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*The New England  
Centenarian Study*



**May 2014**

## **Long Life Family Study Funding Continued Through 2019**

**We** are very pleased to announce that the Long Life Family Study has been awarded a 5 year renewal grant by the National Institutes of Health! In fact, the reviewers of the renewal application were so pleased with the significance and innovation of the study, that the application was given a perfect score. We would not have been able to achieve such a spectacular review had it not been for the enthusiastic and dedicated participation of all of our LLFS families! Therefore we send all of you a huge thank you!

Because of your dedication to the Long Life Family Study (LLFS) we are beginning to understand the secrets of very long, healthy lives. We have published findings indicating that overall, LLFS subjects have much lower rates of age-related diseases and disabilities. By studying families, rather than unrelated individuals, we expect to gain insights into genetic, behavioral and environmental factors that family members have in common that give them such a healthy aging advantage. We cannot thank you



enough for your past, present and future participation in the LLFS. Inside this newsletter, we provide you with some of our key published findings thus far.

Aging is indeed a slow process, but among many LLFS participants, it is even slower! So for us to detect changes over time, we need to call you every year to get updates on how you are doing. Some clinical characteristics however cannot be determined over the phone and so we need to come and visit you in person. With this renewal we are planning to do just that, so please anticipate another home visit from us in the coming couple of years!

**We Can't Wait to See You  
Again!**

This repeated examination will be similar to our first in-person visit with you. We will be in touch with you as we get ready to perform this visit, in order to explain what we will be doing and to come up with a time that works best for you and your family. We are so excited to come see you in person again!

## Telomeres and Long Life

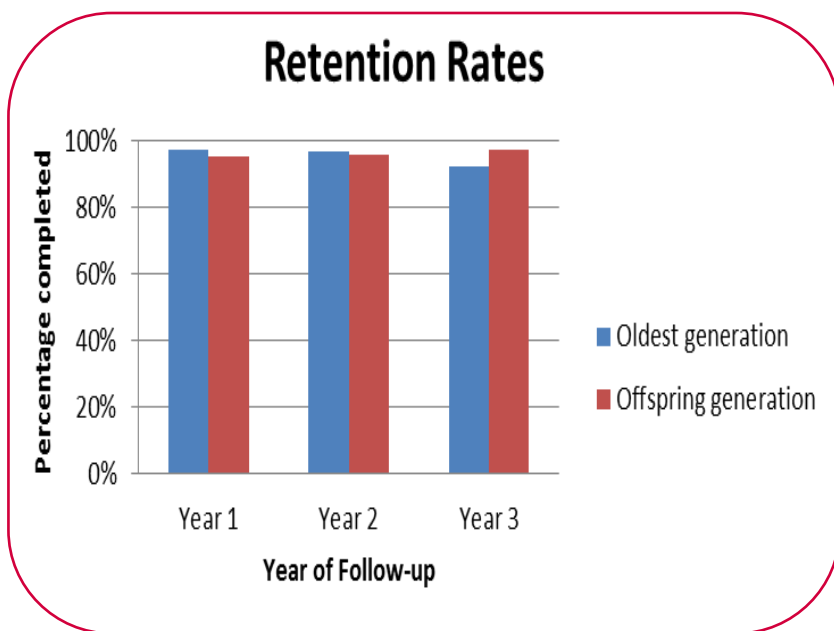
**“We also found that the children of the long-lived participants have longer telomeres”**

Some of the blood sample that we obtained from our Long Life Family Study (LLFS) participants was used to measure the length of their telomeres. Telomeres are structures that help maintain the structural integrity of our chromosomes. Chromosomes contain our DNA or genes. As we age, scientists have noted that telomeres become shorter and shorter, making our chromosomes and subsequently our cells, more vulnerable to damage. In the New England Centenarian Study, we have previously noted that the children of centenarians have longer telomeres which may mean their cells can age more slowly. We went on to determine telomere lengths in the cells of LLFS participants and have found that they also have longer telomeres. Now we are embarking on



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studies to try to understand how and why telomeres are longer in our participants. Presumably, one of the reasons is because of some specific genes that are common amongst LLFS family members that help keep these telomeres long. We are also looking into environmental and life style factors that family members have in common (like diet, not smoking or drinking, exercise etc.).



