

Tenth Annual Diamond Blackfan Anemia International Consensus Conference

Sponsored by:



SATURDAY MARCH 14th

6:00PM Shuttle Service from Ritz Carlton to **Palm Restaurant, Tribeca**
6:30PM **2009 Kick-Off Dinner**
Keynote Speaker: **Stacy Trebing**
Introduction by: **Marie Arturi**

SUNDAY MARCH 15th

8:30 – 9:00 **Breakfast ~ Harbor Vista (Function Level)**

Meetings will be held in Salon II & III (Function Level)

9:00 – 9:20 Welcome Remarks and Introductions
Marie & Manny Arturi, Daniella Maria Arturi Foundation
Dawn Baumgardner, Diamond Blackfan Anemia Foundation

9:20 – 9:45 **Sudip S. Parikh, Ph.D.**
Science Advisor & Professional Staff
United States Senate Committee on Appropriations
Subcommittee on Labor, Health & Human Services, Education, and Related Agencies

Genotype/Phenotype Correlations

Moderators: Jeffrey M. Lipton
Thierry LeBlanc

Introduction

Jeffrey M. Lipton

9:45 – 10:00 **The Past and Future of DBA**
Blanche P. Alter
Clinical Genetics Branch, Division of Cancer Epidemiology and Genetics
National Cancer Institute, Rockville, MD

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- 10:00 – 10:10 **DBA – The Syndrome**
Jeffrey M. Lipton
- 10:15 – 10:25 **Ribosome Biology**
Pierre-Emmanuel Gleizes
- 10:25 – 10:35 Systematic analysis of the role of the human RPS proteins in ribosome biogenesis
Pierre-Emmanuel Gleizes, Marie-Françoise O'Donohue, Valérie Choesmel
- 10:40 - 10:50 Association of the RPL5 and RPL11 Mutations with Craniofacial and Thumb Malformations and Identification of New Sequence Changes in RP Genes in Diamond-Blackfan Anemia.
Hanna T. Gazda, Mee Rie Sheen, Adrianna Vlachos, Valerie Choesmel, Marie-Françoise O'Donohue, Hal Schneider, Natasha Darras, Catherine Hasman, Colin A. Sieff, Peter E. Newburger, Sarah E. Ball, Edyta Niewiadomska, Michal Matysiak, Bertil Glader, Charlotte Niemeyer, Joerg J. Meerpohl, Eva Atsidaftos, Jeffrey M. Lipton, Pierre-Emmanuel Gleizes, and Alan H. Beggs
- 10:55 – 11:10 *Coffee Break*
- 11:10 – 11:20 Remission in Patients with Diamond Blackfan Anemia (DBA) Appears to Be Unrestricted by Phenotype or Genotype
Adrianna Vlachos, Hun Lee, Charalampos Lyssikatos, Eva Atsidaftos, Ellen Muir, Hanna Gazda, Alan H. Beggs, and Jeffrey M. Lipton
- 11:25 – 11:35 Differences in *In Vitro* Erythroid Proliferation in Diamond-Blackfan anemia in conjunction with presence or absence of *RPS19* mutations.
Hélène Moniz, Aurore Crétien, Corinne Hurtaud, Thierry Leblanc, Gil Tchernia, Narla Mohandas, and Lydie Da Costa
- 11:40 – 11:55 Wrap-Up

Potential Drug Treatments for DBA

Moderators: Mitch Weiss
Sarah Ball

- 11:55 – 12:05 Lenalidomide and Dexamethasone promote erythropoiesis in both normal and shRNA infected human CD34+ cells
Anupama Narla, Jocelyn Bosco, Kelly McGowan, Shilpee Dutt, Arati Khanna-Gupta, and Benjamin L Ebert
- 12:10 – 12:20 Characterizing the role of glucocorticoids in red cell development in order to understand the mechanisms of corticosteroid treatment in DBA
Johan Flygare, Harvey F. Lodish
- 12:25– 12:35 **“There’s No Stopping Us”** - The ribosomal read-through of premature stop codons in patients with Diamond Blackfan Anemia
Monica Bessler, Kim Smith-Whitley, Philip J Mason, David B Wilson
- 12:40 – 12:50 Therapeutic Use of the Amino Acid Leucine in the Treatment of Transfusion-Dependent Diamond Blackfan Anemia Patients: A Study in Collaboration with the Diamond Blackfan Anemia Registry
Adrianna Vlachos
- 1:00 – 2:00 *Lunch*

