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REPORT

Why Some People Live So Long! Identifying What Enables Humans to Survive Past 110 in Good Health

By James Clement

Super-centenarians are very rare individuals. They have lived to at least **110 years** of age.

In the United States, there are approximately 54,000 centenarians (people who are **100 years** of age or older). Only about a dozen of these centenarians, however, appear to make it to 110 years old.[1,2]

Worldwide, only about **70** individuals have been verified to be at least 110 years of age or older.[2] Surviving decades longer than their peers — often in far better health — super-centenarians may hold the keys to protection from disease, decline, and early death.

As you read their individual stories you cannot help but notice that many of these extremely long-lived individuals did not take the special precautions that you, I, and other readers of this magazine follow to maximize our health. Yet many of them went their entire lives without illness, and some without ever seeing a doctor.

Sadly, most of us are not as lucky to have been born with such “super” genes.

The **Life Extension Foundation**® is helping to fund an unprecedented project to identify those genetic variations that protect super-centenarians from disease and allow them to live nearly perfectly healthy lives until just shortly before their deaths. The objective is to enable scientists to create therapies that will bring the extraordinary protective powers of super-centenarians to ***everyone***.

In May of 2011, researchers James Clement and Parijata Mackey left for Europe on a journey, partially funded by the Life Extension Foundation® , to study how super-centenarians avoid illnesses and live long, healthy lives.

These two researchers had attended multiple scientific conferences on aging. It was apparent that most life span research was done on short-lived species, such as *C. elegans*, drosophila, and mice. Human studies were largely limited to cells grown in Petri dishes, rather than studies of cells in-vivo. At the time, no one was actively collecting and analyzing large numbers of genetic and molecular profiles of humans who lived to **110 or older**.

Before their journey, James and Parijata surveyed the existing scientific literature for studies on long-lived humans. Special focus was paid to research conducted by Boston University’s Tom Perls and Albert Einstein College of Medicine’s Nir Barzilai. Drs. Perls and Barzilai had conducted extensive demographic and some single nucleotide polymorphism and genome-wide association studies on why these individuals lived so long without diseases.

Nir Barzilai speculated that long-lived individuals possessed genes that protected them from diseases, but neither he nor Tom Perls had been able to uncover these genes. Based on the research they had seen, James and Parijata decided that it was important to focus on individuals over the age of 105, especially men, on the basis that individuals who lived to this age would likely have these protective genes, if such existed.

James and Parijata also investigated the work of the Gerontological Research Group and the *Guinness World Book of Records*, both of which document and verify the identities of individuals claiming to be super-centenarians. Based upon various public and private resources, they then built their own research study list of hundreds of individuals over the age of 105.

THE STUDY'S OBJECTIVE

The objective of James and Parijata's current study involves a double comparison of the genomic and molecular data from extremely long-lived individuals. They first want to see what similarities super-centenarians share, and secondly compare super-centenarians with "normal" individuals, especially those who died having known illnesses, such as cancer, cardiovascular diseases, Alzheimer's, stroke, diabetes, etc.

HEREDITY OF LONGEVITY: (IT'S PARTIALLY IN THE GENES)

In 1996, James Vaupel published a paper showing that, across several thousand Danish twins, approximately **20-26%** of their longevity could be attributed to genetics.[3] However, the mean age of the twins in that study was only 70 years—implying that these individuals likely lacked sufficient "protective genes" to have inherited "super" longevity from their parents.

The same researchers published another study of nonagenarians (persons from 90 to 99 years old) and centenarians, which noted that the discovery of genetic factors associated with exceptional longevity increases with the age of the subjects. This study, and many others, strongly suggests that the genetic component of exceptional longevity gets larger with increasing age, and is especially high for those aged 106 years and older.

