March 2, 2010

Dear Colleague:

With an incidence of just four per million, pediatric myelodysplastic syndrome (MDS) is a heterogeneous group of diseases about which very little is known. Its heterogeneous clinical and laboratory presentation has made it difficult to study and identify novel genetic alterations. Thus, no targeted therapies exist and hematopoietic stem cell transplant (HSCT) is the only therapeutic option for young patients, for whom cure is the goal.

While the initiating events and underlying biology are not clear, the clinical and laboratory presentation often resembles acquired or inherited bone marrow failure disorders. Many constitutional or genetic BMF disorders have a higher incidence of developing secondary MDS.

To better understand pediatric MDS and its relationship to BMF disorders, Children's Hospital Boston is launching an NIH-funded **pediatric MDS and BMF disorder patient registry and tissue bank**. With this registry we seek to improve accuracy of diagnosis in children with MDS and BMF disorders by central and standardized review of morphology, cytogenetics data, molecular analysis and clinical data. Through systematic and in depth analysis, we aim to create a comprehensive database that will allow for improved characterization and understanding of these disorders. Long-term we hope to store well-annotated pediatric MDS and BMF tissue samples for future analysis so we can:

- Define the genetics of childhood MDS.
- Identify pathways for therapy.
- Translate this knowledge to improved outcomes.

Connecting with eligible patients is the first step in the process. Eligibility and exclusion criteria for the tissue bank and registry are outlined below.

Clinical Trial ID #	Pediatric Myelodysplastic Syndrome and Bone Marrow Failure Disorder Patient Registry and Tissue Repository 10-02-0057

Eligibility Criteria	Patients must be <35 years old and have a suspected or known following diagnosis:
	• Suspected or known diagnosis of primary MDS (including familial MDS)
	• Suspected or known diagnosis of secondary MDS
	  ○ Secondary to bone marrow failure disorders
	  ○ Secondary to chemo- or radiation therapy
	• Suspected or known diagnosis of Myeloproliferative Disorders such as
	  ○ Myelofibrosis (MF)
	  ○ Essential Thrombocythemia (ET)
	  ○ Polycythemia Vera (PV)
	• Suspected or known diagnosis of Myelodysplastic (MDS)/Myeloproliferative Disorder (MPD)
	• Suspected or known inherited bone marrow failure disorders such as
	  ○ Fanconi Anemia (FA)
	  ○ Dyskeratosis congenital (DC)
	  ○ Severe Congenital Neutropenia (SCN)
	  ○ Schwachman-Diamond Syndrome
	  ○ Diamond-Blackfan Anemia
	  ○ Bone marrow failure, NOS

	• Acquired Severe Aplastic Anemia and Very Severe Aplastic Anemia
Exclusion Criteria	Patients are not eligible if they meet the following criteria. • Translocation characteristic of de novo AML like t(8;21)(q22;q22) [AML1/ETO fusion gene] t(15;17)(q22;q12) [PML/RAR α rearrangement] inv(16)(p13q22) [CBFβ/MYH11 rearrangement] • Myeloid leukemia of Down syndrome
Patient Evaluation and Data Collection	Every patient will undergo a specific diagnostic evaluation, including diagnostic procedures. No additional procedures are performed for the study. The following information will be obtained: • Patient demographics • Clinical history • Peripheral blood (serum and plasma), bone marrow, and germ line tissue (buccal mucosa swabs or skin biopsies for fibroblasts) • Ancillary information such as cytogenetics and lymph node or chloromas samples, if necessary In regular time intervals (6-12 months), follow up information will be requested.

We aim to enroll 250 patients over the next five years, following each for a minimum of one year. Your help in recruiting participating patients will directly correlate to the success of this initiative and the development of more effective diagnostic and treatment approaches for pediatric MDS.

I am available directly at 617-919-2697 to discuss this registry and how to enroll potential patients. You may also contact Dr. Inga Hofmann, the PI of the study at 617-355-6369 or by emailing us at or mds@childrens.harvard.edu.

Sincerely,

David A Williams M.D.

David A. Williams, MD
Chief, Division of Hematology/Oncology, Children's Hospital Boston
Director of Translational Research, Children's Hospital Boston
Leland Fikes Professor of Pediatrics, Harvard Medical School

Inga Hofmann, MD
Attending in Pediatric Hematology/Oncology/HSCT
Children's Hospital Boston