NIH NATIONAL CANCER INSTITUTE

Summer 2023

Inherited Bone Marrow Failure Syndromes (IBMFS) Study *Newsletter*

Division of Cancer Epidemiology and Genetics • Clinical Genetics Branch

FANCONI ANEMIA CANCER SCREENING STUDY

Do you or a family member have Fanconi anemia (FA)? If so, join the **NCI Fanconi Anemia Cancer Screening Study** to help improve early detection of cancer and clinical care of people with FA.

We invite you to participate in this study if you are an individual with FA and 12 years of age or older.

Children aged 8 to 11 years are eligible if they have areas of concern for cancer in the mouth or the anal/genital areas, or new-onset symptom such as swallowing difficulty.

You may participate in this study if you already participate in other studies at the NCI or elsewhere.

Learn more by visiting marrowfailure.cancer.gov. You can also contact the study team at 1-800-518-8474 or Fanconi@nih.gov.

INHERITED BONE MARROW FAILURE SYNDROME (IBMFS) STUDY UPDATES

Retirement

Stephanie Steinbart, RN, MPH, is a registered nurse who has had an incredibly successful career with 30 years of combined experience in cancer genetics, public health, program management, patient care as well as teaching. Ms. Steinbart served as CGB's referral nurse for more than 20 years and retired in January 2023.

IN THIS ISSUE

Study Recruitment

We have enrolled more than 2,500 participants from 608 families since the study opened in 2002.

Study Website

The IBMFS website was redesigned and launched in April 2023. Please review the updates by visiting marrowfailure.cancer.gov.

For research updates from the study, please visit the Research Highlights page on the IBMFS website: marrowfailure.cancer.gov/ibmfs/research.html.

STUDY TEAM MEMBERS

Principal Investigator

Neelam Giri, M.D., is a pediatric hematologist/oncologist and is the principal investigator of the IBMFS study.

Lead Medical Advisor

Sharon Savage, M.D., is the lead medical advisor for the IBMFS study and is in charge of the telomere biology disorders within the IBMFS study.

Clinical/Scientific Team

Lisa McReynolds, M.D., Ph.D., is a pediatric hematologist/oncologist working on the genomics of IBMFS.

Matthew Gianferante, M.D., M.P.H., is a pediatric hematologist/oncologist working on the genetics of Diamond Blackfan anemia.

Maryam Rafati, M.D., is a medical geneticist working on novel IBMFS gene and variant discovery.

Fellows

Joseph Deng, B.S., is a post-baccalaureate fellow working on the risk of cancer in Fanconi anemia.

Rachel Hendricks, B.S., is a post-baccalaureate fellow working on gene discovery in the IBMFS.

Special Volunteers

Sonia Bhala, B.S., a former post-baccalaureate fellow under the mentorship of Dr. Sharon Savage, is back as a special volunteer. She is working on dyskeratosis congenita and related telomere biology disorders.

Marena Niewisch, M.D., is a pediatric hematologist/oncologist characterizing the genotype-phenotype correlations in dyskeratosis congenita and related telomere biology disorders.

Blanche P. Alter, M.D., M.P.H., is the founder of the NCI IBMFS Study. She continues to be involved as a Special Volunteer.

Scientific Support

Cecilia Higgs, M.H.S. program manager, leads the regulatory matters of the study and manages the study files, including the protocol, consent documents, and submissions to the Institutional Review Board.

Study Support

Ann Carr, M.S., C.G.C., is a genetic counselor with many years of experience in both cancer and pediatric genetics.

Debbie Flamish, M.A., is a research assistant helping with many logistical aspects of the study.

Lisa Leathwood, R.N., is the lead research nurse and study manager for the IBMFS study.

Maureen Risch, R.N., is a clinical research nurse for the IBMFS study.

Please visit the NCI IBMFS website
https://marrowfailure.cancer.gov/
for full biographies and to find out more about the key staff members and their roles in the study.

NEW PROTOCOL DEVELOPMENTS, UPDATES, AND COLLABORATIONS

Update about the Telomere Biology Disorders (TBDs) Needs Assessment Study

NCI researchers launched a study in September 2021 that aims to identify the informational, social, and emotional needs of individuals and families living with TBDs.

Many thanks to those of you who have completed the study!

Study Description: Social science and medical researchers at the NCI (Ms. Wilsnack, Dr. Camella Rising, Dr. Sharon Savage, Dr. Sadie Hutson, and others) collaborated with Team Telomere leaders to design a needs assessment study for individuals and families living with dyskeratosis congenita (DC) or a related TBD. To be eligible to participate in the study, you must be:
· 18 years old or older AND:

- An individual diagnosed with DC or a related TBD OR
- A caregiver of an individual with DC or a related TBD OR
- A bereaved parent or spouse of an individual who died of complications of DC or a related TBD

How to Participate: The NCI researchers would be grateful for your participation. The study involves two components:

a) completing an anonymous online survey that should take no more than 20 minutes and
b) completing an approximately 1-hour confidential telephone interview.

You may choose to complete only one component of the study (either the survey or the interview). If you complete BOTH the online survey and interview, you will have the option to choose either a $30 electronic gift card to Target or Amazon as acknowledgement of your time and effort. If you are interested in participating in the study or have any questions, please contact Camella Rising, PhD, MS, RDN at 240-276-5262 or camella.rising@nih.gov.