Tom Perls of Boston University has published a study suggesting that "the older you are, the healthier you've been."[4]

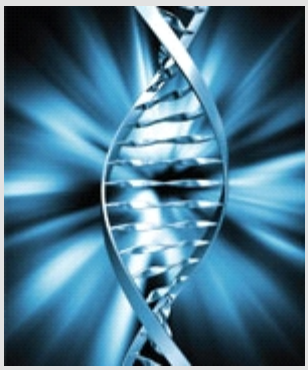
Perls' group found that the siblings of centenarians have roughly a **3.5 times *greater*** chance of reaching 100 years of age than siblings of non-centenarians.[5]

Even more astounding, the siblings of male super-centenarians have a **17-times greater** chance of living to 100 than that of the general population.[5]

Super-Centenarians
Both **Christian Mortensen** (age 115) top, and **Walter Breuning** (age 114), second from top, loved their cigars. **Dorothy peel** (age 110) said she owed her longevity to drinking a mid-afternoon glass of sherry and an evening glass of whiskey every day (she quit smoking at age 104).

WHAT YOU NEED TO KNOW

Uncovering the Genetics of Extreme Longevity



- Super-centenarians are very rare individuals that have lived to at least **110 years** of age.
- Worldwide, only about **70** individuals have been verified to be at least 110 years of age or older.
- **Life Extension Foundation**®-funded research will soon be underway to identify those genetic variations that protect super-centenarians from disease and allow them to live nearly perfectly healthy lives until just shortly before their deaths.
- Boston researchers have found that the siblings of centenarians have roughly a **3.5 times *greater*** chance of reaching 100 years of age than siblings of non-centenarians.
- Even more astounding, the siblings of male super-centenarians have a **17-times greater** chance of living to 100 than that of the general population.

WHOLE GENOME SEQUENCING: $350,000 - $99,000 - $20,000 - $10,000 - AND DROPPING

In early 2008, Dan Stociescu became the second human in the world to buy the full sequence of his genome. Dan paid $350,000 for this honor with the intent of helping to propel the direct-to-consumer genomics business forward.

In 2009, James Clement had his complete genome sequenced for $99,000. By early 2010, whole-genome sequencing had dropped to $10,000 to $20,000 a person—if you could afford to do large batches of genomes. Sequencing costs were falling nearly an order of magnitude about every two years.

James and Parijata decided that they would spend the next few years collecting the DNA of individuals over the age of 105. This would enable them to sequence and study this precious DNA once costs had dropped to an affordable level. They approached wealthy individuals and the Life Extension Foundation® to raise money for this project, and with a very limited budget, set out to meet super-centenarians around the world.

When conducting interviews with these long-lived individuals, James and Parijata would ask about lifestyle practices and whether they had longevity in their families. It turned out that, more often than not, they had led pretty normal lives, including smoking and drinking throughout most of their lives. Only a few reported that they had been active in sports or had regularly exercised.

DR. LEILA DENMARK: 1898 - 2012. LIVED 114 YEARS

In March 2011, James and Parijata visited the Athens, Georgia, home of Mary Denmark Hutcherson. Mary lived with her 113-year-old mother, **Dr. Leila Denmark.**

Born February 1, 1898, Leila became a schoolteacher and then a pediatrician who practiced medicine for more than 70 years. Denmark helped develop a whooping cough vaccine and wrote a well-regarded parenting book, *Every Child Should Have a Chance*, now in its 14th printing.

Leila Denmark was the only woman in her graduating class of 1928 at the Medical College of Georgia, and only the third woman to graduate from the college. As co-developer of the whooping cough vaccine in the 1920s and 1930s, she was awarded the 1935 Fisher Prize. She continued to practice until she retired in 2001. At 103, she was the oldest practicing physician in the United States. Among her many other awards, Denmark was named Atlanta's Woman of the Year in 1953.

She was among the first physicians to say that second-hand smoke posed a danger to children, and counseled that enjoying what you do and a good diet were two keys to good health.

