



Li-Fraumeni Syndrome (LFS) Study Newsletter

Division of Cancer Epidemiology and Genetics • Clinical Genetics Branch

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MESSAGE FROM THE NCI LFS STUDY TEAM

We thank you for your continued involvement with the NCI Li-Fraumeni Syndrome (LFS) Study. As our study enrollment has grown, so has the study team. We added clinicians, laboratory scientists, and a new genetic counselor. To meet our team members, see page 4.

World-renowned LFS expert, **Dr. Maria Isabel Achatz**, has

joined our study team as a co-principal investigator, alongside Dr. Sharon Savage. Dr. Achatz has been working closely with LFS families since 2003, in the clinic and through epidemiological and molecular studies. Her group identified the high occurrence of a founder mutation among the general population in the South/Southeastern regions of her native Brazil.

RESEARCH HIGHLIGHTS

Risk of First and Subsequent Cancer in the NCI LFS Study

The NCI study team recently conducted and published the first analysis of cancers in our study participants. We evaluated the types and number of cancers in 286 individuals with *TP53* mutations from 107 families. For females, the risk of cancer was highest after age 20, due primarily to breast cancer. For males, the risk of cancer was higher in childhood. The types of cancers developing in people who had already had one cancer were similar to the types of first cancers. This study and those

published by other groups is helping us better understand the types of cancers and age of onset in people with LFS. In the future, we hope to use these data to refine our cancer screening practices.

Mai PL, Best AF, Peters JA, DeCastro RM, Khincha PP, Loud JT, Bremer RC, Rosenberg PS, Savage SA. [Risks of first and subsequent cancers among *TP53* mutation carriers in the National Cancer Institute Li-Fraumeni syndrome cohort.](#) *Cancer* 2016 Aug 6. [Epub ahead of print] PMID:27496084.

Cancer Screening for Patients with LFS

In June 2016, the NCI study team presented results of cancer screening tests for 100 study participants at the annual meeting of the American Society of Clinical Oncology. In addition, we are working collaboratively with at least eight institutions from around the world to combine data across study populations. We are in the process of analyzing the data and summarizing our findings in scientific manuscripts. We will share these results with you once they are published.

Emotional, Social and Spiritual Support in LFS Families

In addition to studying the effect of LFS on cancer risk and physical health, the NCI LFS study team also evaluates emotional and social well-being. In a review of 65 study participants we found that this group seemed to be coping well. They reported little distress, with a few exceptions. Friendships, in addition to nuclear family and family of origin, were often deep and enduring and provided an important source of information, as well as tangible, emotional, and spiritual support. Organized religion was important in some families, typically from mainstream traditions. Other participants reported a spiritual or humanist outlook on life and nature that sustained them.

Peters JA, Kenen R, Bremer R, Givens S, Savage SA, Mai PL. [Easing the burden: Describing the role of social, emotional and spiritual support in research families with Li-Fraumeni Syndrome.](#) *J Genet Couns* 2016 Jun;25(3):529-42. PMID:26621765.

Participants' Interest to Receive Results from Genomic Research Testing

As you know, a major component of our study involves analyzing genetic material you provided. These tests result in primary, secondary and "incidental" findings. Often the health implications of "incidental" results are unclear. As part of the informed consent process for participants we regularly ask whether you wish to receive these results. A recent survey of adults in our study revealed that the vast majority of you wanted this information. To learn more about the survey results, you can read the abstract or full report.

Loud JT, Bremer RC, Mai PL, Peters JA, Giri N, Stewart DR, Greene MH, Alter BP, Savage SA. [Research participant interest in primary, secondary, and incidental genomic findings.](#) *Genet Med* 2016 Apr 21. [Epub ahead of print] PMID:27101135.

UPDATES FROM THE NCI LFS STUDY

Family Interview Study

In 2012, we launched the Family Interview Study as an extension of our psychological and social research conducted in the LFS study. The purpose of the interviews is to explore and understand the ways in which families with LFS communicate with and support each other in ways that may or may not be related to their health. Jennifer Young, MA, MS, LGMFT, a trained couples and family therapist, conducts in-depth interviews with two or more family members during their visits to the NIH Clinical Center. She explores the specific challenges that arise in navigating a wide range of individual and family issues that might be affected by the presence of LFS.

