RESEARCH NOTE

Chromosomal changes in ageing

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Introduction

Ageing as a phenomenon, and the possibilities of postponing, reversing or abolishing it, have fascinated humans for a very long time as both mythology and history testify (Joshi 2005). In the past couple of centuries, scientists proposed a number of ageing theories, but none of them was completely satisfactory. Current theories regarding proximal causes of ageing can be classified into two major categories: theories invoking a program directing ageing and stochastic theories. Programmed ageing theories assume the existence of a purposeful genetic program that determines the ageing process. In contrast, stochastic or error-based theories suggest that ageing is driven by random, accidental events that cause mutations and/or deregulation of cellular processes, and finally lead to cellular dysfunction and senescence (Hayflick 2000, 2007; Semsei 2000). Considerable progress in identifying genes involved in the ageing process has been made in genetically tractable model organisms such as, yeast, the nematode *Caenorhabditis elegans*, the fruitfly *Drosophila melanogaster* and mice (Guarente and Kenyon 2000). These studies have revealed several specific genes that appear to regulate ageing, such as *age-1* and *clk-1* in nematodes, *sir-2* in yeasts, *Tor, mth* and *Indy* in flies and *klotho* in mice (Takahashi *et al*. 2000; Christensen *et al*. 2006). Studies performed on *D. melanogaster* have shown that diet plays an important role in longevity, too (Joshi *et al*. 1996).

Recent studies in humans have uncovered a number of genes with a potential role in longevity and disease. Good examples are "disease-protective alleles" such as, *APOE* and *APOE2*, *APOC3*, and some HLA variants, which have been described in higher frequency in centenarians (Lao *et al*. 2005).

Changes in chromosomal structure or function are also strongly associated with ageing, although it is not yet clear whether these changes are part of the cause or a consequence of ageing. Cellular ageing is associated with a higher frequency of cells with various chromosomal aberrations. Cytogenetic studies in presenescent cells from elderly people showed an increase in the frequency of cytogenetic changes (Bolognesi *et al*. 1999; Wojda *et al*. 2006). Lymphocytes obtained from elderly persons demonstrate an increased number of DIC and RING chromosomes, suggesting a lot of damaged DNA (Davidovic 1995). The goal of the present study was to determine the frequency of chromosomal aberrations in different age groups and try to link these observations to the process of ageing.

Methods

The study group was recruited from a random sample of 106 hospitalized elderly persons (over 65 years) and divided them into six age subgroups (65–69, 70–74, 75–79, 80–84, 85–89, and over 90 years). The control group ($n = 42$) was selected among younger persons, ranging from 5 years to 50 years old and divided them into three subgroups (5–14, 18–20 and 45–50 years). Cytogenetic analyses were performed on lymphocytes obtained from peripheral blood, cultured by a slightly modified Moorhead method. Samples were scored for all chromosomes, ring chromosomes, acentric fragments and chromatid or chromosome breakages. Among numerical changes, only tetraploid cells and endoreduplications were considered important. Statistical analysis was performed by Chi-square test, and probabilities of less than 0.05 were considered significant.

Results

The frequency of chromosomal aberrations was higher in elderly persons (6.08%), as compared to the groups of younger individuals (2.92%, 3.2%, 4.6%, respectively, for the control subgroups) ($P < 0.01$). Regarding subgroups among the elderly, we have found the following frequency distribution of chromosomal aberrations: 9.3% (65–69 years), 6.8% (70–74 years), 6.7% (75–79 years), 3.5% (80–84 years), 5.3% (85–89 years) and 4.8% (over 90 years old) (figure 1).

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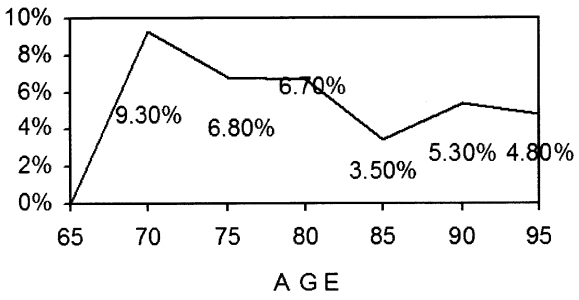

Figure 1. Chromosomal aberration frequency in elderly humans.

Discussion

The effects of ageing in humans appear to be a combination of the influence of genetically programmed phenomena and exogenous environmental factors, and that takes place at the cellular level (Wojda and Witt 2003). Many processes that occur in somatic cells as a consequence of DNA replication (accumulation of DNA errors or mutations that outstrip repair processes e.g. telomere shortening and deregulation of apoptosis) cause replicative senescence in human cells (Fenech 1998; Wojda and Witt 2003). Such genetic instability could be one of the basic proximal reasons for senescence, and it is also often associated with cancer and various disorders of immune system (Cutler 1992).

In our study, we found a higher frequency of chromosomal aberrations in the elderly, compared to the younger control population. Our results are similar to those published by Wojda *et al*. (2006), who found that ageing is marked by a higher level of chromosomal aberrations. These findings together imply that cytogenetic aberrations could be considered as potential biomarkers of ageing, especially as detection of chromosome aberrations in old people is a relatively simple method for verification of the genetic instability.

From the data of our study, we were surprised by the relatively low percentage of chromosomal aberrations in the "oldest old" (aged 80 years or above), which was comparable to the percentage found in the younger control population. This finding corresponds to an earlier finding of low level of chromosomal abnormalities in centegenerians (Wojda *et al*. 2006). In light of these facts, we can assume that very old people had the slower rate of accumulation of genetic damage throughout their lives. Thus, the relatively low level of chromosomal aberrations in the "oldest old" people is likely to be both a consequence of their genetic stability and a contributing factor to their attainment of advanced age. They are practically in the same position as the normal middle-aged population (Davidovic 1999) and represent the special subgroup of elderly - the "privileged one" (Davidovic *et al*. 2003). Recent research has shown that although there is an exponential increase in adult mortality with age, it declines in the "oldest old" population (late-life mortality plateau). The discovery that at least some measures of ageing appear to plateau in late life is a significant discovery in ageing research (Mueller and Rose 1996; Rose *et al*. 2006; Mueller *et al*. 2007). We believe that our findings regarding chromosomal aberrations in the "oldest old" population are in accordance with the work of Mueller and Rose (1996), which dealt with ultimate or evolutionary causes of ageing.

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