The 11th International SDS Scientific Congress

June 5-8 2025, Cincinnati Ohio

Summary

Eleventh SDS Congress Review by Geneticist

The meeting began with Deana introducing Dr. Johanna Rommens, a renowned geneticist and molecular biologist, who presented a review of the Eleventh International Medical and Scientific Congress on Shwachman-Diamond Syndrome (SDS), held in Cincinnati in June, 2025. Dr. Rommens discussed the overall meeting structure focused on SDS with lecture sessions, discussion-based events, and a poster session, as well as a special social event at the Cincinnati Museum Center. She also highlighted the Dr. Peter Durie Keynote Lecture given by Dr. Akiko Shimamura. The presentation ended with Dr. Rommens noting the interactive nature of the congress and the valuable feedback provided by attending family members.

SDS Care Challenges

Dr. Rommens discussed challenges faced by families and individuals with SDS, including the need for lifelong care, age-appropriate education, and management of medication costs. She highlighted the importance of commitment to research and need for continued investigations into all aspects of variability in presentation including hematological and non-hematological features of the syndrome. The meeting also addressed the challenges of transitions in care, particularly from pediatric to adult care, and explored strategies to make these transitions smoother, such as overlapping phased approaches or access to combined pediatric and adult care centers.

Ribosome Function in Shwachman-Diamond Syndrome

Dr. Rommens provided a detailed overview of ribosome function and its relevance to SDS, explaining how loss-of-function variants in genes like SBDS, EFL1 and DNAJC21 lead to ribosome maturation defects. She described the complex process of ribosome assembly, highlighting the multiple steps and many factors involved, and explained how mutations in SDS-associated genes disrupt the final stages of ribosome maturation, resulting in reduced protein synthesis. Dr. Rommens also discussed the potential for developing therapeutic approaches, such as modulation of interactions of late maturation factors, and highlighted ongoing research efforts to understand the roles of ribosomes and protein levels in different cell types and tissues. (Note added, SRP54 appears to play a role in an alternate facet of ribosome activity.)

Advancements in SDS Research Technologies

Dr. Rommens discussed emerging developments in model organisms and organ-on-a-chip technology for studying SDS and its cell and organ consequences, and toward their potential to help test therapeutic strategies. She highlighted newer approaches toward patient diagnoses, including broader use of genetic sequencing and the potential for newborn screening.

Clonal hematopoiesis in Patients with SDS

Dr. Rommens explained how the long-recognized chromosomal changes noted in blood and marrow cells of patients are now appreciated as a reflection of somatic evolution in blood stem cells. With the benefits of improved DNA sequencing, and ability to detect more subtle gene sequence alterations, the full extent of changing blood stem cells (*i.e.* clonal hematopoiesis) can be appreciated. She described how clones

develop as stem cells acquire genetic changes, with measures of variant allele frequency to assess the proportion of cells carrying these changes. Dr. Rommens highlighted two key driver genes that appear common in SDS clonal hematopoiesis. The first is EIF6, that when reduced, appears to provide a survival advantage to stem cells thus allowing better growth despite missing SBDS. The second, TP53, is typically responsible for multiple 'guarding' functions for cells but is known to be associated with cancer development and of concern when both gene copies become disrupted.

From research findings to benefits for SDS

Dr. Rommens indicated enthusiasm for ongoing research, striving toward better understanding of the abilities of organs and cells with SDS, and how they maintain balance toward stresses. Also, the implications of clonal hematopoiesis yield hope toward improved bone marrow surveillance given the potential for better definitions of high- as well as low-risk features to guide treatment decisions for patients. She highlighted ongoing international studies and apparent potential for preemptive bone marrow transplantation, while acknowledging the complications associated with such procedures. Dr. Rommens also touched on the needs for further research into additional causal genes and recognition of consequences and improved interventions for all organs affected in SDS.

Dr. Rommens acknowledged Cincinnati Children's, the organizing team and all the speakers, and expressed willingness to answer questions.