Our participant retention rate is the percentage of participants (from all of those who originally joined the study) who provided follow-up information. As you can see from the graph, our rates are consistently high, over 90% for both generations. This is an exceptionally good rate

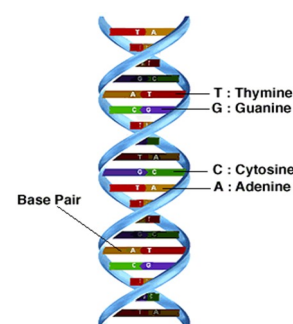
## On the Trail of Genetic Factors that can Contribute to Longevity

One of the most exciting aspects of the Long Life Family Study, and one of its major goals, is the possibility that we may discover new genetic secrets of healthy aging and longevity. Studying people who are related and also have a trait in common, like longevity, can be a very powerful approach to discovering variations in genes that they have in common (and not in common) that could be important to achieving a very healthy old age. One of the interesting things we are finding is that some families likely have some genetic variations that are relatively rare in the general population that afford some type of protection against aging and age-related diseases. Furthermore, one family might have a particular rare or set of rare variants while another family might have a different set. Using an approach called genetic linkage, we are finding that one such set may be related to protection against diabetes while another set could be related to telomere

length (please see the article about telomeres on the previous page).

### Base-Pairs

A Base-Pair is a rung of the ladder of our DNA, made up of two nucleotides. There are four possible nucleotides and it is the many different sequences of these base pairs that are the blue prints of our genes. We all have the same genes, but it's the tiny variations in specific base pairs of our genes that make us genetically different from one another. In the Long Life Family Study we look for variations that family members have in common that explain their healthy longevity.



### FUN FACT

*From the blood samples that you provided, we have analyzed about 2.5 million genetic variants, known as single nucleotide polymorphisms or SNPs (pronounced "snips"). Now that is no small feat!*



**The University of Southern Denmark LLFS Study Site.** There are 3 American study sites that enrolled and now annually keep in touch with the LLFS participants, and one study site in Denmark, in Northern Europe that does exactly the same thing. Why Denmark? Having a study site in Denmark gives LLFS investigators the opportunity to study long living families in another part of the world and to take advantage of those cultural and environmental differences in better understanding the determinants of longevity. The Danish site also has some unique advantages like church books and other databases that keep meticulous vital records of all families in Denmark going back to the 16th century! Their system of universal health care also allows access to participants' complete health records since they were born. These preliminary results suggest that part of the explanation for the exceptional survival in these Danish families is health behavior.



## LLFS Recent Findings

### MIDDLE AGED MOTHERS LIVE LONGER

Early in the New England Centenarian Study in the late 1990s, we published an article in *Nature* magazine stating that about 20% of the centenarian women in the study had a history of having at least one of their children beyond the age of 40 years. This was about four times the rate of women also born around 1900 but who survived to just average life expectancy. We interpreted these findings to indicate that being able to have a child beyond the age of 40 years was a marker of the woman's reproductive system aging relatively slowly and not having age-related diseases that could decrease fertility, like diabetes and cardiovascular disease.

Now we have looked at our LLFS data and we are seeing a similar pattern among the female LLFS participants. Our statistician colleagues at Boston University School of Public Health, Fangui Sun and Paola Sebastiani, have found that LLFS women who had at least one of their children beyond the age of 33 years had a two times greater chance of living to very old age (the top 5th percentile of survival) compared to participants who didn't give birth beyond the age of 29 years. The findings once again support the observation that older maternal age (without the assistance of fertility technologies) can be a marker of slower aging and increased likelihood of living to advanced age.

Our observation also has ramifications for why there might be genes that allow women to live much longer beyond the age of menopause. Having genes that allow a person to age more slowly could help a woman be fertile for a longer period of time and therefore have the opportunity to have more children. These genes then also help her live at least 15 years after the birth of her last child to successfully rear them to the age that they are independent. Protective genes would also allow women to reach the age of grandparenthood or even great-grandparenthood, so they can help take care of and insure the survival of younger generations.

