gov/pubmed/24388329>
- Identified FAM111B mutations as a cause of an SDS-Like disorder with exocrine pancreatic insufficiency. <https://www.ncbi.nlm.nih.gov/pubmed/26495788>
- In collaboration with Dr. Seiamak Bahram identified SRP54 mutations as a cause of an SDS-Like disorder. The characterization of this gene provides diagnosis for patients who present with features of SDS and advances our understanding of these diseases. <https://www.ncbi.nlm.nih.gov/pubmed/28972538>
- In collaboration with Dr. Daniel Link, discovered that TP53 mutations frequently developed in individuals with SDS at an early age. The efforts of understanding why people with SDS are at increased risk to develop bone marrow failure and leukemia are ongoing. The goal is to find markers that will help identify patients at high risk may allow individualized surveillance and treatment.  
<https://www.ncbi.nlm.nih.gov/pubmed/29092827>
- In collaboration with Dr. Eirini Papapetrou and with Dr. Carl Novina, discovered that the TGFbeta pathway is hyperactivated in the bone marrow of individuals with SDS. Drugs to inhibit the TGFbeta pathway might improve blood counts. <https://www.ncbi.nlm.nih.gov/pubmed/31039138>

**Some of the questions the registry is focused on:**

- What are the major health complications over the life of someone with SDS? How many people stay healthy? What are the chances that someone with SDS will develop severely low blood counts, MDS or AML? Can we predict who will develop bone marrow failure, MDS or AML?
- Can we prevent medical complications of SDS? Can we develop better treatments?
- How can we educate the medical community about SDS? How can we serve as a resource of information for families?

Next, **Dr. Kas Myers**, co-director of the SDS Registry, walked us through an abundance of data from the registry highlighting the impact SDS has on various organ systems. The larger the sample size (i.e. the more patients participate), the more meaningful and significant the conclusions will be.

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**increased participation in the registry has helped to better understand the other aspects of SDS beyond the blood and bone marrow**

Some of the findings that she shared included that

- Congenital anomalies are more common in patients with SDS than previously thought and can be severe and significantly impact health and quality of life
- Many patients with SDS have changes in their bones and bone density that are significant and require ongoing medical care
- Patients with SDS are not always short or very thin as previously thought and doctors should still consider testing for SDS regardless of physical size
- Most patients with SDS do not have clinical problems with immune function that lead to significant infections beyond that expected with neutropenia.
- Some potential new clinical complications of SDS were described.
- There is a wide variation in the type and amount of neuro-cognitive involvement in patients with SDS

We also had a rare opportunity to hear directly from **Dr. Mark Fleming**, a Boston Children's Hospital hematopathologist, who is an expert in bone marrow examinations for SDS. He highlighted the importance of seeking advice from experienced SDS centers when it comes to problems with the bone marrow of SDS patients, especially if a bone marrow transplant is being considered. Diagnosing MDS and other complications of SDS is difficult and requires expert evaluation. The rules and expectations of "normal" don't apply. The SDS registry is available as a resource to answer questions.

Dr. Shimamura added that in order for the bone marrow samples to be most helpful for the SDS registry, they need the clinical reports including the pathology report, cytogenetics, and FISH (fluorescent in-situ hybridization). Increasingly, centers are performing somatic mutation analysis on marrow exams so those should also be forwarded to the Registry. It is critical to remember to send these reports to the registry when they become available after a biopsy. The registry doesn't repeat these clinical tests on the marrow samples, but rather reserve these precious samples for new research. Some hospitals are better than others at sending the reports to the registry, and often patients' assistance is needed. Feel free to reach out to the SDS Registry research nurse if you need help obtaining the marrow reports.

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**There is hope that Treosulfan will offer a great new treatment option for SDS patients who need a transplant.**

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After the morning break, several talks focused on MDS, leukemia, and their respective treatments. Outcomes of MDS and leukemia were discussed. **Dr. Shimamura** discussed the indications for regular surveillance of the bone marrow, in an effort to identify dangerous changes early enough, when treatment options are most effective. Early results suggest that regular surveillance is associated with better long term survival rates, but larger numbers of patients are needed to assess this.