She avoided eating too much sugar, a substance medical researchers are now beginning to suspect contributes to a number of health problems, including cancer. Those principles seemed to serve her well. Her parents died relatively young. Many of her 11 brothers and sisters — she was the third of 12 children — had heart disease, but Denmark enjoyed good health up until the last few years of her life.

Retirement came at age 103. World travel followed until age 106. She then left Alpharetta and came to Athens to live with Hutcherson, her only daughter. While there she enjoyed a few years of gardening before experiencing the first of a series of mini-strokes. This eventually led to her death at age 114.

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Health

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JAMES “DOC” SISNETT: GOING ON 113 YEARS

James Sisnett was born in the tropical paradise of Barbados on February, 22, 1900. At nearly 113 years of age, he’s the oldest man in the Western hemisphere. Visiting Sisnett on the week of his 111th birthday, James and Parijata enjoyed a celebration that attracted many of the island’s top officials, including the Minister of Health. Sisnett’s nearly fifty living descendants flew in from around the world.

A perpetual grin seems to constantly delight those surrounding James Sisnett. He enjoys breadfruit, cognac, and flirting with the cheery nurses at his retirement home. One of his many granddaughters remarked that he has, “the memory of an elephant, the appetite of a truck driver, and a wicked sense of humor.” The next few days would prove how right she was.

Sisnett has enjoyed a remarkable bill of health throughout his life. At his birthday celebration he described the only doctor’s visit of his youth. With a mischievous twinkle in his eyes (and that perpetual grin) he relayed his story. “I had a toothache when I was nine years old. I was taken to the doctor, and do you know what the doctor did? He gave me a glass of rum! A nine-year-old boy, given rum! But it worked — my tooth didn’t hurt anymore.”

It would be the only “medicine” he’d ever need.

Currently, Sisnett has no known illnesses, suffering only from a hearing loss — which, as his family revealed, chuckling, sometimes serves as an excuse for Sisnett to pretend not to hear if he doesn’t want to listen to someone. Cataract surgery was performed successfully when he reached age 106.

A remarkable memory rivals Sisnett’s sharp sense of humor. Remembering names, faces, places, dates, and events has never posed a problem. The friendly ease with which he greeted his hundred or so guests by name made clear just how sharp his mind remains.

James Sisnett witnessed a century of the changed and unchanged on the island. He pointed out the new developments on the hillsides, and marveled at the unchanging nature of the white beaches, the pine forests, and the waves crashing upon the rocks.

Standing on the island’s western coast, we looked East across to Africa. There is no land between Barbados and Africa, nothing to slow the rough waves that crash upon the island’s western shore. The loud crashing where land meets sea is said to be a reminder of the cries of countless Africans, captured and enslaved, who perished on slave ships during the brutal crossing to the Americas. It’s a solemn reminder; history feels ever so close, standing with a man only one generation removed from this terrible chapter in our past.

Sisnett shared a strong connection to historical events with other “super” individuals. **Mississippi Winn**, a lovely southern belle, beauty and charm still apparent at 113 years of age, was born the daughter of two freed slaves.

Sisnett’s family is every bit as remarkable as the man himself. Despite inheriting type I diabetes from Sisnett’s first wife, his children lack the severe complications typical of the disease. All of his children look decades younger than their biological ages. His family shares his contagious wit, strength, intelligence, and sense of humor, and glow with such a warmth and kindness, they made the visit unforgettable. Their selfless contributions to this research can result in treatments or cures not just for diseases such as type I diabetes, but also for heart disease, cancer, neurodegenerative disorders, and so much more.

JOHANNES HEESTERS: 1903 - 2011. LIVED 108 YEARS

In September 2011, James, Parijata, and Kemal Akman, a graduate student at the Ludwig-Maximilians-Universität in Munich, visited **Johannes Heesters** at his home in Starnberg, Germany. Mr. Heesters, born in 1903, was primarily a singer and actor throughout his life. Although born in Holland, he spent most of his life in Germany and Austria. He enjoyed champagne and chain-smoked for nearly a century.