DBA Models

Moderators: Mohandas Narla
Benjamin Ebert

- 2:00 – 2:10 Generation of Mouse Models of Diamond-Blackfan Anemia Associated with Point Mutations in the RPS19 and Other Ribosomal Subunit Genes
David M. Bodine, Emily E. Devlin, Lydie DaCosta, Mohandas Narla and Gene Elliott
- 2:15 – 2:25 Multiple Defects in Embryoid Bodies Derived from Mouse Rps19-Haploinsufficient Embryonic Stem Cells: Implications for Diamond Blackfan Anemia
Sharon Singh, Abdallah Nihrane, Sehba Dsilva, Jeffrey M. Lipton, Steven R. Ellis, and Johnson M. Liu
- 2:30 – 2:40 Signaling Pathways Affected by RPS10 & RPL11 Deficiency in Zebrafish and Hematopoietic Cells
Kathleen Sakamoto, Kenji Morimoto, Nadia Danilova, and Shuo Lin

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- 2:45 – 2:55 Generation of a mouse model for RPS19-deficient Diamond-Blackfan anemia by reduction of RPS19 using shRNA.
Stefan Karlsson, Pekka Jaako, Johan Flygare, Karin Olsson
- 3:00 – 3:10 Titration of p53 in ribosomal protein mouse mutants causes a spectrum of cutaneous and hematologic phenotypes
Kelly McGowan, Christopher Park, Laura Attardi, Irving Weissman, Greg Barsh
- 3:15 – 3:25 *Coffee Break*
- 3:25 – 3:35 Human RPS19 Protein Structure and the Generation of Induced Pluripotential Stem Cells from Diamond Blackfan Anaemia Patients
Alan J. Warren, Til Buender, Ludovic Vallier, Mark Bycroft, Stefan M. Freund, Niklas Dahl
- 3:40 – 3:50 Diamond Blackfan anemia: What's the 5S ribonucleoprotein subcomplex got to do with it?
Steven R. Ellis, Joseph B. Moore IV, Elisa Pavesi, Irma Dianzani, Jason Farrar, Robert J. Arceci, Adrianna Vlachos, Jeffrey M. Lipton, Johnson M. Liu
- 3:55 – 4:10 Wrap-Up
- 4:10 – 5:10 **Poster Session**
Moderators: George Buchanan
 Irma Dianzani

Diamond-Blackfan Anemia at the National Cancer Institute
Blanche P. Alter and Neelam Giri

Characterization of a Mouse Model of Diamond-Blackfan Anemia Associated with the RPS16R62W Point Mutation
Emily E. Devlin, Lydie DaCosta, Mohandas Narla, Gene Elliott and David M. Bodine

The Effect of Ribosomal Protein Mutations on Zebrafish Early Hematopoiesis
Alison M. Taylor, Caroline E. Burns and Leonard I. Zon

DBA French group: ongoing studies in the clinical field
Thierry LeBlanc, P.-E. Gleizes, I. Marie, L. Da Costa.

