

# DBA Newsletter

Volume 6, Number 4 • When we all work together, anything is possible!

## Daniella Maria Arturi Foundation Sponsors Productive Conference

The Diamond Blackfan Anemia Foundation, Inc., has teamed with the Daniella Maria Arturi Foundation to co-sponsor this year's meeting which will be held the beginning of April in New York City. The Diamond Blackfan Anemia Fourth International Consensus Conference promises to be well attended by international researchers and physicians.

The Diamond Blackfan Anemia Third International Consensus was held April 29-30, 2002 in Baltimore, Maryland. The Diamond Blackfan Anemia Foundation, Inc. is grateful to the Daniella Maria Arturi Foundation which hosted this most productive and encouraging meeting. The following are brief summaries of the topics discussed.

Dr. Sarah Ball of London presented her work on an in vitro model for DBA, which demonstrated the response of normal and DBA red cell precursors to erythropoietin and the partial corrective response to steroids. Dr. Ball also reported on the extended follow-up of patients with DBA in the United Kingdom.

Lydie DaCosta, working in Berkeley, California presented evidence that mutations in some portions of the RPS19 gene affect both the quantity of RPS19 produced, and where that protein is located in the cell.

Jason Fixler, also at Berkeley, reported on his work with the Drosophila model of DBA. Homozygous minute type fruit flies have a decreased production of red cell equivalents.

Dr. Jeffrey Lipton from New Hyde Park, New York, reviewed the DBA registry families who have multiple members with DBA. He pointed out the diversity and variable penetrance that this disease can exhibit.

Jean Delaunay from Bicetre, France, showed that among patients with DBA and mutations in the RPS19 gene, some individual mutations associate with one another.

Hanna Gazda, working from Boston, reported on her efforts to find additional Diamond Blackfan genes. Concentrating on the 8p region, she has correlated the mutations found in this region with genes reputed to code for ribosomal proteins in this area.

Patricia Shi reported that in the NIH experience with stem cell mobilization using G-CSF, this technique appears to produce an adequate number of stem cells with only mild side effects.

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Stefan Karlsson, from Lund, Sweden, has been able to achieve production of RPS19 RNA in affected cells by transduction techniques.

Dr. Janis Abkowitz, from Seattle, showed that in patients who responded to Reglan for Diamond Blackfan Anemia, the response is durable. She reported however, that if the prolactin levels of the patient do not increase in response to Reglan treatment, there is also no hematologic response .

Dr. Blanche Alter, from the NIH, pointed out that many bone marrow failure syndromes have an increased risk of cancers and that these cancers often occur earlier in life than in the general population. She is studying these results with particular regard to differences in cancer and noncancer cases which may provide insights into both the causes of cancer and the effects of bone marrow failure syndromes. The website to find more details about this project or to volunteer as a subject is [www.marrowsfailure.cancer.gov](http://www.marrowsfailure.cancer.gov).

Dr. George Buchanan of Dallas, Texas, and Dr. Adrianna Vlachos of New Hyde Park, New York, led a spirited discussion of guidelines for diagnosis and management of DBA.

On May 1st, the National Heart, Lung and Blood Institute of the

National Institutes of Health sponsored the DBA workshop. Dr. Pankaj Qasba of Bethesda, Maryland, coordinated the program.

This workshop included discussion of the previous day's research, as well as discussion by Yigal Dror of the apoptosis in inherited marrow failures. Leonard Zon reported on his use of zebra fish as a model system for the genetics of blood formation and Edward Davey reported on investigations of what proteins may interact with the RPS19 protein outside of the ribosome itself. Colin Sieff of Dana-Farber ably summarized the day's activities.

In addition to the conference, the Daniella Maria Arturi Foundation has also been working with lobbyists to pass a DBA bill. It has recently been confirmed that DBA language has been included in the Congressional Record, the Senate Labor, Health, and Human Services appropriations bill. This requires the National Heart, Lung, and Blood Institute (NHLBI) to report to the congressional committee their progress regarding DBA. The NHLBI is developing a comprehensive research strategy to investigate it's genetic predisposition to cancer, advanced treatment options, and gene therapy. The NHLBI is also urged to consider ways to enhance the DBA Registry so that it may better facilitate research in this field.