When asked why he refused to retire, Heesters once quipped: “Should I just sit around at home, waiting for them to come and get me? I wouldn’t dream of it.”

Mr. Heesters posed for photos with James and Parijata and told them stories about his acting career, and sang a song for them. His wife, actress Simone Rethel, whom he married following the death of his first wife, presented them with an autographed copy of her book, in which she dispels the misconception that old age means illness, disability, and nursing homes. In December 2010, the 107-year-old Heesters announced that he had quit smoking for his then 61-year-old wife, Simone, saying, “She should have me as long as possible.” Johannes Heesters passed away on Christmas Eve, 2011.

RHYS THOMAS LEWIS: 1903 - 2012. LIVED 108 YEARS

James and Parijata arrived in the UK and set up temporary headquarters in a small house in the university town of Oxford, near the center of England. They gathered the names and addresses of as many people as they could find who were over 105 years old, and began contacting them. About a dozen individuals agreed to meet with them and to provide DNA samples. Many of these individuals exceeded their expectations as to their health and vigor.

Shane Mackey, a biology student at the University of Chicago, and brother of Parijata Mackey, and James visited the home of Rhys Lewis and his son Peter, in Wokingham, UK.

Long life ran in Mr. Lewis’ family, with two of his sisters, Doris Williams and Megan Samuel, living until 102 and 99. Both passed away last year. Rhys was born in Wales on September 17, 1903.

A few lifestyle details were provided by his son, Peter. “He used to smoke, but gave up some years ago. He drank in moderation: he loved a glass of sherry for example, but that’s all. He ate well but not to excess, and disliked any ‘foreign’ food! He loved a good fry-up, fish and chips, and roast beef, and used to grow his own on an allotment.”

The family lived a modest life but “full of argument,” especially on politics but also history and economics (“which we inherited, and have passed on to our children”). “He lived frugally (like many of his generation, having survived two world wars) and was a keen saver. His will left over half a million pounds - he received two pensions (state plus teachers). He left such a sum because he invested very wisely, both directly in shares and through unit trusts.

“He could also become very angry (right to the end), and was especially angry at being hospitalized (a broken hip and hemorrhoids).” His son, Peter, continued his commentary. “I wonder if he suffered short-term memory loss towards the end, because this seems to be a problem with some old people, that they forget their accidents and can’t understand why they are in hospital!

“But his long-term memory improved (surprisingly) as he aged, having time to excavate his sub-conscious I suppose. He even came up with stories from his childhood I had never heard before. For example, Rhys left home at 13 to become a miner, but continued to improve himself by taking night school and eventually leaving mining to attend Swansea University. Before he retired at 67 years of age, he was head of history at Easthampton Park College of Education in Berkshire.”

Rhys died on July 4, 2012, just a few months short of his 109th birthday, the oldest living Welshman, at that time.

SOCIAL, OUTGOING, HAPPY, NEARLY ILLNESS-FREE AND OTHERWISE “NORMAL”

According to the Max Plank Institute, super-centenarians make up only **0.05 per million** of the population. After meeting several dozen centenarians and super-centenarians, James and Parijata have concluded that they are indeed very special people, both biologically and in personality. Nearly all of them were quite social, outgoing individuals with cheerful dispositions. These genetically fortunate individuals lived nearly illness-free lives, with many of them never having seen a doctor, all the while having smoked, drank, and generally having lived very average lifestyles.

One typical story was recounted by a retirement home director, who shall remain nameless. A stomach virus swept through their community. It killed several residents, and made residents and staff alike ill for weeks. The super-centenarian in question got

sick the night of the outbreak—but by the next morning he was fully recovered, and asked for his regular breakfast. The manager said he'd never seen anything so amazing for someone of that age. Wouldn't we all like to be as resilient as this super-centenarian?

