Summary of the 2009 International Consensus Conference from DBAF's Research Director, Steven Ellis, PhD

This year represents the 10th anniversary of the Diamond Blackfan Anemia International Consensus Conference. I have been attending these conferences since 2004. From my viewpoint this year's conference was one of the most far reaching and important conferences from both the clinical and scientific perspectives.

Where once there were few treatment options for DBA, novel therapies are moving forward into clinical trials with others in various stages of development. We heard from Dr. Adrianna Vlachos (New York) who is coordinating the North American clinical trial for the efficacy of leucine as treatment for DBA. While there have been published reports of small trials where DBA patients have been given leucine and anecdotal reports from sporadic families trying leucine, a carefully controlled clinical trial is necessary to truly address its efficacy and address any potential adverse side effects. Plans for this trial are nearing completion and patient accrual should begin soon! Dr. Vlachos also reported on a clinical trial being considered for the use of lenalidomide as a therapeutic option for DBA. This trial will be led by Dr. Bertil Glader (Palo Alto). Initially this trial will be limited to a small number of adult patients because of the potential for serious adverse side effects. Dr. Monica Bessler (St. Louis) presented a novel idea for using a drug currently under clinical trials for a number of different genetic diseases that may be efficacious in ~ 20% of DBA patients with a particular class of mutations. What is interesting about this drug is that it doesn't matter which gene the mutation is in, it just targets the type of mutation. Thus, we could have designer drugs specific for some DBA patients and not others. Drs. Narla (Boston) and Johan Flygare (Boston/Lund) presented work on the mechanisms by which steroids promote erythropoiesis in DBA patients. These studies are yielding fascinating new insights. Dr. Flygare wants to use this insight to create a method for screening thousands of chemicals for properties similar to steroids. Compounds identified in this manner would be lead compounds for drug development with the hope that drugs could be found that act like steroids but have fewer side effects. As I hope you can tell, there was considerable excitement at this meeting relating to possible new treatments for DBA.

Where once there were none, we now have several animal models for DBA. In the past most laboratory studies on DBA relied on tissue culture cells and yes, even Brewer's yeast. As you might expect, these cell based models lack the complex physiology of a complete organism and, so while valuable, are limited especially for matters like drug testing and understanding factors like why mutations in ribosomal protein genes selectively affect the production of red blood cells. We heard reports on three mouse models of DBA from Drs. David Bodine (Washington D.C.), Kelly McGowan (Palo Alto), and Stefan Karlsson (Lund). We also heard about zebrafish models for DBA from Drs. Sakamoto (Los Angeles) and Taylor (Boston). Recent technological developments have allowed scientists to create embryonic stem cell-like cells from adult cells. These cells, called induced pluripotent stem cells, allow investigators to study complex developmental questions in cell based models. Drs Warren (Cambridge, England) and Lensch (Boston) described studies using this class of cells, whereas Dr. Singh (New York) spoke on similar studies using mouse embryonic stem cells. Again, with so many possible models to choose from, progress on the translational research front should move forward rapidly.

Where once there was RPS19, we now have a total of six genes known to be affected in DBA. Dr. Gazda (Boston) reported on the identification of two new DBA genes, with other genes identified, but not as yet confirmed. Dr. Vlachos (New York) reported studies trying to correlate the gene affected in DBA patients with various clinical parameters associated with the disease. Interesting relationships are being found. One of the goals of this type of study would be to determine if knowledge of gene affected could give physicians insight into how well a patient might respond to therapy or perhaps even go into remission. Dr. Moniz (Paris) reported that cells from patients with different types of mutations behaved differently in cell culture adding fuel to the fire that the nature of the gene affected will likely influence clinical presentation. I could go on and on about remarkable new insight being uncovered at the basic science level pertaining to the underlying molecular basis for DBA. As this is my own research area, I am hoping all remaining investigators focusing their time and energies in this area will forgive my cutting this discussion short. Let me just close by saying without the foundations laid by these studies on the basic science side of DBA: Drs. Gleizes (Toulouse, France), Fumagalli (Cincinnati), Dianzani (Novara, Italy), Meerpohl (Freiburg, Germany),

Pospisilova (Czech Republic), Keel (Seattle), Dahl (Uppsala, Sweden) Mason (St. Louis), Tailor (Toronto), Loreni (Rome), Caywood (Baltimore), and Sieff (Boston), I doubt we would have seen all the progress discussed above.

In closing, let me reiterate my view that the 10th annual Diamond Blackfan Anemia International Consensus Conference sponsored by the Daniella Maria Arturi Foundation and co-sponsored by the Diamond Blackfan Anemia Foundation was a smashing success, with outcomes that should transform the lives of patients and families affected by DBA in the near future.