

Geriatrics Section, Department of Medicine  
Boston Medical Center, Boston, MA, USA

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## Happy Spring!

We would like to express our sincerest wishes for a happy and healthy 2013 to all of our New England Centenarian Study participants and their families!



*The New England  
Centenarian Study*

## Recent Findings

As you might recall from our previous newsletter, the research that many of you are contributing to is greatly enhancing our understanding of how some people live to extreme old ages. We know from studies like the Seventh Day Adventist Health Study that most people, if they take good care of themselves with good health related behaviors (e.g. don't smoke, minimize red meat and alcohol in your diet, regularly exercise, effectively manage your stress) have a genetic makeup that can get them to their mid to late eighties.

**Protective Genes.** However, to live beyond the late eighties, our studies support the hypothesis that for older and older ages, special combinations of many genes play a greater and greater role. We used to think that these combinations must exclude variations of genes that are bad for you, but our work and that of the Leiden (Netherlands) Longevity Study show that nonagenarians and centenarians have just as many of most of these disease-associated genes as the general population. Therefore we believe that many of the genetic variants that are required to facilitate living to very old ages are protective. These genes likely slow the rate of aging and decrease one's risk for age related diseases (e.g. Alzheimer's disease, heart disease, stroke, diabetes and cancer).

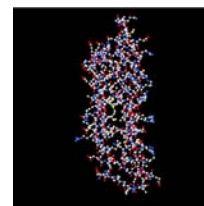
**The Lamin A Gene.** One really interesting study that the NECS recently participated in involves research of the Lamin A gene. One variation of this gene causes a very rare genetic



disease called Hutchinson-Guilford Disease. Only 1 newborn in 4 million has this disease. Many believe that Hutchinson-Guilford Disease is the opposite of surviving to very old age – rather people with this

disease appear to have many of the problems associated with aging including vision problems, hardening of the arteries (called atherosclerosis), hair loss, osteoarthritis and increased rates of heart attack and stroke but at very young age. Their average life expectancy is about 20 years.

In a study senior authored by Francis Collins, the Director of the National Institutes of Health, the NECS helped determine that there is a different variation of the Lamin A gene that is associated with exceptional longevity. So this is a story of two sides of the same coin, where one variation of the gene has a very powerful effect as the cause of a very debilitating and lethal disease and the other variation may be very good for a person but its effect is likely quite modest and just one of many genetic variations that together help a person achieve healthy aging and extreme old age.



## The Apolipoprotein E Gene.

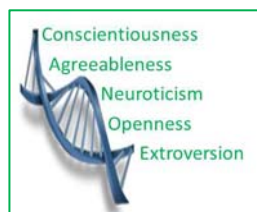
Another 2-sided coin story is this gene that plays an important role in transporting certain forms of cholesterol and fats in our blood stream.

Apo E also helps break down and clear beta amyloid plaques that build up in the brains of people with Alzheimer's disease. There are three major variations of the Apo E gene: E2,

E3 and E4. People who have inherited the E4 variation from a parent are at increased risk for Alzheimer's as well as atherosclerosis because this variation is not as effective as the others in clearing amyloid and certain forms of fat and cholesterol that are bad for you. Inheriting the E4 variation from both parents makes matters even worse. Our work in the Long Life Family Study shows that members of families that cluster for longevity tend to have low rates of the E4 variation and increased frequency of the E2 variation. However, other studies show that inheriting the E2 variation from both mom and dad is not necessarily good for you either. Therefore, more research is needed to understand if and how the E2 variant might provide at least some benefit.



The Long Life Family Study (LLFS) is now in its seventh year. Boston Medical Center is one of four Study Centers that help run the National Institute on Aging-funded Study, collect initial and follow-up data from the 4,900 subjects and 560 families in the Study and analyze the tremendously valuable data collected from our subjects. In the cases of a number of families, we have subjects enrolled in both the New England Centenarian Study and the Long Life Family Study.



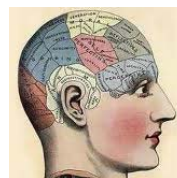
In another investigation of LLFS data, our very own Stacy Andersen led a study to determine if LLFS subjects have any personality traits in common. Personality traits were measured using the NEO Five Factor Inventory questionnaire which scores answers in the five domains of personality: conscientiousness, agreeableness, neuroticism, openness to experience and extraversion. We found that members of the offspring generation scored low in neuroticism and high in extraversion compared to population norms. These findings are similar to findings we made with the NECS offspring. Interestingly, the older generation scored within "average" for the general

population. Some people believe that as one gets older, they become more withdrawn, less open and more set in their ways. Our data do not support these assumptions.

Another question we have asked is if there are any associations between the personality traits that we have observed to be associated with healthy aging and specific genetic variants and the answer is yes. In a study conducted in collaboration with researchers from the Baltimore Longitudinal Study on Aging, we not only confirmed several associations that study had made but we also found several others. These findings are currently under review for publication in the Journal *Frontiers of Genetics of Aging*.



Further regarding our LLFS subjects, many of you will notice that we have recently added a couple of new questionnaires that address the possible connection between sleep habits, activity levels and longevity. We thank you all very much with all of your helpful answers to these questionnaires.