### Genetic Terminology

- **Genome** – An organism's complete set of DNA, including all of its genes.
- **Genome Wide Association Scan – GWAS** - A way for scientists to identify genes involved in human disease or trait, like longevity. This method searches the genome for small variations, called single nucleotide polymorphisms or SNPs (pronounced "snips"), that occur more frequently in some people than in other people. Most are normal variations but some are related to disease risk or longevity. A study can look at hundreds or thousands of SNPs at the same time.
- **Genetic variants** – Differences between one gene and another due to small differences in the DNA code.
- **DNA** - Deoxyribonucleic acid - The chemical name for the molecule that carries genetic instructions in all living things. The DNA molecule consists of two strands that wind around one another to form a shape known as a double helix.
- **Chromosomes** - An organized package of DNA found in the nucleus of the cell. Humans have 23 pairs of chromosomes. Each parent contributes one chromosome to each pair so that offspring get half of their chromosomes from their mother and half from their father.
- **Genes** - The basic physical code for a biologic trait such as eye color or protein structure. Genes are passed from parents to offspring and contain the information needed to specify traits. Humans have approximately 23,000 genes arranged on their chromosomes.
- **SNPs** - Single nucleotide polymorphisms - A variation of a single base pair of DNA. Same as a genetic variation. Scientists are studying how SNPs in the human genome correlate with disease, longevity, drug response, and other clinical characteristics.

## Cognitive Function in Long-Lived Families Study

Stacy Andersen, the New England Centenarian Study and Long Life Family Study Project Manager, has completed her dissertation which included 170 participants from long-lived families of the Long Life Family Study and 141 participants without familial longevity. In the older generation, she found that people without familial longevity had higher education yet they still performed at levels similar to people with familial longevity, even though higher education is usually associated with better cognitive performance. This suggests that long-lived family participants may have genetic or environmental advantages associated with being part of a long-lived family that may preserve cognitive function through other pathways. In the offspring generation, she found that participants from long-lived families had better scores on a test of attention than participants without familial longevity. She also analyzed the role of cognitive reserve in test scores. Cognitive reserve is built up by life experiences such as reading, playing games, and lifetime job complexity. It is believed to prevent cognitive impairment resulting from brain dam-

age from aging and neurodegenerative processes. Stacy found that people from long-lived families had lower levels of indicators of cognitive reserve even though they had cognitive test scores similar to people with higher levels of cognitive reserve, indicating once again that being part of a long-lived family may lead to preserved cognition through other pathways. People without familial longevity may be more reliant on better education and more cognitive reserve to achieve similar test performance to people from long-lived families.

Stacy hopes to generate many more results with additional data analysis which will be shared soon. She also wishes to thank everyone who so generously donated their time to take part in the study. She couldn't have done it without you!

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## Staff Updates

**Stacy Andersen** has, on top of all her other responsibilities, completed her dissertation using data from the Cognitive Function in Long-Lived Families study. She graduated on May 17th with her PhD in behavioral neuroscience from Boston University School of Medicine. She is also recently engaged and is planning a wedding for the fall of 2014. **Lori Feldman** has finished her third and final year of her Master's in Social Work from Salem State University. Her concentration is older adults/end of life and, after graduating

on May 15th, she will be leaving the LLFS (after seven years!) to work with older adults in a social work capacity. **Jesse Gass** continues to pursue her interest in mental health and hopes to apply to doctoral programs in clinical psychology next year. **Tara Neary** has been accepted to Boston University School of Medicine and will be starting in the fall. She also plans to run her first marathon in the spring! **Dr. Tom Perls**, Director of the New England Centenarian Study and the Boston Study Center of the LLFS

*Continued on page 6*

## Gerontological Research Meeting

The 2013 Gerontological Society of America's Annual Scientific Meeting was held in New Orleans, Louisiana and we once again had the privilege of presenting. The NECS staff were well-represented in poster sessions and symposia.

- Dr. Perls led the Long Life Family Study's symposium titled, "The Long Life Family Study and The Genetic and Phenotypic Study of Exceptional Aging." Each Study Center of the LLFS presented some of their key research, and Professor Paola Sebastiani from Boston University's School of Public Health presented findings on the genetic makeup of exceptional longevity.
- Stacy Andersen presented a poster titled, "Centenarians delay retirement and driving cessation," showing that centenarians relatively delay retirement and driving cessation by up to a decade. The ability to work and drive longer may indicate preserved physical and cognitive function of centenarians compared to the general population of the same birth cohort.
- Jesse Gass' poster was titled, "Never-Married Status in the New England Centenarian Study (NECS)." She found that rates of having never



married/remaining single were substantially lower in centenarians than in the general population. She also found that the association between marriage and longevity is stronger for men. These findings support previous research that for most people, marriage is associated with lower mortality.

