Summer 2014

Li-Fraumeni Syndrome (LFS) Study *Newsletter*

Division of Cancer Epidemiology and Genetics • Clinical Genetics Branch

National Cancer Institute

Dear LFS Study Participant,

We want to update you on the progress of the LFS study and express our sincere appreciation for your continued support and participation. This newsletter contains information about:

- The current status of our Study
- Ongoing tissue collection efforts
- An invitation to complete a new survey effort
- A link where the archived videocast of the 2nd International LFS Association (LFSA) and the Li-Fraumeni Exploration (LiFE) Consortium meeting can be accessed
- Informational websites and other resources about LFS
- A selected bibliography of publications by LiFE Consortium members
- Study Team updates

LFS Study Update

The NCI LFS Study (NCI 11-C-0255) began recruitment in 2011. Since opening the study, we have had an overwhelming response. We have enrolled over 400 individuals from 105 families. New families and family members are being evaluated and enrolled to the study.

We continue to employ a broad research approach in our efforts to understand:

1. The effectiveness of a comprehensive cancer screening regimen
2. The types of cancers that can develop among individuals with LFS
3. The role of the *TP53* gene in the development of cancers in LFS
4. Other genes that may be associated with cancer development in families where no *TP53* mutation has been identified
5. Environmental factors that might modify risk of developing cancer for individuals with LFS

To reach these study goals, we collect a large amount of data and specimen, including:

- Personal and family history questionnaires
- Biological specimens such as blood or tumor samples
- Dietary and physical activity questionnaires
- Medical and pathology records

We also want to learn about how individuals cope with being a member of a family at high genetic risk of cancer. This will help us better understand the needs of family members and consequently be able to provide more useful support. We

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

gather information on participants' emotional, social, educational, and communication views and concerns using questionnaires and personal interviews.

We are also evaluating a cancer screening regimen for LFS study participants with a variety of imaging methods such as MRIs and ultrasounds as well as physical examination and blood tests. The goal of the screening regimen is to detect cancer at an early stage, where treatment might be more effective. Eligible mutation-positive individuals are invited to the NIH Clinical Center in Bethesda, Maryland, for the screening component. This effort is on-going, and we continue to invite individuals to participate in the screening project.

In addition, we have recently added new research objectives to the LFS Study, including:

Physical Activity and Diet (PAD) Pilot Study: Research shows that diet and exercise are important for one's health and may change cancer risk. In 2013, we started a pilot study to assess the feasibility of colleting detailed information from study participants on physical activity patterns and dietary intake over the course of one year. Once a month, participants are asked to complete an internet-based questionnaire recalling either their activity or dietary intake over the previous 24 hours. Results of this pilot study are expected to shape the next steps in our studying lifestyle as a potential modifier of cancer risk.

A Pilot Study of Metformin in Patients with a Diagnosis of Li-Fraumeni Syndrome (NCI 14-C-0005) is currently enrolling eligible participants. Metformin is an oral medication that has been used to treat diabetes for decades. Recent studies indicate that metformin may also help prevent cancer. Drs. Farzana L. Walcott and Antonio T. Fojo of the NCI Medical Oncology Branch are conducting a clinical trial to determine the safety of metformin in individuals with LFS who take the medication over a short period of time. If you are interested in learning more about this study, you can find more information at *https://www.clinicaltrials.gov/*, the study number is NCT01981525.

Use of Social Media and the Internet: We are conducting a survey of LFS family members to help us understand how the internet and social media are used to communicate and share health information about LFS. We would appreciate your sharing with us if and how you use the internet and social media for this purpose. The information gathered will help us develop strategies to support the communication of health information among family members. If you choose to complete the attached survey, please use the accompanying instructions to return it to us.

Fresh tissue collection efforts. The ability to obtain and retain a sample of fresh tissue at the time of surgery is a high priority for the study. The collection of these surgical specimens is essential to our research efforts to understand the underlying genetic changes that result in the transformation of normal tissue into cancer. If you are to have a biopsy or surgery, please call the LFS Study Research Nurse, Janet Bracci, R.N. (301-212-5265) if you are willing to contribute to the tissue collection. With your permission, Janet will work with your local healthcare providers and local institution to collect and transport the material to our biospecimen repository.

Effects of *TP53* mutations on the genome. Several studies are underway that will evaluate the DNA of individuals with and without *TP53* mutations in order to better understand the molecular consequences of these mutations.