ABOUT THE ANDROCYTE RESEARCH TEAM

James Clement, the CEO of Androcyte, was a lawyer who, over the past decade, became increasingly involved with healthy life-extension, cryonics, and transhumanism.

James's previous leadership roles included serving as the COO for the Maximum Life Foundation and as the Executive Director of the World Transhumanist Association. He is currently a member of the Board of Directors of the Alcor Life Extension Foundation®. In 2008, James co-founded and published **h+ Magazine** with his friend and mentor Dan Stoicescu, a wealthy philanthropist who holds a PhD in medicinal chemistry. h+ Magazine focused on promoting research in nanotechnology, biotechnology, information science (artificial intelligence), and cognitive science, and became a very successful online magazine, having nearly a half-million readers a month.

Parijata Mackey's honors began with the Silver Knight in Science Award from the *Miami Herald* in 2005, for her work on Drosophila genetics. She was selected as a DHS Scholar, and received a scholarship to study molecular biology, computational neuroscience, and philosophy at the University of Chicago, where she later taught and founded the synthetic biology research program. Additional research experience includes genetic engineering and synthetic biology at the University of Chicago, mechanisms of aging and DNA damage at Barry University, and pathogen bioinformatics at Lawrence Livermore National Laboratory.

Dr. Michael Fossel is the Principal Investigator for this Supercentenarian Research Study. Currently Dr. Fossel is a Physician Executive at HPG Resources, and previously served as a professor of Clinical Medicine at Michigan State University and as editor of the *Journal of Anti-Aging Medicine*. He is best known for his views on telomerase therapy as a possible treatment for cellular senescence. Dr. Fossel has written numerous articles on aging and ethics for the *Journal of the American Medical Association* and *In Vivo*, and he published a book titled *Reversing Human Aging* in 1996. An academic textbook by Dr. Fossel entitled *Cells, Aging, and Human Disease* was published in 2004 by Oxford Press.

Dr. George Church is the lead Scientific Advisor of this project. Dr. Church is Professor of Genetics at Harvard Medical School, Director of the Center for Computational Genetics. His 1984 Harvard PhD thesis included the first direct genomic sequencing method, molecular multiplexing tags, which lead to automation & software used at Genome Therapeputics Corporation for the first commercial genome sequence—which was performed on the pathogen, *Helicobacter* in 1994. He helped initiate the Human Genome Project in 1984, and is widely regarded as a pioneer in personal genomics and synthetic biology.

SUMMARY

James and Parijata continue to collect DNA samples from the extremely long-lived while focusing on the analysis of the dozens of whole-genomes thus far sequenced. They are now working with their chief scientific adviser, Dr. George Church of Harvard Medical School, to identify the variations that protect these individuals from disease and allow them to live nearly perfectly healthy lives until just shortly before their deaths.

Life Extension Foundation® has agreed to advance this research by sponsoring a gene-expression research study. Blood tests will be used to look at bio-markers that have been discovered that relate to the biological age of an individual's various organs as compared to their chronological age. This Life Extension Foundation®-sponsored research study should begin sometime in mid-2013.

REFERENCES

1. Available at: http://www.census.gov/prod/cen2010/briefs/c2010br-09.pdf. Accessed January 10, 2013.
2. Available at: http://www.grg.org/Adams/E.HTM. Accessed January 10, 2013.
3. Herskind AM, McGue M, Holm NV, Sørensen TI, Harvald B, Vaupel JW. The heritability of human longevity: A population-based study of 2872 Danish twin pairs born 1870–1900. *Human Genetics*. 1996;97(3):319-23.
4. Hitt R, Young-Xu Y, Perls T. Centenarians: The older you get, the healthier you've been. *Lancet*, 1999;354(9179):652.
5. Perls TT, Wilmoth J, Levenson R, et al. Life-long sustained mortality advantage of siblings of centenarians. *Proc Natl*

Acad Sci USA. 2002;99:8442-47.