### **The Cognitive Function in Long-Lived Families Study**

Since December, 2010, we have been enrolling Long Life Family Study participants who live within 3 hours of Boston for participation in a 3 hour in-person study of cognition called the Cognitive Function in Long-Lived Families Study. As a major part of her PhD thesis work, Stacy Andersen is studying if specific cognitive functions remain intact into very old age in the LLFS family members. To date, we have enrolled 160 participants from long-lived families. In addition, we have enrolled 85 participants who are not members of these families. We are truly thankful to all who have agreed to participate in this additional study and hope to be able to report our findings soon.



### **Fruition**

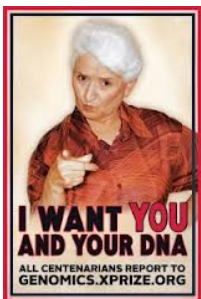
The LLFS is at a very exciting stage right now because we have analyzed all of the blood samples from our subjects for genetic data.

We are now in the process of analyzing those data to find genes that are playing roles in the longevity and healthy aging of our family members.



The reinsurance company Swiss Re has, for a long time, been very interested in factors that enhance a person's chances for healthy aging and longevity. When we were given the opportunity by the Society of Actuaries to present a paper on this topic, Swiss Re was most generous in providing the New England Centenarian Study with funding for this work. Since late last year, three Masters of Public Health graduate students from the Boston University School of Public Health have joined us to transfer all of the New England Centenarian Study's family pedigree data into a special database that will allow us to much better understand patterns of inheritance for exceptional longevity.

**Leslie Pierce, Samantha Xia, and Kelly Salance** have been working hard to carefully input these data and to also further research the families in order to fill in any missing data. We will be performing the data analysis later this spring and will look forward to presenting our findings at the Society of Actuaries Living to 100 international conference, held in Orlando next January.



### *The Archon Genomics X Prize*

For the past year the NECS has led the recruitment effort for the Archon Genomics X Prize. The purpose of an X Prize is to sponsor a competition to facilitate scientific advances. In

this case, the purpose is to markedly advance the technology necessary to accurately

determine a person's genetic code which is made up of about 3 billion bits of information. The 10 million dollar prize will be given to the laboratory or company that can extremely accurately decode the entire genetic codes of 100 centenarians in less than 30 days at a cost of less than \$1000 per subject. Once the competition is over, all of the generated data will be analyzed by the New England Centenarian Study and other groups that help with the enrollment of subjects for this effort.

### **Staff Updates**

**Stacy Andersen**, Project Manager, is finishing up data collection for her dissertation for her Ph.D. in Behavioral Neuroscience at Boston University and is working on transcription and data analysis. **Lori Feldman** is in her second of three years of her Masters of Social Work program at Salem State University. **Jesse Gass** continues to pursue her interest in mental health and hopes to apply to doctoral programs in clinical psychology next year. **Tara Neary** recently returned from a service trip to Kenya where she volunteered at a hospital and orphanage. She will be applying to medical school this spring for admission in the fall of 2014.



**Dr. Tom Perls** was promoted to Professor of Medicine and Geriatrics. He also has an appointment in the Division of Graduate Medical Sciences. This summer he will be leading two symposia at the World Congress of Gerontology and Geriatrics. The first symposium will report on the coordinated efforts of seven centenarian studies from around the world. The second symposium will be on anti-aging quackery. At the Congress, Tom will also be receiving the Congress' Busse Biomedical Research Award in recognition of significant contributions to aging research.



## Centenarian Highlight



Reverend John Wesley Annas, Jr. was born in N. Attleboro, Massachusetts in 1904. His father was a minister in a Methodist Episcopal church and served for over 40 years.

Now, in Leesburg, Florida, at age 108, John can say that he has served the church for over 40 years, just like his father before him. What has helped him accomplish so much? "Love God and trust fellow man, you don't spend time worrying."

Formally retired at age 65 in Syracuse, NY, the bishop assigned John to another parish for another five years. After that ended, he "got restless" and asked to be assigned to another church, and then another, and yet another, until he finally retired from giving regular sermons when he was almost 80 years old.

John and his first wife, Anita, moved to Florida in 1995 after Anita saw John wrestling their snow-blower out of a ditch at age 91. At that point she decided it was time to move to warmer climates. They spent several years together in Florida before Anita passed away. John proudly claims three children, eight grandchildren, and numerous great-grandchildren.

John finds great inspiration in Abraham Lincoln and has been reciting a presentation he prepared about him, "Lincoln," for many years. He took portions from John Drinkwater's play, "Abraham Lincoln," and created a 30-minute one-man show where he plays the parts of five different characters, including Lincoln and his wife. It was during one of these presentations that John's current wife, Lenore, caught sight of him. Lenore saw his Lincoln presentation at the town hall and arranged to have him present it at the library. They got to know each other, married in 2007, and now share a wonderful and full life together.