Collaboration with investigators in Brazil. We are collaborating with investigators at two institutions in Brazil who follow a large number of LFS families. Common questionnaires have been developed and many exciting studies are planned.

Useful Resources

- **NCI LFS study website:**
  http://www.lfs.cancer.gov

- **Li-Fraumeni Association**
  www.lfsassociation.org
  The LFS Association is comprised of families who are affected by Li-Fraumeni Syndrome. The organization hopes to educate, raise awareness and find better screening programs and treatments for LFS.

- **LiFE Consortium:** Li-Fraumeni Exploration Consortium
  http://epi.grants.cancer.gov/Consortia/single/life.html

  The mission of the LiFE Consortium is to:

  - Foster communication among investigators studying Li-Fraumeni Syndrome
  - Promote collaborative research projects for topics not easily addressed in a single study in order to advance our understanding of LFS and its impact on affected families, which will lead to improved clinical care
  - To provide a platform for joint activities between professionals and associations of patients and families to promote support, education and awareness, both among families and in the society at large

The second Li-Fraumeni Syndrome Conference occurred on Oct 25-26, 2013, at the Dana-Farber Cancer Institute, Boston, MA. The conference was sponsored by Dana-Farber Cancer Institute, LiFE Consortium, and the LFS Association, and was attended by families as well as clinicians and researchers. A video-cast of the conference can be viewed at:
http://www.lfsassociation.org/li-fraumeni-syndrome-conference/

Disclaimer: We are providing web addresses to internet sites for informational purposes and for your convenience. Please note the following:

- When you view a non-NCI website, you are subject to the privacy and security policies of the owners/sponsors of that external website.
- NCI does not endorse organizations that sponsor external websites. In addition, NCI does not endorse products or services that such organizations may offer. Furthermore, NCI does not control or guarantee the currency, accuracy, relevance, or completeness of information found on external websites.

Selected Recent Publications

Mai PL, Malkin D, Garber JE, et al., Li-Fraumeni syndrome: report of a clinical research workshop and creation of a research consortium. *Cancer Genet* 2012; 205(10):479-87. PubMedCentral: *http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3593717/*

Malkin D. Li-Fraumeni Syndrome. *Genes Cancer* 2011; 2(4):475-84. *http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3135649/*

Masciari S, Dillon DA, Rath M, et al. Breast cancer phenotype in women with *TP53* germline mutations: a Li-Fraumeni syndrome consortium effort. *Breast Cancer Res Treat* 2012; 133(3):1125-30. *http://www.ncbi.nlm.nih.gov/pubmed/22392042*

Ognjanovic S, et al., Sarcomas in *TP53* germline mutation carriers: a review of the IARC *TP53* database. *Cancer* 2012; 118(5):1387-96. *http://onlinelibrary.wiley.com/doi/10.1002/cncr.26390/full*

Sorrell AD, et al., Tumor protein p53 *(TP53)* testing and Li-Fraumeni syndrome : current status of clinical applications and future directions. *Mol Diagn Ther* 2013 Feb; 17(1):31-47.
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3627545/

Wang PY, et al., Increased oxidative metabolism in the Li-Fraumeni syndrome. *N Engl J Med* 2013; 368(11):1027-32.
http://www.nejm.org/doi/full/10.1056/NEJMoa1214091#t=article

Greetings from the NCI-LFS Research Team

LFS Team (from left to right): *Nicole Dupree-Battle, MPH, Janet Bracci, RN, BSN, Sylvia Nqwa, BA, Jennifer Loud, RN, CRNP, DNP, June Peters, MS, CGC, Phuong Mai, MD, MS, Renee Bremer, MS, Katie Loughlin, MPH, Sharon Savage, MD, Kathy Nichols, RN, BSN*
Not pictured: *Stephanie Steinbart, RN, MPH, GCN*

The LFS study team includes a group of experts who bring their own special perspective to the project. Studying the many aspects of familial/hereditary cancer disorders requires the knowledge and expertise of disciplines such as cancer genetics doctors and nurses, genetic counselors, study managers, data coordinators and research assistants.

Are you relocating or changing your phone number? Please contact **Janet Bracci, R.N.,** at 301-212-5250

If you want to refer someone, please contact **Stephanie Steinbart, R.N.,** our referral nurse, at 301-212-5250 or 800-518-8474.

Study E-mail is NCILFS@westat.com

We want to thank you again for your participation in the NCI LFS Study. Studies like this are possible only with a mutual collaboration among families and researchers. Every person's contribution is important to the success of the whole study.