As 2014 rapidly approaches I thought I would take this opportunity to do a year-end review of 2013 from a decidedly DBA-centric point of view. Below are some of the highlights from 2013 with an occasional nod back to 2012 and beyond.

- **January 2013 – The first clearly documented case of DBA presenting during fetal development**

A study led by a group in France documented the first case of hydrops fetalis in a fetus harboring a mutation in the RPS19 gene(Da Costa, Chanoz-Poulard et al. 2013). These studies suggest that DBA may be under diagnosed and contribute to miscarriages in the general population. Moreover, this finding has significant implications for genetic counseling in families with a history of DBA and more broadly in the general population.

- **June 2013 – Opening of the leucine trial for transfused DBA patients**

Building on preliminary data from the Czech Republic and several animal models for DBA, the Cohen Children's Medical Center announced that the trial for leucine in transfused DBA patients is now open. The ability of leucine to ameliorate phenotypes in animal models of DBA has raised considerable hopes for this treatment, but anecdotal reports from studies in humans have been conflicting (Pospisilova, Cmejlova et al. 2007, Jaako, Debnath et al. 2012, Payne, Virgilio et al. 2012). This carefully controlled clinical trial should get definite answers on the ability of this treatment to reduce transfusion requirements for DBA patients.

- **July 2013 – Opening of a clinical trial for the safety and efficacy of Sotatercept in adults with transfusion dependent Diamond Blackfan anemia**

The North Shore Long Island Jewish Health System has opened a trial to investigate the safety and dosing of Sotatercept as an agent to stimulate the production of red blood cells in adult patients with DBA. Sotatercept (ACE-011) is an experimental drug that has been shown to increase the number of red blood cells in human subjects (Sherman, Borgstein et al. 2013). Because of the novelty of this drug and its limited safety data in human populations, this trial is currently restricted to adult DBA patients. Nevertheless, this trial shows how new treatments for DBA may arise from unexpected quarters and be rapidly transitioned into new clinical trials.

- **July 2013 – Despite being the ribosomal proteins whose names will change most dramatically in the new ribosomal protein nomenclature, ribosomal proteins L5 and L11 (along with their compatriot 5S rRNA) continued to bubble to the surface as critical proteins involved in DBA pathogenesis**

Groups in the United States and the United Kingdom both published papers on the role of the RPL5/RPL11/5S rRNA subcomplex in signaling ribosome stress to p53 activation as a potential means for the enhanced cell death seen in erythroid progenitors in DBA patients (Donati, Peddigari et al. 2013, Sloan, Bohnsack et al. 2013, Teng, Mercer et al. 2013). *The Thomas laboratory has received funding from the DBA Foundation to continue work on alternative mechanisms of cell death in DBA patients harboring mutations in RPL5 and RPL11.*

- **August 2013 - The first induced pluripotent stem cells created from DBA patients**

Researchers at Children's Hospital of Philadelphia took cells from the skin of a DBA patient and reversed these cells back to state similar to that of embryonic-like stem cell capable of differentiating into virtually any cell type within the body (Garcon, Ge et al. 2013). These cells will be very important tools for understanding the molecular basis of DBA and may some day be used therapeutically to treat the disease. *Dr. Ge has received funding from the DBA Foundation to continue her work on IPS cells from DBA patients.*

- **July 2012 / Dec 2103 – Non-ribosomal protein genes and DBA**

In 2012, GATA1 became the first DBA gene that coded for something other than a ribosomal protein. At the American Society of Hematology Meeting in December of 2013, a group of investigators spearheaded by individuals at the National Human Genome Research Institute reported three new non-ribosomal protein genes that appear to be responsible for DBA. Like the GATA1 gene, these genes have only been identified in a small number of patients. These results illustrate the growing complexity of the underlying molecular basis of DBA. The same group of investigators also used advanced genomic technology to identify a small deletion of the *RPS14* gene in a patient diagnosed with DBA (Vlachos, Farrar et al. 2013). This finding altered the diagnosis for this patient from DBA to $5q^-$ syndrome. As a result of the change in diagnosis, this patient was treated with lenalidomide and has shown a favorable response. These results illustrate the importance of identifying the underlying genes affected in ALL patients suspected of having DBA. *Drs. Vlachos, Bodine and Ellis, involved in these studies have all received research support from the DBA Foundation that contributed to these studies.*

**Citations**


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