TBDs Needs Assessment Study Team

- Sadie Hutson, Ph.D., R.N., W.H.N.P-B.C., F.A.A.N.P., is a senior investigator on the team.
- Camella Rising, Ph.D., M.S., R.D.N., is a research fellow and an investigator on the team.
- Rowan Forbes Shepherd, Ph.D., is a postdoctoral fellow and an investigator on the team.
- Catherine Wilsnack, M.S.W., L.M.S.W., is a special volunteer. She is currently a doctoral student and an investigator on the team.
- Emily Pearce, M.P.H., is a predoctoral fellow and doctoral student studying the experience and management of medical uncertainty for individuals with TBDs and their families. She is part of the psychosocial research team.
- Ashley Thompson, M.S., is a board-eligible genetic counselor. She studies the genetics of telomere biology disorders and is also part of the psychosocial research team.

Update from the DC and Telomere Biology Group

The Clinical Care Consortium for Telomere-associated Ailments (CCCTAA) was officially formalized in April 2021, and 18 institutions have signed onto the agreement to-date. The CCCTAA Database study was approved by the NIH Institutional Review Board in June 2022. This study is focused on telomere related research and will serve as a resource to researchers. Institutions have begun to enter data into the database, and we look forward to providing more updates as this effort progresses.

RECENT PRESENTATIONS AND PAPERS FROM THE IBMFS STUDY

Presentations

Avascular necrosis and minimal trauma bone fractures in patients with dyskeratosis congenita. Niknafs A, Niewisch MR, Savage SA, Giri N.

American Society of Hematology 64th Annual Meeting, December 2022

Telomere shortest length assay (TeSLA) defines the distribution and accumulation of the shortest telomeres in dyskeratosis congenita. Raj H, Niewisch MR, Lai T-P, Wang Y, Spellman SR, Aviv A, Gadalla SM, Savage SA.

American Society of Hematology 64th Annual Meeting, December 2022

Publications

Genotype-phenotype and outcome associations in patients with Fanconi anemia: the National Cancer Institute cohort. Altintas B, Giri N, McReynolds LJ, Best A, Alter BP. *Haematologica*, 2023.

This comprehensive study of a large cohort of patients with Fanconi anemia provides a detailed assessment of physical abnormalities and clinical outcomes in relation to Fanconi anemia genes, mutation pathways and type of genetic variants.

Next-generation sequencing errors due to genetic variation in *WRAP53* encoding TCAB1 on chromosome 17. Savage SA, Jones K, Teshome K, Lori A, McReynolds LJ, Niewisch MR. *Human Mutation*, 2022.

This study discusses the diagnostic utility and limitations of genomic sequencing findings in the context *WRAP53* variants and highlights the importance of accurate interpretation of clinically actionable variants.

Shwachman Diamond syndrome: narrow genotypic spectrum and variable clinical features. Thompson AS, Giri N, Gianferante DM, et al. *Pediatric Research*, 2022.

This study of the NCI IBMFS cohort highlights the importance of a multidisciplinary team approach in the diagnosis and management of patients with Shwachman Diamond Syndrome due to their diverse clinical presentations, involving multiple organ systems, despite a narrow genotypic spectrum.

Disease progression and clinical outcomes in telomere biology disorders. Niewisch MR, Giri N, McReynolds LJ, et al. *Blood*, 2022.

This long-term study of the clinical manifestations of telomere biology disorders (TBD) created a foundation for incorporating the mode of inheritance into evidence-based clinical care guidelines and risk stratification in patients with TBDs.

Fanconi anaemia: A syndrome with distinct subgroups. Alter BP, Giri N, McReynolds LJ, Altintas B. *British Journal of Haematology*, 2022.

This study discusses that people with Fanconi anemia who are diagnosed as adults are distinct from those diagnosed during childhood. People diagnosed with FA as adults may not have hematological problems or obvious physical findings that are characteristics of FA diagnosed during childhood but may have come to attention through family studies or due to early onset cancer or severe complications of cancer treatment.

Risk of cancer in heterozygous relatives of patients with Fanconi anemia. McReynolds LJ, Giri N, Leathwood L, Risch MO, Carr AG, Alter BP. *Genetics in Medicine*, 2022.

This study of parents, grandparents, and siblings of patients with Fanconi anemia enrolled in our cohort shows that the risk of cancer is not increased in people who carry a single copy of a pathogenic variant in a FA gene. This does not apply to carriers of gene variants in *BRCA1, BRCA2, PALB2, BRIP1,* and *RAD51C*.

Genotype-cancer association in patients with Fanconi anemia due to pathogenic variants in *FANCD1* (*BRCA2*) or *FANCN* (*PALB2*). McReynolds LJ, Biswas K, Giri N, Sharan SK, Alter BP. *Cancer Genetics*, 2021.

This review of world literature of FA describes the types of early childhood embryonic cancers that are seen only in patients with FA due to pathogenic variants in *FANCD1* and *FANCN* and not in FA caused by pathogenic variants in other FA genes. Surveillance for these specific cancers is recommended for patients with *FANCD1* and *FANCN* genotypes.

Thank you for participating in our

Inherited Bone Marrow Failure Syndromes (IBMFS) study!

The strength of our study is in our participants.