- In a poster titled, "Age of Onset and Prevalence of Dementia in Centenarians Using 3 Different Assessment Tools," Tara Neary presented data on how three dementia assessment tools used in the New England Centenarian Study compared in determining the presence and age of onset of dementia in centenarians. She found that self-report is adequately sensitive only for severe cognitive impairment, whereas a memory test is the most sensitive measure of cognition used in our studies. An informant questionnaire, the Dementia Questionnaire, is especially useful in our study population because it can be administered for subjects with sensory impairments that prevent direct testing with a memory test.

### Staff Updates continued

is also a geriatrician at Boston Medical Center and professor of medicine at Boston University School of Medicine. He was recently honored with the Ewald W. Busse Research Award. One of the most prestigious in the field of gerontological research, the award is given every four years in conjunction with the World Congress of Gerontology and Geriatrics in Seoul, Korea.

### NECS Staff Photo



From left to right: Stacy Andersen, Jesse Gass, Tara Neary, Lori Feldman, and Dr. Tom Perls.

## Recent Publications



Sebastiani P, Bae H, Sun FX, Andersen SL, Daw EW, Malovini A, Kojima T, Hirose N, Schupf N, Puca A, Perls TT. [Meta-analysis of genetic variants associated with human exceptional longevity.](#) *Aging (Albany NY)*. 2013;5(9):653-61.



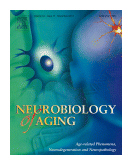
Cosentino S, Schupf N, Christensen K, Andersen SL, Newman A, Mayeux R. [Reduced prevalence of cognitive impairment in families with exceptional longevity.](#) *JAMA Neurol*. 2013 Jul;70(7):867-74.



Bae HT, Sebastiani P, Sun JX, Andersen SL, Daw EW, Terracciano A, Ferrucci L, Perls TT. [Genome-wide association study of personality traits in the long life family study.](#) *Front Genet*. 2013 May 8;4:65.



Sanders JL, Minster RL, Barmada MM, Matteini AM, Boudreau RM, Christensen K, Mayeux R, Borecki IB, Zhang Q, Perls T, Newman AB. [Heritability of and mortality prediction with a longevity phenotype: The healthy aging index.](#) *J Gerontol A Biol Sci Med Sci*. 2013 Aug 2.



Barral S, Cosentino S, Costa R, Andersen SL, Christensen K, Eckfeldt JH, Newman AB, Perls TT, Province MA, Hadley EC, Rossi WK, Mayeux R; Long Life Family Study. [Exceptional memory performance in the Long Life Family Study.](#) *Neurobiol Aging*. 2013 Nov;34(11):2445-8.



Elo IT, Mykyta L, Sebastiani P, Christensen K, Glynn NW, Perls T. [Age validation in the long life family study through a linkage to early-life census records.](#) *J Gerontol B Psychol Sci Soc Sci*. 2013 Jul;68(4):580-5.



Sebastiani P, Sun F, Andersen SL, Lee J, Wojczynski MK, Sanders JL, Yashin AJ, Newman AB, and Perls TT. [Families enriched for exceptional longevity also have increased health-span: findings from the long life family study.](#) *Front Public Health* 2013, doi: 10.3389



Perls T. [The reappearance of procaine hydrochloride \(gerovital h3\) for antiaging.](#) *J Am Geriatr Soc*. 2013 Jun;61(6):1024-5.



Lee JH, Cheng R, Honig LS, Feitosa M, Kammerer CM, Kang MS, Schupf N, Lin SJ, Sanders JL, Bae H, Druley T, Perls T, Christensen K, Province M, Mayeux R. [Genome wide association and linkage analyses identified three loci-4q25, 17q23.2, and 10q11.21-associated with variation in leukocyte telomere length: the Long Life Family Study.](#) *Front Genet*. 2014;4:310.