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## **Donations Made to Honor DBA Patients**

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Donations were made and/or fundraisers were held in 2002 in honor of the following DBA patients. The Diamond Blackfan Anemia Foundation, Inc. and all DBA families thank the families of these patients. It is through their efforts and generosity that we are able to continue funding approved research projects.

Philip Ash	Alexandria Hartmann	Ryan Simmons
Kevin Ballina	Natalie Hianik	Michael Sinatra
Justin Baumgardner	Michael Joyce	Carson Souza
Lizzie Bell	Cameron Lanore	Ryan Spring
James Bohuski	Jason Lingham	Jeffrey Vink
Tracey Brochin	Samuel Manning	Christopher & Matthew Vroman
Paula & Sarah Browning	Paige Mauch	Andreas Wagner
Kate Burnette	Andrew & Michael McCaughey	Dan Wagner
Sean Cadden	Nancy McSweeney	Atleigh Whitman
Gail Coughlin	Kylie Monica	Paul Witzgall
William Fair	Sage Orvis	Marissa Ybarra
Gabriella Ferrari	John-Paul Quintero	Keir Zangrando
Brianne Fitzmaurice	Kyle Rashford	
Shayna Goldrich	Kyle Rose	
Kathleen Grace Green	Coleson Shaw	<i>In memory of Katie James</i>



# **DBAF Able to Grant \$158,357.00 to Scientists Because of Others' Generosity**

DBA families and friends have once again made possible grants for DBA research to world-renowned physicians.

One grant entitled "Gene Expression During Erythropoiesis in Diamond-Blackfan Anemia" for \$82,357.00 was awarded to Mahmut Y. Celiker, MD, Jeffrey Lipton, MD, PhD, Steven Arkin, MD, and Adrianna Vlachos, MD, of Schneider Children's Hospital, New Hyde Park, New York.

The long term objective of this study is to apply the information gathered about the pathophysiology of DBA, to develop new treatment modalities, to optimize the current treatment methods, and eventually bring a cure to all patients with DBA. In the short term, the goal is to better understand the mechanism by which red blood cell production termed erythropoiesis fails in patients with DBA. The Diamond Blackfan Anemia Registry provides an invaluable tool to study the pathogenesis, treatment, and prognosis, of DBA and offer opportunities to improve outcome in these patients.

Kathleen M. Sakamoto, MD, of the University of California, Los Angeles, was awarded \$25,000.00 for a study titled: "AML in Diamond-Blackfan Anemia: Molecular Basis and Therapeutic Strategies." The focus of this research is understanding the molecular basis of leukemia and developing new strategies to treat myeloid leukemia. The study will shed new light on the mechanism of disease and risk for leukemia in DBA patients.

The DBAF also awarded \$10,000.00 for the Biolron 2003 World Congress on Iron Metabolism at the National Institutes of Health, Bethesda, MD, May 4-9, 2003.

Iron Chelation and Iron Overload in Sickle Cell Disease, Thalassemia, Diamond-Blackfan Anemia and Other Iron Loading Anemias will be discussed at this conference.

The Diamond-Blackfan Anemia Fourth International Consensus to be held in early April, 2003 was co-sponsored by the DBAF for \$25,000.00.

A grant for \$16,000.00 was awarded to Dr. Gil Tchernia of Bicetre Hospital, France. The objective of this research project is to study the role of ribosomal protein S19 (RPS19) erythropoiesis and to define the link between a mutation in the gene and the occurrence of the disease. New insights generated by this study could help design new therapeutic strategies for the treatment of patients affected by DBA.