Physical Activity and Diet Pilot Study

In 2014, we launched a pilot study on Physical Activity and Diet (PAD) in LFS families. This was the first step towards determining whether it is feasible to collect these complex data from our study participants. A random sample of participants were invited to provide information about their daily diet and physical activity using a web-based questionnaire. The pilot was successful and we are now exploring opportunities to conduct a larger study to understand whether modification of diet and physical activity could improve the overall health and well-being in LFS families.

WHAT'S NEW IN LFS?

Updated Results from the “Toronto” Protocol

Drs. Anita Villani, David Malkin, and colleagues, reported results of their intensive cancer screening protocol for 89 people with pathogenic variants (i.e., mutations) in *TP53*. Of that group, 40 underwent cancer surveillance (also known as screening). From the 49 who initially declined surveillance, 19 people opted to participate. Patients were followed for an average of 32 months. Forty tumors were detected in patients who did not have symptoms. The screening protocol is very intensive with annual whole body and brain MRI, breast MRI for women, and blood work every 3-4 months for everyone, as well as abdominal ultrasound every 3-4 months for children. The researchers concluded that people undergoing surveillance had improved overall survival, compared with those who did not follow this intense regimen. These results are promising, but data from more studies will be helpful in developing the best approach for individual patients. We and the rest of the international LiFE consortium members are actively working towards this goal.

Villani et al. [Biochemical and imaging surveillance in germline mutation carriers with Li-Fraumeni syndrome: 11- year follow-up of a prospective observational study](#). *Lancet Oncology* 2016 Sep;17(9):1295-305. PMID:27501770.

RESOURCES

In order to further connections through social media, NCI helped to establish the first recognized LFS hashtag. Be sure to use #LiFraumeni when posting to Twitter, Facebook, and Instagram:

<http://www.symplur.com/healthcare-hashtags/lifraumeni/>.

LiFE Consortium and LFS Association Conference

The 3rd Annual Li-Fraumeni Syndrome Exploration (LiFE) Consortium and LFS Association Conference was held in Columbus, OH, June 1-3, 2016. An international gathering of families, doctors, nurses, genetic counselors, nutritionists, and basic scientists, presented the latest information about LFS. There were also moving testimonials from families, friends, and survivors. For a photo gallery, and to learn more about this and prior conferences, visit the **LFS Association** website at:

<http://www.lfsassociation.org/reach2016gallery/>

Living LFS family support group:

<http://www.LivingLFS.org>

For video excerpts of the meeting visit YouTube:

https://www.youtube.com/playlist?list=PLsq0zkSXkPNNIfE_uOMmYfFMOzNPDzdYc

Check our study website for updates in between newsletters, view study team bios, and more:

<http://www.LFS.cancer.gov>

To learn more about the Healthcare Hashtag Project:

<http://www.symplur.com/healthcare-hashtags/>.

Healthcare Hashtag Project, a free open platform for patients, caregivers, advocates, doctors and other providers that connects them to relevant conversations and communities.

MEET THE NCI LFS STUDY TEAM



From left: Kelvin Andrade, Rosamma DeCastro, Talia Wegman-Ostrosky, June Peters, Nicole Dupree, Kathy Nichols, Megan Frone, Jennifer Loud, Renee Bremer, Sharon Savage, Maria Isabel Achatz, Janet Bracci, Payal Khincha, Katie Beebe, Maureen Risch, Jenni Young, Sylvia Ngwa.

Missing: Diana Merino

Clinicians: Sharon Savage, Maria Isabel Achatz, Jennifer Loud, Payal Khincha, Rosamma DeCastro

Research Nurses: Janet Bracci, Kathy Nichols, Maureen Risch

Genetic Counselors: June Peters, Megan Frone

Data Manager and Research Assistants: Renee Bremer, Katie Beebe, Nicole Dupree, Sylvia Ngwa

Research Fellows: Kelvin Andrade, Talia Wegman-Ostrosky, Jenni Young, Diana Merino

Please see the NCI LFS website at: <http://www.lfs.cancer.gov> to find out more about the key staff members and their roles on the study.