## Centenarian Highlight

When Edythe Kirchmaier drove her first car – a Model T – at the age of 16, she never imagined that she would still be behind the wheel nearly 90 years later. To commemorate this milestone, Edythe was recently given a brand new Honda Civic by an anonymous donor. It is fitting that this act of kindness was bestowed



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upon Edythe, a woman who has dedicated her life to helping others. Describing herself as “a caring, giving person with a love for life,” she says, “I just love the universe – there isn’t anybody I don’t like.” Edythe has long sought to connect with people and make the world a better place. At 105-years-old, she doesn’t plan on stopping anytime soon.

From a very young age in Springfield, Ohio, Edythe’s mother instilled in her “a need to care for others.” Her mother had a large victory garden, which fed the family and the neighborhood, and she was known for taking in those who were less fortunate and giving them a meal in exchange for a few hours of work. It was her mother’s generous spirit, Edythe says, that inspired her to pursue a career in social work.

Edythe began her studies at Ohio State University at a time when women were just beginning to enter higher education and she says “women were ready for it.” Afterwards, she moved to Chicago, where she completed two semesters of graduate work and then took a position at the Illinois Emergency Relief Commission, a job that was to change her life. There, she met her future husband, Joe, who was also a social worker, and they were married in 1938. They relocated to California, had a son,

Raymond, in 1940, and a girl, Mary, in 1943. The family eventually settled in Santa Barbara, where Edythe still lives in her home of 65 years.

Good genes, a healthy lifestyle, and a positive attitude are the three factors to which Edythe attributes her longevity, adding that she has “to give God some credit!”. It’s important, she says, to maintain a positive outlook and avoid dwelling on the negative, insisting that “you never get too old to enjoy life.” The activity that gives her the most joy is volunteering for Direct Relief, a medical aid organization that serves people around the world. She has worked as a volunteer for them for more than 40 years and currently serves as spokeswoman. Other favorite activities include making crafts, participating in senior groups, attending luncheons and church functions, and spending time with her 6 grandchildren and 17 great-grandchildren.

Edythe has lived through more than a century of remarkable changes. Among those, she believes that the birth of aviation and the internet were the most significant because they brought people closer together. In fact, as Facebook’s oldest registered user and with more than 30,000 followers, she sets a living example. For her 105th birthday, she launched a Facebook campaign to gather support for Direct Relief, even appearing on national television with Jay Leno and Ellen DeGeneres. She gets a kick out of being recognized in public now, but doesn’t let it go to her head. When asked to name the most memorable events in her life, she responds, “All of them. I’ve enjoyed every minute of my life. I have no regrets.”



**Our heartfelt gratitude goes out to The Samowitz Foundation for generously funding this year's newsletter and other activities.**

## Funding and Philanthropic Support

Funding of our research primarily comes from the National Institute on Aging (NIA), a member institute of the National Institutes of Health (NIH).

Over the previous year we were extremely fortunate to receive a research grant from the reinsurance company Swiss Re, which funded our work investigating the family trees of centenarians. We are studying those data to determine patterns

of longevity in families and how to use those family survival data to determine an individual's own chances of living to very old age.

If you might be interested in contributing funds for our research efforts, please do not hesitate to contact us. Dr. Perls can be reached at 617-638-6688 or email him at: [thperls@bu.edu](mailto:thperls@bu.edu).

## Recruitment

We are always looking for participants throughout North America for our studies. If you know of any centenarians age 105 and older who may be interested, please call our study toll-free at 1-888-333-NECS (6327) or email Stacy Andersen ([stacy@bu.edu](mailto:stacy@bu.edu)).

## Send us your pictures!

We love getting your pictures! Please send us your photographs — email it or send it through the mail! We make regular submissions to various media and we love being able to include photographs of our amazing participants. If we decide to use your photo for any reason, we will contact you and your family first to obtain permission.

If you wish, we will be happy to return any mailed photographs to you. Our mailing address is on the front page. Email photos to [stacy@bu.edu](mailto:stacy@bu.edu) and make sure to include proper credit to the photographer.

## Websites of Interest:

### Our studies

[www.bumc.bu.edu/centenarian](http://www.bumc.bu.edu/centenarian)

[www.bumc.bu.edu/supercentenarian](http://www.bumc.bu.edu/supercentenarian)

[www.longlifefamilystudy.org](http://www.longlifefamilystudy.org)

**A website about anti-aging quackery and growth hormone**

[www.hghwatch.com](http://www.hghwatch.com)

**The Life Expectancy Calculator**

[www.livingto100.com](http://www.livingto100.com)

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