Next, **Dr. Kas Myers** (including slides from **Dr. Lauri Burroughs** from the Fred Hutchinson Cancer Research Center) talked about Bone Marrow Transplants and Treosulfan. Treosulfan appears to be as effective as other transplant approaches, but has the advantage of significantly less toxicity. This is important for SDS patients, as SDS patients are particularly sensitive to toxicity and suffered poor outcomes with classic BMT regimens. There is hope that Treosulfan will offer a great new treatment option for SDS patients who need a transplant. This treatment is already approved in Europe. Now, there is a new clinical trial under development in the United States.

**Dr. Grover**, a pediatric gastroenterologist at Boston Children's Hospital and part of the scientific advisory board of the SDS Registry, wrapped up the morning sessions with a more lighthearted discussion of GI complications. He explained what happens when the pancreas doesn't perform its digestive function, the importance of ensuring proper nutrition and supplementation with fat soluble vitamins and key minerals as needed. He also talked about the liver, and his upcoming efforts to study liver complications in SDS patients.

After a delicious lunch with time to network with families, doctors, and researchers, we switched gears to discuss cutting edge research.

First, **Dr. Coleman Lindsey**, Dana Farber Cancer Institute, introduced his collaboration with the SDS Registry and the Shimamura lab to study the significance of various clones that can come up in SDS patients. He introduced a model to learn and predict which clones are more dangerous than others. Hopefully this research - which hinges on the registry and patient participation - will help predict which patients should move to transplant and what the best time would be.

Next, **Dr. Jessica Pollard**, Dana Farber/ Boston Children's Hospital, described several clinical trials in collaboration with the SDS Registry for new treatments of MDS and AML in the context of SDS, aimed at further improving outcomes. The SDS Registry is available to answer questions about clinical trials for MDS and AML.

**It is very important to ensure proper nutrition and supplementation with fat soluble vitamins and key minerals -- as needed.**



**The SDS Registry is available to answer questions about clinical trials for MDS and AML.**

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**NEW HOPE: A new program to apply gene editing technology based on CRISPR to correct SBDS mutations in blood stem cells**

Finally, **Dr. Christian Brendel** and **Dr. Dan Bauer**, Boston Children’s Hospital, wrapped up the scientific portion of the day with their presentation on gene therapy for SDS. Their team in collaboration with the SDS Registry started a new program to apply gene editing technology based on CRISPR to correct SBDS mutations in blood stem cells. The idea is that the corrected stem cells could then be used for a transplant in the same patient they came from, eliminating the risks of graft-versus-host-disease, reducing other side effects, increasing successful engraftment and offering an option for patients who don’t have other suitable stem cell donors available.

After the afternoon break, **Nancy Cincotta**, LCSW, MPhil, Psychosocial Director Camp Sunshine, conducted a session on finding shared experiences and support between families. It was a great tool to get to know each other, and voice our concerns, worries, pain and joy.

Lastly, family representatives of the registry **Nicole Shen** and **Dr. Eszter Hars** wrapped up the meeting by sharing their stories. Their perspectives on why the SDS Registry is such a critical component of finding the best treatment options, developing new ones, and ultimately finding a cure for SDS ended the day on an inspirational note. On behalf of the patient community, they thanked Dr. Shimamura, Dr. Myers, and all the registry staff for all their hard work and dedication over the past 10 years.

Here is to progress and finding a cure! Cheers!

## IMPORTANCE OF YOUR PARTICIPATION

By Maggie Malsch and Sara Loveless  
Research Nurses, SDRS

We literally cannot make progress in the treatment of SDS and its complications without your participation in the Registry.

If you would like to provide blood and marrow samples during your regular care at your home hospitals, we need your help getting them (plus the clinical reports afterward) to us. **Please request a Bone Marrow Kit (specimen collection kit) a month before your procedure.** It contains instructions for your medical team, specimen collection tubes, and a pre-filled shipping label.

Please also check in with your local registry site periodically to ensure that your medical and contact information are up-to-date, and that your release forms are current.

“ **If you have a Bone Marrow Biopsy coming up within a month or two, please request your kit from us ASAP!** ”



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