*The Diamond Blackfan Anemia Foundation, Inc., its officers, directors, and volunteers are not responsible for the information in this newsletter. The DBA Newsletter is for informational purposes only and does not constitute medical opinion or advice. Consult your personal physician as to whether any information in this newsletter may be useful in your specific case.*

Abstracts of many of these articles can be read online at: <http://www.ncbi.nlm.nih.gov/entrez/query.fcgi>

- **Marrow failure.**  
D'Andrea AD, Dahl N, Guinan EC, Shimamura A.  
Hematology (Am Soc Hematol Educ Program). 2002;:58-72.  
PMID: 12446419
- **Allogeneic stem cell transplantation using non-myeloablative conditioning regimens: results of the Mexican approach.**  
Ruiz-Arguelles GJ.  
Int J Hematol. 2002 Aug;76 Suppl 1:376-9.  
PMID: 12430885
- **Piebaldism in diamond-blackfan anaemia: a new phenotype?**  
Costa LD, Fixler J, Berets O, Le lanc T, Willig TN, Mohandas N, Tchernia G.  
Br J Haematol. 2002 Nov;119(2):572. No abstract available.  
PMID: 12406103
- **Study of 22 Egyptian patients with Diamond-Blackfan anemia, corticosteroids, and cyclosporin therapy results.**  
El-Beshlawy A, Ibrahim IY, Rizk S, Eid K.  
Pediatrics. 2002 Oct;110(4):e44.  
PMID: 12359817
- **Familial transient erythroblastopenia of childhood is associated with the chromosome 19q13.2 region but not caused by mutations in coding sequences of the ribosomal protein S19 (RPS19) gene.**  
Gustavsson P, Klar J, Matsson H, Forestier E, Henter JI, Rao S, Seip M, Skeppner G, Dahl N.  
Br J Haematol. 2002 Oct;119(1):261-4.  
PMID: 12358933
- **Gene transfer improves erythroid development in ribosomal protein S19-deficient Diamond-Blackfan anemia.**  
Hamaguchi I, Ooka A, Brun A, Richter J, Dahl N, Karlsson S.  
Blood. 2002 Oct 15;100(8):2724-31.  
PMID: 12351378
- **Response of Diamond-Blackfan anemia to metoclopramide: evidence for a role for prolactin in erythropoiesis.**  
Abkowitz JL, Schaison G, Boulad F, Brown DL, Buchanan GR, Johnson CA, Murray JC, Sabo KM.  
Blood. 2002 Oct 15;100(8):2687-91.  
PMID: 12351372
- **Blackfan-Diamond anemia and dyserythropoietic anemia presenting with increased nuchal translucency at 12 weeks of gestation.**  
Souka AP, Bower S, Geerts L, Huggon I, Nicolaides KH.  
Ultrasound Obstet Gynecol. 2002 Aug;20(2):197-9.  
PMID: 12153674
- **Pneumocystis carinii pneumonia in patients with Diamond-Blackfan anemia receiving high-dose corticosteroids.**  
Huh WW, Gill J, Sheth S, Buchanan GR.  
J Pediatr Hematol Oncol. 2002 Jun-Jul;24(5):410-2.  
PMID: 12142794
- **Transcription factor GATA-4 is not involved in Diamond-Blackfan anaemia.**  
Cmejlova J, Pospisilova D, Cmejla R.  
Haematologica. 2002 Jul;87(7):ELT30. No abstract available.  
IPMID: 12091145
- **The effect of thrombopoietin on erythroid progenitors in Diamond-Blackfan anemia.**  
Kawasaki H, Nakano T, Kohdera U, Kobayashi Y.  
Int J Hematol. 2002 May;75(4):382-4.  
PMID: 12041668
- **Clinico-haematological profile of pure red cell aplasia in children.**  
Marwaha RK, Bansal D, Trehan A, Marwaha N, Varma N.  
J Trop Pediatr. 2002 Apr;48(2):113-6.  
PMID: 12022425
- **Multiple cerebral aneurysms and the Diamond-Blackfan syndrome.**  
Trivedi RA, Watts C, Kirkpatrick PJ, Gillard JH.  
J Neurol Neurosurg Psychiatry. 2002 May;72(5):678-9. No abstract available.  
PMID: 11971069
- **Managing anemia in a pediatric office practice: Part 2.**  
Segel GB, Hirsh MG, Feig SA.  
Pediatr Rev. 2002 Apr;23(4):111-22. Review. No abstract available.  
PMID: 11927743

# DIAMOND BLACKFAN ANEMIA FOUNDATION, INC.

## POSITION TO BE FILLED

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We're Growing! The Diamond Blackfan Anemia Foundation, Inc. is pleased to announce that because of our continued growth and desire to fund more research, we are hiring a research director. The foundation is now accepting applications for this position. If you know a physician in your local hospital who would be interested, please share the job description with them.

