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Fundamental and Molecular Mechanisms of Mutagenesis

Mutation load and human longevity

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Abstract

Since paternal age at reproduction is considered to be the main factor determining human spontaneous mutation rate (Crow, J. (1993) Environ. Mol. Mutagenesis, 21, 122–129), the effect of paternal age on human longevity was studied on 8,518 adult persons (at age 30 and above) from European aristocratic families with well-known genealogy. The daughters born to old fathers (50–59 years) lose about 4.4 years of their life compared to daughters of young fathers (20–29 years) and these losses are highly statistically significant, while sons are not significantly affected. Since only daughters inherit the paternal X chromosome, this sex-specific decrease in daughters' longevity might indicate that human longevity genes (crucial, house-keeping genes) sensitive to mutational load might be located in this chromosome.

Keywords: Mutation load; Human longevity; Paternal age; Spontaneous mutations; Genealogy

Paternal age at reproduction is considered to be the main factor determining human spontaneous mutation rate [1] and, according to the mutation theory of aging [2], might have long-term effects on offspring longevity [3]. We report a strong inverse relationship between father's age at reproduction and daughter's (not son's) longevity.

The results of long-term follow-up of 8518 persons from European aristocratic families with known genealogy (taken from more than 120 genealogical publications listed elsewhere [4]) are presented in Table 1.

Note that daughters born by old fathers lose about 4.4 years of their life and that these losses are statistically highly significant ($p < 0.01$, Student's test = 3.1), while sons are not significantly affected. Since only daughters inherit the paternal X chromosome, this sex-specific decrease in daughters' longevity might indicate that human longevity genes (crucial, house-keeping genes) sensitive to mutational load might be located in this chromosome [4].

Although a strong inverse relationship has been shown between daughters' longevity and paternal age at reproduction, this does not prove a cause and effect, and other confounding factors (maternal age, in particular) may be involved. Our preliminary studies showed, however, that maternal age at reproduction was not important in the range of 20–40 years

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Table 1
Human longevity and sex differential in longevity as a function of father's age at reproduction

Paternal age at reproduction [b] (years)	Mean age at death [a] ± standard error (years)		Sex differential in life span (years)
	Daughters (sample size)	Sons (sample size)	
20–29	66.5 ± 0.7 (592)	61.3 ± 0.4 (1238)	5.2 ± 0.8
30–39	65.9 ± 0.5 (1214)	60.8 ± 0.3 (2580)	5.1 ± 0.6
40–49	64.4 ± 0.7 (694)	60.5 ± 0.4 (1543)	3.9 ± 0.8
50–59	62.1 ± 1.2 (206)	60.3 ± 0.7 (451)	1.8 ± 1.4

[a] Human longevity was calculated for adults (those who survived by age 30) born in 18th and 19th centuries. The data for those born in 20th century were excluded from the analysis in order to have unbiased estimates of longevity for extinct birth cohorts.
[b] Data are controlled for father's longevity (all fathers lived 50 years and more) in order to eliminate bias caused by correlation between father's and offspring life span.

[4]. Larger epidemiological studies are planned and may cast more light on the long-term effects of paternal age at reproduction.

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