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EDITORIAL

# Age editorial

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Exceptional human survival has been a topic of fascination since time immemorial and is an area of increasing interest to the gerontological community. Investigating the extremes of human survival may yield clues that can help us better understand aging across the entire human lifespan. Nevertheless, despite the growing importance of this phenotype, there is remarkably little agreement among gerontologists as to what exceptional survival (ES) means or how to best study it (NIH 2001).

The most obvious and simple definition for ES is survival past a specified exceptional or extreme age. For most researchers, and the general public in fact, the age of 100 years has generally been considered to be quite exceptional. While this is certainly an exceptional age for most human populations, the study of exceptional human survival should take into account population-specific secular trends in life expectancy and other demographic effects, genetic effects, sex-specific effects, lifestyle, psychological, social and other environmental factors, as survival to a given age is less exceptional in some populations than others (NIH 2001).

With these factors in mind, this issue of AGE presents five different studies of exceptional human survivors, each of which adds further understanding to this complex phenotype. Four of these studies focus on centenarians, still a rare phenotype that occurs in only 10 per 100,000 persons in most modern countries, but as high as 50 per 100,000 in Okinawa, Japan's westernmost prefecture (Willcox et al. 2006). There are less than a dozen major research groups that investigate the centenarian phenotype, mainly in the U.S., Japan and Europe.

Several approaches have been used to investigate the genetic and environmental factors involved in this phenotype. The first comprehensive investigation of the centenarian phenotype began in the mid 1970s with the study of a geographically and genetically isolated group of centenarians in Okinawa, Japan (Sanabe et al. 1977; Takata et al. 1987; Willcox et al. 2006), and has been followed by studies of other ethnic groups, including Swedes (Samuelsson et al. 1997), Danes (Andersen-Ranberg et al. 2001), other Japanese (Shimizu et al. 2003; Kojima et al. 2004) and Italians (De Benedictis et al. 1999; Caselli et al. 2006), among others. Other centenarian studies focus on admixed populations from the continental U.S., including those in Georgia (Poon et al. 1992; Martin et al. 2002) and New England (Perls et al. 1999). Finally, other researches investigate particular ethnic groups of centenarians, such as Ashkenazi Jews (Barzilai et al. 2003).

In this issue of AGE, Willcox et al. point to the importance of genetic factors in exceptional human survival, reviewing the evidence from diverse studies

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and highlighting findings from over 30 years of work on the long-lived Okinawans, who have among the world's highest prevalence of exceptional survivors. The paper concludes with a robust discussion on the challenges that we face when integrating environmental information with the vast amount of genetic information that is now achievable with high-throughput genotyping methods. Johnson et al. focus on the nutritional aspects of centenarianism in the state of Georgia, USA, indicating the significant challenges facing those who have achieved centenarian status in maintaining adequate nutritional intake. Given the well-known association between caloric restriction and longevity in animal models, it would be interesting to know if these centenarians were lifelong undereaters or if this is a byproduct of being frail and elderly, with few community resources.

Two studies explore the link between personality and ES, an interesting but under-explored area. The study by Martin et al., an exploration of personality patterns from the Georgia Centenarian Study, analysed whether there might be a special combination of personality traits that define centenarians. Indeed, this study discovered that low levels of neuroticism, high levels of competence and high extraversion was notable in this group of exceptional survivors compared with younger controls. In the other study of personality, Masui et al. found that centenarians in Tokyo had high scores in the specific personality traits of conscientiousness, openness and, like their Georgian counterparts, extraversion. This result was obtained using a novel model that estimated personality change with age from longitudinal data in the younger elderly. Researchers from the Tokyo Centenarian Study speculate that these personality traits contribute to longevity through health-related behaviours, stress reduction and adaptation to the challenging problems of the "oldest old."

In the final paper, Yashin et al. take a prospective approach to understanding the risk for survival to older ages. Yashin et al. used longitudinal data from seven physiological indices over the lifespan of individuals from the Framingham Study. These researchers developed a method for assessing one's potential for living a long life based on physiological trajectories of change observed at younger ages in longer-lived individuals and shorter-lived individuals. Deviation from age-specific physiological indices constructed from body mass index (BMI), blood pressure, cholesterol and other risk factors at younger ages was able to predict mortality at older ages.