Though John has macular degeneration and some hearing loss, he keeps very busy by

visiting with friends, reading (with the aid of a magnifier that projects onto a screen), responding to the continual requests to present his "Lincoln" piece, and leading the occasional sermon. He and Lenore published a collection of his poems that he delivered at Christmas sermons over a period of 50 years. He recites his poems with ease and joy, all from memory.

John credits his terrific longevity to his upbringing. "The good lord gave my mother and father good genes that they passed onto me. We ate simple but very nourishing food like oatmeal – not rich cake."



## Gerontological Research Meetings

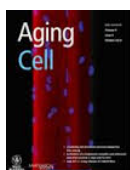
The Gerontological Society of America's Annual Scientific Meeting is our usual big annual academic meeting every year. Our last GSA meeting was a particular treat because it took place in sunny San Diego! Nearly all of the NECS staff presented research findings at the meeting in November.

- Dr. Perls organized and led the Long Life Family Study's symposium titled, "Phenotypic and genetic survival advantages of Long Life Family Study subjects". Each Study Center of the LLFS presented some of their key research. Professor Paola Sebastiani from Boston University's School of Public Health presented our findings on personality traits and their associations with specific genetic variations.
- Stacy Andersen presented a poster titled, "Feasibility of neuropsychological testing in the oldest old: It can be done!" which described findings from the Cognitive Function in Long-Lived Families Study. She found that by choosing tests that minimized demands on hearing, vision, and writing and by organizing the tests to allow for multiple sessions, all participants were able to complete all of the testing. Most importantly, no tests were altered allowing

for a standardized testing of all participants with ages ranging from 41 to 103 years.

- Tara Neary's poster was titled, "Centenarian Clock Reading" which presented data from a Clock Reading Test that was administered to 26 participants over the age of 100. Participants were shown clock face drawings with or without numbers and were asked to read the time indicated on each clock. We identified errors in clock reading and categorized them into eight error types. Common error types included switching the minute and hour hands and misreading the minute hand by five minutes or the hour hand by one hour. Tara found that clock reading error types can reveal conceptual (understanding the meaning of a clock face) and/or perceptual (being able to identify and understand visual characteristics) deficits in cognitive function.
- In a poster titled, "Depression prevalence rates and ages of onset in the Long Life Family Study (LLFS) and the New England Centenarian Study (NECS) cohorts," Jesse Gass presented data on depression prevalence and incidence amongst NECS and LLFS subjects. She found that NECS centenarians delayed depression the longest, followed by LLFS participants, LLFS controls, and NECS controls. Furthermore, when a quarter of the participants in each group had developed depression, centenarians showed more than a 15-year delay in depression compared to controls. These results suggest that centenarians and those with familial longevity are more likely to delay the onset of depression.

## Recent Publications



Conneely KN, Capell BC, Erdos MR, Sebastiani P, Solovieff N, Swift AJ, Baldwin CT, Budagov T, Barzilai N, Atzmon G, Puca AA, Perls TT, Geesaman BJ, Boehnke M, Collins FS.

Human longevity and common

variations in the LMNA gene: a meta-analysis. *Aging Cell*. 2012;11:475-81.



Schupf N, Barral S, Perls T, Newman A, Christensen K, Thyagarajan B, Province M, Rossi WK, Mayeux R. **Apolipoprotein E and familial longevity.** *Neurobiol Aging*. 2012; S0197-4580.



Michael Anson R, Willcox B, Austad S, Perls T. **Within and between-species study of extreme longevity.** *J Gerontol A Biol Sci Med Sci*. 2012;67(4):347-50.



Andersen, SA, Sun, JX, Sebastiani, P, Huntly, J, Gass, JD, Feldman, L, Bae, H, Christiansen, L, Perls, TT. **Personality Factors in the Long Life Family Study.** *Journals of Gerontology, Series B: Psychological Sciences and Social Sciences* December 28, 2012 (print version pending)



Sebastiani P, Perls, TT. **The genetics of extreme longevity: Lessons from the New England Centenarian Study.** *Frontiers in Genetics of Aging* November 30, 2012 (online)  
[http://www.frontiersin.org/Genetics\\_of\\_Aging/10.3389/fgene.2012.00277/abstract](http://www.frontiersin.org/Genetics_of_Aging/10.3389/fgene.2012.00277/abstract)

## Funding and Philanthropic Support



GLENN FOUNDATION  
FOR MEDICAL RESEARCH



Funding of our research primarily comes from peer-reviewed competitive grants provided by the National Institute on Aging (NIA) and the National Heart Lung and Blood Institute (NHLBI), both of the National Institutes of Health (NIH). We are extremely thankful to the Glenn Medical Foundation which provided a grant award to Dr. Perls to study the basic biological mechanisms of aging and to the reinsurance company, Swiss Re, for their support of our study of familial transmission of longevity.

Marty and Paulette Samowitz have been wonderful friends to the Centenarian Study and without their support this newsletter and other key activities would be impossible.

We have many additional studies that we are desperate to conduct but we can't because of our funding constraints. If you would like to speak with Dr. Perls about any particular funding interest that you might have, 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. 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 your family to obtain permission.

If you wish, we will be happy to return any photographs to you.

### 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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