

The 11th Annual DBA International Consensus Conference

By: Steven R. Ellis, Ph.D

It was a dark and stormy night that kicked off the 11th annual DBA International Consensus Conference. And while the atmosphere outside on this March evening in New York City was forbidding, the ambiance inside was warm and collegial as clinicians, scientists, and numerous other interested parties gathered to begin this year's conference. After an introduction by Marie Arturi who regaled the audience with inspirational poetry and photography, researchers heard motivational talks from Janet Pereira whose son Jack has DBA, and Congresswoman Carolyn McCarthy, a longtime supporter of DBA research. These talks set the tenor for meeting, fostering a common bond among meeting participants to continue the remarkable progress in the DBA field witnessed over the past few years.

Susan Shurin, acting director of the National Heart Lung and Blood Institute, began the scientific sessions by describing the NHLBI's strategic plan to support crosscutting translational research to further understanding and treatment options for a myriad of human diseases including DBA. Continued progress in DBA research depends on our ability to recruit young investigators into the field. With young investigators like Anu Narla, who followed with a talk on the perspective of a young investigator entering the field, I think it is clear that the future looks bright for DBA research.

One of the major features of this year's conference that really stood out in my mind is how the recent explosion of animal models for DBA has altered discussions at the meeting. While basic ribosome biology remains an undercurrent of most talks, the animal models have shifted the focus to hematopoiesis and other parameters relevant to the disease state. You can tell by the expansive discussions after each talk engaging both clinicians and scientists that the field is maturing to the point where basic science discoveries are being translated into clinical applications. There were 4 talks on mouse models of DBA (Mason, Bodine, Abkowitz, and Jaako), and 2 talks on zebrafish models (Taylor and Lin). There was also considerable interest in induced pluripotent stem cell models (Agarwal, Loh) and mouse embryonic stem cell models (Goldberg) for DBA, both of which promise to shed light on how ribosomal protein haploinsufficiency disrupts developmental pathways.

The translational research theme was present throughout this year's meeting. Fumagali and Flygare presented recent studies on novel approaches to DBA therapy while Vlachos, Pospislova and Glader discussed

the status of clinical trials for leucine and lenalidomide. Alter reported on cancer risk in DBA patients and Ball led a spirited discussion on strategies to revise the DBA consensus document with regular updates. Gene discovery for DBA appears at a crossroads. Gazda and Farrar reported that when virtually all of genes encoding ribosomal proteins were examined in patients in North American Registries, almost half of the patients did not have readily identified mutations. These observations indicate that the search for new genes needs to be broadened either through the analysis of other genes involved in ribosome synthesis or by using recent advances in genome-wide research to analyze virtually every gene in a DBA patient. Pre-rRNA processing studies can potentially be used to determine whether a patient has a mutation in a gene that affects ribosome biogenesis, and Leblanc reported on studies developing this tool for potential diagnostic and gene discovery applications.

Ribosome biology emerged from the shadows in the last session where hot topics continued to be the extent to which nucleolar stress signaling to p53 activation (Monitz, Arceci) or altered translation (Horos, Loreni) or both (Du, earlier session) contribute to the clinical features of DBA. Gleizes ended the scientific portion of the meeting by showing the effects of ribosomal protein haploinsufficiency on nucleolar dynamics during the cell cycle.

In addition to oral presentations at the meeting a poster session was held which included reports on protein (Dianzani), gene (Da Costa, Dahl), and patient (Vlachos, Kartal, Meerpohl) databases. There was also a poster reporting work on the enhanced severity of iron overload in DBA patients (Quarello).

Last but certainly not least, the meeting ended with talks from officials from the National Heart Lung and Blood Institute (Qasba) and the National Institute of Diabetes and Digestive and Kidney Disease (Bishop) on funding opportunities for DBA research.

I would be remiss if I didn't take this opportunity to provide a special note of thanks to Lauren Carroll and Shannon Scott for their behind the scene efforts that keep these meetings running smoothly.

The annual DBA International Consensus Conference continues to be the premier venue for bringing together International experts on all facets of Diamond Blackfan anemia for a weekend of intense and stimulating presentations.