These studies of the ES phenotype, all using different methods, point to at least one common conclusion—ES is a complex phenotype and reflects genetic and environmental as well as stochastic factors that vary across the lifespan. Further study of this phenotype will likely require ever more complex statistical models that incorporate both genetic and environmental data. This type of innovative work will likely require collaboration between researchers from diverse disciplines, in much the same way as the separate fields of genetics and epidemiology recently converged to form the new field of genetic epidemiology. We hope that the papers presented in this issue of AGE reflect this collaborative spirit and that this helps to bring us a small step closer to understanding the complexities of aging and exceptional human survival.

## References

Andersen-Ranberg K, Schroll M, Jeune B (2001) Healthy centenarians do not exist, but autonomous centenarians do: a population-based study of morbidity among Danish centenarians. J Am Geriatr Soc 49(7):900–908

Barzilai N, Atzmon G, Schechter C, Schaefer EJ, Cupples AL, Lipton R, Cheng S, Shuldiner AR (2003) Unique lipoprotein phenotype and genotype associated with exceptional longevity. JAMA 290(15):2030–2040

Caselli G, Pozzi L, Vaupel JW, Deiana L, Pes G, Carru C, Franceschi C, Baggio G (2006) Family clustering in Sardinian longevity: a genealogical approach. Exp Gerontol 41(8):727–736

De Benedictis G, Rose G, Carrieri G, De Luca M, Falcone E, Passarino G, Bonafe M, Monti D, Baggio G, Bertolini S, Mari D, Mattace R, Franceschi C (1999) Mitochondrial DNA inherited variants are associated with successful aging and longevity in humans. FASEB J 13(12):1532–1536

Kojima T, Kamei H, Aizu T, Arai Y, Takayama M, Nakazawa S, Ebihara Y, Inagaki H, Masui Y, Gondo Y, Sakaki Y, Hirose N (2004) Association analysis between longevity in the Japanese population and polymorphic variants of genes involved in insulin and insulin-like growth factor 1 signaling pathways. Exp Gerontol 39(11–12):1595–1598

Martin P, Long MV, Poon LW (2002) Age changes and differences in personality traits and states of the old and very old. J Gerontol B Psychol Sci Soc Sci 57(2):P144–P152

U.S. National Institutes of Health, U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health, National Institute on Aging (2001)

Report of the National Institute on Aging Advisory Panel on Exceptional Longevity (APEL). NIH publication no. 01-4951

Perls TT, Bochen K, Freeman M, Alpert L, Silver MH (1999) Validity of reported age and centenarian prevalence in New England. Age Ageing 28(2):183–197

Poon LW, Clayton GM, Martin P, Johnson MA, Courtenay BC, Sweaney AL, Merriam SB, Pless BS, Thielman SB (1992) The Georgia Centenarian Study. Int J Aging Hum Dev 34(1):1–17

Samuelsson SM, Bauer Alfredson BB, Hagberg B, Samuelsson G, Nordbeck B, Brun A, Gustafson L, Risberg J (1997) The Swedish Centenarian Study: a multidisciplinary study of five consecutive cohorts at the age of 100. Int J Aging Hum Dev 45(3):223–253

Sanabe E, Ashitomi I, Suzuki M (1977) Social and medical survey of centenarians. Okinawa J Public Health 9:98–106

Shimizu K, Takeda S, Noji H, Hirose N, Ebihara Y, Arai Y, Hamamatsu M, Nakazawa S, Gondo Y, Konishi K (2003) Dietary patterns and further survival in Japanese centenarians. J Nutr Sci Vitaminol 49(2):133–138

Takata H, Suzuki M, Ishii T, Sekiguchi S, Iri H (1987) Influence of major histocompatibility complex region genes on human longevity among Okinawan-Japanese centenarians and nonagenarians. Lancet 2(8563):824–826

Willcox BJ, Willcox DC, He Q, Curb JD, Suzuki M (2006) Siblings of Okinawan centenarians share lifelong mortality advantages. J Gerontol A Biol Sci Med Sci 61(4):345–354