A Profile of James Clement's Supercentenarian Research

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Should James Clement's name remain well-known in association any of the present day work on human longevity, one would hope it will be as one of the pioneers to first organize trials of senolytic therapies in humans, via his Betterhumans organization. This is far from the only research interest of this citizen scientist, however, and in past years he has put in a great deal of time and effort to expand what is known of the genetics and biochemistry of supercentenarians, rare individuals who survive past the age of 110. That is the focus of the article here.

For my part I think that the genetics of supercentenarians are not the place to look for meaningful therapies to lengthen life. After all, these individuals are still very frail, enormously impacted by the damage of aging. So far as past genetic assessments have shown, there isn't much of a difference between the survivors and the dead in any given birth year. A tiny fraction of people beat the odds even when the odds are long, and that may well be all there is to it: chance in complex system. Still, rare discoveries such as that announced yesterday keep the hope alive that there is some genetic rarity in supercentenarians that might be more relevant to future medicine. Regardless, I see the path forward as something other than genetic mapping. Instead it is that of senolytics and other forms of therapy that aim to periodically repair the damage that causes aging before it rises to pathological levels, to prevent and turn back aging, not just slow it a little.

Quote:

The full genetic sequences of some three dozen genomes of North American, Caribbean, and European supercentenarians being made available this week by a nonprofit called Betterhumans to any researcher who wants to dive in. A few additional genomes come from people who died at 107, 108 or 109. If unusual patterns in their three billion pairs of A's, C's, G's and T's - the nucleobases that make up all genomes - can be shown to have prolonged their lives and protected their health, the logic goes, it is conceivable that a drug or gene therapy could be devised to replicate the effects in the rest of us.

The rare cache of supercentenarian genomes, the largest yet to be sequenced and made public, comes as studies of garden-variety longevity have yielded few solid clues to healthy aging. Lifestyle and luck, it seems, still factor heavily into why people live into their 90s and 100s. To the extent that they have a genetic advantage, it appears to come partly from having inherited fewer than usual DNA variations known to raise the risk of heart disease, Alzheimer's disease and other afflictions.

That is not enough, some researchers say, to explain what they call "truly rare survival," or why supercentenarians are more uniformly healthy than centenarians in their final months and years. Rather than having won dozens of hereditary coin tosses with DNA variations that are less bad, scientists suggest, supercentenarians may possess genetic code that actively protects them from aging. But the effort to find that code has been "challenged," as a group of leading longevity researchers put it in a recent academic paper, in part by the difficulties in acquiring supercentenarian DNA.

The DNA sequences being released this week were acquired almost single-handedly by James Clement, 61. A professed citizen-scientist, Mr. Clement collected blood, skin, or saliva from supercentenarians in 14 states and seven countries over a six-year period. The usefulness of such a small group for a genetic study is unclear, which is one reason Mr. Clement's company Androcyte, now defunct, has turned into a crowdsourcing project. So despite the limitations of Mr. Clement's database, several prominent researchers have already expressed interest in it. "This could show the utility of starting a bigger collection."

There was, nominally, the prospect of making money. But with a business plan that, even to some of his investors, sounded more like a research project, Mr. Clement seems to have undertaken the task largely because it provided the chance to act on a longstanding interest in human longevity, including his own. A self-described transhumanist who eats mostly low-glycemic vegetables and nuts and walks seven miles a day, Mr. Clement has accumulated an eclectic résumé that includes starting a brew pub, practicing international tax law, and cofounding a futurist magazine. He harbors what he prefers to call a "healthy love of life," rather than an aversion to death, and he is possessed of an apparently genuine conviction that longer lives would make humans more humane.

"My hat was off to someone who was willing to take the time out of his life to go get these precious specimens," said *Dr. George Church*, the Harvard geneticist, who has devoted a portion of his laboratory to research into the reversal of aging. The kind of ultrarare mutations that supercentenarians might harbor, *Dr. Church* believed, were not likely to be detected with standard techniques, which scan only the places in the genome where DNA is already known to vary between individuals.

To look for as-yet-uncataloged variations would require sequencing all of the supercentenarians' six billion genetic letters, a far more expensive procedure. When he and Mr. Clement first discussed the idea in 2010, the cost was about \$50,000 per genome. But the price was falling. And with the financial support of a handful of like-minded wealthy individuals who agreed to invest in the exploratory phase of the project, "it just seemed," Mr. Clement said, "like something I could do."

Link: https://www.nytimes.com/2017/11/13/health/supercentenarians-genetics-longevity.html