High frequency of RPL5 and RPL11 gene mutation in Italian patients with Diamond-Blackfan anemia (DBA)
Irma Dianzani for **Ugo Ramenghi**, Paola Quarello, Emanuela Garelli, Adriana Carando, Maria Francesca Campagnoli, Alfredo Brusco

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Stem cell transplantation in Diamond-Blackfan Anemia: A retrospective analysis

Jorg Meerpohl, Strahm B, Kartal M, Bernardo ME, Lang P, Matthes-Martin S, Schulz A, Schmugge M, Fischer A, Locatelli F and Niemeyer CM

Analysis of ribosomal protein genes in Diamond-Blackfan anemia patients from the Czech National DBA Registry

Dagmar Pospisilova, Jana Cmejlova, Jan Stary, Zdena Cerna, Radek Cmejla

DBA in the UK: new directions

Josu De La Fuente, Sarah Ball

5:10 – 5:25 Wrap-Up

5:30 – 8:30 Cocktail Reception ~ Skyline Vista ~ Function Level

MONDAY MARCH 16th

8:30 - 9:00 **Breakfast ~ Harbor Vista (Function Level)**

9:00 – 9:10 Modeling Congenital Marrow Diseases Using Human Pluripotent Stem Cells
M. William Lensch, Ph.D.

Instructor in Pediatrics, Harvard Medical School Affiliate Faculty and Faculty Advisor for Education, Harvard Stem Cell Institute Senior Scientist, George Q. Daley Laboratory
HHMI/Children's Hospital Boston Division of Hematology/Oncology

Cell Biology

Moderators: Steven Ellis
Monica Bessler

9:15 – 9:25 Potential mechanistic links between the erythroid failure of *Flycr*-deleted mice and Diamond-Blackfan Anemia
Sioban Keel and Janis L. Abkowitz

9:30 – 9:40 Prolonged cell cycle with distinct arrests in RPS19 and RPS24 deficient primary fibroblasts from Diamond Blackfan Anemia patients
Niklas Dahl, Jitendra Badhai, Anne-Sophie Fröjmark, Edward Davey, Jens Schuster

9:45 – 9:50 X-inactivation and clonal hematopoiesis in Diamond Blackfan anemia
Philip J. Mason, Kraig Young, Quillan Huang, Adrianna Vlachos, Jeffrey M. Lipton, Monica Bessler

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- 9:55 – 10:05 Expression of FLVCRI cDNA Rescues Erythroid Differentiation in a Cell Culture Model of Diamond Blackfan Anemia: Implications for a Potential Gene Therapy Treatment for DBA
Chetan Tailor, Simon P. Duffy, Michelle A. Rey, Yigal Dror
- 10:05 – 10:15 *Coffee Break*
- 10:15 – 10:25 PIM1 Kinase Plays a Role in the Response to Ribosomal Stress of DBA Cells
Fabrizio Loreni, Valentina Iadevaia, Sara Caldarola, Stefan Karlsson, Irma Dianzani
- 10:30 - 10:40 Fibroblasts from patients with Diamond-Blackfan anaemia show abnormal expression of genes involved in protein synthesis and amino acid metabolism.
Irma Dianzani, Federica Avondo, Paola Roncaglia, Helena Krmac, Nicoletta Crescenzo, Emanuela Garelli, Marta Armiraglio, Anna Aspesi, Carlotta Castagnoli, Maria Francesca Campagnoli, Ugo Ramenghi, Stefano Gustincich, Claudio Santoro
- 10:45 – 10:55 Down-regulation of RPL35a and RPS19 in the UT7-EPO cell line results in cell cycle arrest at G2/M
Robert J. Arceci, Emi H. Caywood, Jason E. Farrar, Michelle Nater, Jeffrey M. Lipton
- 11:00 - 11:10 Nucleolar Stress and p53 Mediated Erythroid Failure in Diamond Blackfan Anemia
Colin A. Sieff and Harvey F. Lodish
- 11:15 – 11:45 *Wrap-up*
- 11:45 – 11:55 Update from the NHLBI
Pankaj Qasba, Ph.D.
Program Director
Blood Diseases Branch
Division of Blood Diseases and Resources
National Heart, Lung, and Blood Institute, NIH
- 11:55 – 12:05 Summary of the "Ribosomes and Their Role in Disease" Meeting
Terry Rogers Bishop, Ph.D.
Hematology Program Director
DKUHD/NIDDK/NIH
- 12:05 – 12:15 Closing Remarks
Marie and Manny Arturi
- 12:15 Lunch & Departure