**Goal:** Maximize the DBAF's efforts to fund research.

**Title:** Research Director ("RD")

**Retainer:** Negotiable

**Description:** *The Diamond Blackfan Anemia Foundation, Inc. (DBAF) is seeking a person to lead its effort to maintain and enhance relationships with Bone Marrow Failure (BMF) researchers and related research institutions. Duties would include the following:*

1. Regular and frequent contact with known BMF researchers to stay abreast of current and proposed research efforts.
2. Discover and initiate discussions with BMF researchers not presently known to DBAF.
3. Represent the DBAF Board at relevant medical conferences.
4. Report to DBAF Board at its quarterly meetings.
5. Assist in the assessment and processing of research grant proposals.
6. Establish research goals and objectives, and develop strategies to achieve such goals and objectives
7. Other related duties as determined by the DBAF.

This is not a full-time position. It is anticipated that the RD would devote (TBD)% of his/her time to the above-described duties. The DBAF would enter into an independent contractor relationship with the RD (as opposed to an employee/employer relationship).

**Qualifications:** Ideally, the candidate is an MD and/or PhD with relevant credentials and appropriate research background, and is currently involved in BMF research. The RD must have his/her own office and related support.

**About the DBAF:** The Diamond Blackfan Anemia Foundation, Inc. (DBAF), founded in 1994, generates funds for the purpose of furthering, by clinical study, laboratory research, publication and teaching, the knowledge of the disorder known as Diamond Blackfan Anemia.

The DBAF is a 501(c)(3) not-for-profit corporation registered with the Charities Bureau of New York State Department of Law, 120 Broadway, New York, New York 10271.

**Contact Person:** Interested parties should contact Andrew J. Wagner at:

GSC Partners  
500 Campus Drive, Suite 220  
Florham Park, NJ 07932  
973-437-1022  
973-437-1037 (fax)  
awagner@gscpartners.com

# DBA Families Loved Camp Sunshine!!



Group shot of DBA kids at Camp Sunshine.



The 6-8 year old group do their skit at Camp Sunshine.

What a great place! New friends, great doctors, plenty of food, and loads of fun filled the DBA family week, July 14-29, 2002 at Camp Sunshine near Portland, Maine.

For those who have been there before, the campus has relocated. It is a new facility east of its previous location and is now more "hotel like."

Approximately thirty-five DBA families were greeted by welcoming staff and volunteers after entering through various sized doors: small, medium, or large. Guests were then taken on a brief tour of the facilities. A volunteer happily carried the campers' luggage to their rooms for them. Each spacious room slept six and was quite comfortable. This warm welcome

helped us all settle in for a busy, productive, and fun week

at Camp Sunshine!

On the first day of camp, the children were separated by age into groups. During the week they enjoyed swimming, archery, canoeing, art, singing, campfires, a talent show,

computers, a live musical production, paddle boating, a costume

party, an obstacle course, soccer, a sleep-

over, tether ball, and the list goes on. The children were kept very busy and enjoyed their counselors and new friends. It was hard for many of the kids to say good-bye at the end of the week.

Adults also participated in many activities. They played games with the teens, developed skits, and enjoyed a great gourmet (adults only) meal with karaoke afterwards. They also had several psychosocial sessions led by Nancy Cincotta of New York City. In addition to the activities and social events, doctors addressed the adults several days during the week.

Doctors who spoke included Dr. Stefan Karlsson, Sweden; Dr. Blanche Alter, Maryland; Dr. Niklas Dahl, Sweden; Dr. Jeffrey Lipton, New York; and Dr. Hanna Gazda, Massachusetts. Dr. Vlachos was scheduled to speak but was injured prior to camp and was unable to attend. She was missed and is now doing fine.

Dr. Karlsson is working on DBA gene therapy. He is optimistic that gene therapy will be available for DBA patients within the next five years or so.

Dr. Niklas Dahl is continuing his work on RPS19; he informed attendees that the knock-out mouse is not viable. This was disappointing, but the research continues to progress.

