NEWSLETTER

Visit 2 Study Update

We are very grateful for your continued participation in the Long Life Family Study and with your help we have reached the very exciting midpoint of the Visit 2 phase of our study. For those of you who have completed a second home visit, we have enjoyed seeing you in person again! It has been our pleasure to have an opportunity to touch base with you during this important phase of LLFS. If we have not yet contacted you for Visit 2, we will be within the next year. It is important to us that we see you in person if at all possible so that we can gain a better understanding of the mechanisms behind achieving a long and healthy life. Everyone in the LLFS will be contacted once per year for our usual surveillance follow-up call.

With your help, we have assembled and maintained contact with an exceptionally long lived and special cohort! As of July 14, 2016, 1922 participants have been seen across all four field centers (Columbia University, University of Pittsburgh, Boston University and University of Southern Denmark) for Visit 2. Currently, our oldest living participant is 105 years of age. Additionally, we have 31 participants who are over age 100 and many of them are very active and healthy. Of the 1922 participants seen during Visit 2, 24% are in the oldest generation and 76% are in the offspring generation. We have also enrolled 361 spouses of offspring and 98 new participants from already enrolled families. Each family member, regardless of age or whether s/he is a blood relative, is a critically important part of this groundbreaking investigation into the secrets of longevity.

The Columbia University team in NYC has visited **469** participants of a total of **802** participants who we plan to see for Visit 2. Aside from visiting our participants in the local tristate area, we have also recently travelled to see our participants who reside in California, Arizona, Missouri, Nevada, Virginia, North Carolina, Florida, etc. Since your participation in this study is crucial for aiding us to determine the secrets to living a long and healthy life, iwe have been happy to traverse the country to meet with you again. With careful collaboration among the US field centers, we may ask your permission to be visited by a different field center that has a trip planned to your region of the country.

Please continue to keep us posted on how you and your family members are doing . We cannot continue to understand the keys to exceptional survival without each of you. If you have any questions about LLFS, which is funded by the National Institute on Aging of the National Institutes of Health, contact us at the Columbia University Field Center via our toll-free telephone number at 1-800-304-4317.

We look forward to visiting you and/or speaking to you soon!

LLFS Research Update

The LLFS researchers have made many recent discoveries about longevity which have been published in scientific journals as well as proudly presented at national and international scientific meetings. Since LLFS began, we have published 36 papers in major scientific journals. Some of our current advances and areas of interest include:

Comparing Families in the Long Life Family Study Across Five Health Systems

Is your exceptional survival because of a gene that promotes health and longevity, or is it because of your healthy environment and behavior, or maybe a combination of both? We wanted to determine if there are families in LLFS who have a lot of family members that are much healthier than you would expect on more than one system in the body. Are the LLFS families who have a lot of members with exceptionally healthy memory also the families who have a lot of members with exceptional strength? We identified a group of LLFS families who are healthier than one would expect on at least one of the following systems: memory, grip strength, pulmonary, blood pressure, and metabolism. We found that families did not appear to be exceptionally healthy on multiple systems: there were no families who were exceptionally healthy on all five systems, 2 families were exceptionally healthy on four systems, and only 4 families were exceptionally healthy on 3 systems. This suggests unique pathways to healthy aging in each system. Each family may have a unique set of genes or a unique combination of genes and environment. It also supports the need to focus on specific systems as we pursue additional genetic sequencing.

LLFS Using Cutting Edge Genetic Sequencing Techniques

The Long Life Family Study is looking for familial genetic changes that promote healthy aging by utilizing a novel DNA sequencing technique developed at Washington University in St. Louis. The method - known as MDiGS for **M**ultiplexed **Di**rect **G**enomic **S**election - allows the team to precisely target specific regions of the genome. These large regions contain many genes and were identified in previous LLFS experiments as areas where families may share genetic changes that result in one or more exceptional health outcomes (blood sugar, longevity, heart health, cognitive ability and many others). MDiGS will allow us to sift through the millions of genetic units in these regions in hundreds of LLFS participants to identify the precise genetic changes in all members of families that have exceptional health features. A project like this hasn't been attempted before on this scale. The unique family structure of the LLFS population and the tremendous infrastructure of genetic technology at Washington University are a perfect match to discover new clues to living a long and healthy life.

Why are we using a Digital Pen during the Visit 2 Examination?

For those of you who have already completed your second in-person visit, you may remember that we asked you to use a different type of pen for the written portions of the memory and thinking tests. This digital pen allows us to record your written and drawn responses and play them back as a short video at a later time. It also allows us to study precise measurements that we would not be able to track with a traditional pen. In fact, the Framingham Heart Study also uses this pen and has looked at differences in “ink time” (time spent drawing on the paper) versus “think time” (time spent thinking about what to draw or write with the pen off of the paper). We plan to compare values for participants from the Long Life Family Study to those from the Framingham Heart Study. This novel measure will also allow us to study changes in drawing and writing that may be related to cognitive decline and perhaps can be detected much earlier than more traditional measures.

USE NEXT TIME IN DECEMBER

We have been working hard to analyze the information collected during our meetings with you. As a result of your continued participation in the annual phone interviews and the most recent home visits, we have made the following recent discoveries about longevity which have been published in various scientific journals within the past year. Additionally, we have also very proudly presented some of these findings at recent national and international scientific meetings:

1. ***Physical activity and pulmonary health —*** *Using the information we have collected from our study participants, we have discovered that both physical activity and pulmonary health appear to be two key heritable factors closely associated with longevity. This means that, if you are a member of a family of long-lived individuals, you may be more likely to engage in physical activity and have better pulmonary health, thereby increasing your likelihood of living a longer and healthier life.*

2. Alzheimer's disease— *One of our most recent findings involves the discovery that LLFS participants appear to carry fewer risk alleles (a form of a gene arising from a mutation) for Alzheimer's disease compared to unrelated spouses. This may suggest that participants of long-lived families may be at a lower risk of getting Alzheimer's disease which is a condition that involves memory loss typically among those over age 65.*

2. Telomere length

We have been continuing our investigation of telomere length. As previously mentioned, researchers have found that longer telomere length, in white blood cells, appears to be a heritable trait which has been associated with living a longer life. Alternatively, shorter telomere length has been found to be associated with dementia and other age-associated processes. Our most recent finding, resulting from LLFS participants, involves a newly-identified rare gene, associated with telomere maintenance, which appears to be associated with exceptional survival.

Additionally, a second paper on telomere length was recently published which supports previous findings and further indicates that, among our participants in the offspring generation, those who are more-closely-related to the elderly probands have a longer telomere length than those less-closely-related such as unrelated spouses.

4. Maternal age at birth

We have also recently found that LLFS participants, who had their last child when they were older than 33 years of age, were more likely to live a longer life than women who had their last child by age 29 years of age. This suggests that older maternal age may predict a greater likelihood of longevity.