Dr. Dahl and Dr. Karlsson are working together and are in need of more patients on RPS19 to do preliminary RPS19 gene therapy research. Increasing the number of RPS19 patients will decrease the amount of time it will take for gene therapy to begin in qualified DBA patients. If you already know you have the mutation on RPS19 and would be willing to donate samples please e-mail Dr. Niklas Dahl at [niklas.dahl@genpat.uu.se](mailto:niklas.dahl@genpat.uu.se).



Josh, Lisa, and Tyler Lorenz launch their wish boats at Camp Sunshine.

Dr. Alter has successfully coordinated a registry at the National Cancer Institute for all bone marrow failure patients and is encouraging all DBA patients to contact her office in order to complete the registration forms. This registry involves cancer in bone marrow failure patients and is separate from the Diamond Blackfan Anemia Registry (DBAR) in New York City. Forms do need to be completed for both registries at this time. If interested in this study please call Lisa Leathwood at 1-800-518-8474 or e-mail her at [lisleathwood@westat.com](mailto:lisleathwood@westat.com). More information is also provided on the study Web site at <http://marrowfailure.cancer.gov>.

Dr. Lipton updated families on the DBAR (Diamond Blackfan Anemia Registry) in New York. He spoke about the success and failure of bone marrow transplant in DBA patients. More patients are registering but complete information is lacking on many patients. Please do your part and make sure your forms are up-to-date and complete. You can contact the DBAR toll free at 1-888-884-3227.



**Volunteers at Camp Sunshine.**

**Three adult DBA patients and mom participate in the boat launch at Camp Sunshine.**

Dr. Gazda informed patients about the genetic research being conducted on chromosome 8. She is in need of blood samples from DBA families with more than one affected DBA family member. Please contact her by e-mail at [Hanna\\_Gazda@dfci.harvard.edu](mailto:Hanna_Gazda@dfci.harvard.edu) if your family would be willing to donate blood for her research.

DBA families will hopefully be attending Camp Sunshine again in the summer of 2004. We hope to see you all there!

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## **A Clinical Trial of Metoclopramide in the Treatment of Diamond Blackfan Anemia in Pediatric Patients**

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Richard Harris, MD, Stella Davies, MB, BS, PhD, and Samuel C. Blackman, MD, PhD, of Cincinnati Children's Hospital and Medical Center are conducting a research study that will investigate the role of the hormone prolactin in the treatment of Diamond Blackfan Anemia. This study proposes to treat patients with DBA with metoclopramide, a medication commonly used to prevent nausea and vomiting. A recent pilot study by Janet L. Abkowitz, MD, has shown metoclopramide causes a dose-dependent increase in the level of the hormone prolactin and has increased the red blood cell count in three of nine patients with DBA.

The purpose of this study is to confirm these findings in additional children with DBA. In those who respond, the hope is to

reduce dependence on steroids and/or blood transfusions and avoid the complications associated with these therapies. Dr. Harris will identify patients with DBA currently receiving medical care at Cincinnati Children's Hospital. These patients will be contacted by the investigators and invited to participate in the study. If the patient is under the care of a physician other than Dr. Harris and you would like to be part of this study, your attending physician will be contacted by telephone by the investigators and informed of the study methods, risks, and benefits of their IRB approved protocol. The investigators are hoping to recruit patients to be part of this study and will work with your physician. As this is not a randomized trial, all eligible patients will be invited to participate. If you would like more information contact Dr. Blackman at (513)636-4200.



Diamond Blackfan Anemia Foundation, Inc.  
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West Seneca, NY 14224

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# *Diamond Blackfan Anemia Registry*

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For those of you needing to contact or mail medical records to the  
Diamond Blackfan Anemia Registry (DBAR), please use the following information.

***MAILING ADDRESS:***

Diamond Blackfan Anemia Registry  
c/o Dr. Adrianna Vlachos  
Schneider Children's Hospital  
Division of Pediatric Hematology/Oncology and Stem Cell Transplantation  
269-01 76th Avenue  
New Hyde Park, NY 11040

***TOLL-FREE PHONE NUMBER:***

1-888-884-DBAR

***EMAIL ADDRESS:***

Dr. Vlachos can also be reached by e-mail at:  
avlachos@lij.edu.