

## Genetic Stability and Aging

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### Letter to Editor

Biological aspects of aging are interdisciplinary topics in gerontology and geriatrics. Aging begins at the cellular level and then spread to tissues and organs. Knowledge of mechanisms guiding aging at the cellular level improves our understanding of what happens to the human organism. It is generally accepted that the organism aging is accompanied by accumulation of mutations and genetic instability [1]. The number of publications devoted to the aging research at the genomic level each year increases. But asking some questions raises others.

A great contribution to this field was made by researchers who used somatic cells maintained *in vitro*. Hayflick was the first who demonstrated the cell aging. He stated [2] that normal human cells were limited to divide while prior it had been declared that expanded human cells are immortal. In other words, it was found that these cells underwent a certain number of population doubling and then die. The process is developed gradually, growth rate reduces, cells acquire modified morphology and drastic changes at the molecular level. These findings made these cells as a widely-used model of the aging processes. Later the research was mostly focused on cultured human mesenchymal stem cells (MSC). These cells also exhibit limited proliferation potential varied depending on the donor and tissue origin. MSC reside *in vivo* and facilitate repair of damaged tissues over the lifespan of the organism. There is an emerging body of evidence that their altered function plays an important role in diseases of aging.

It is widely accepted that the organism lifespan is genetically controlled. On the other hand, aging is caused by accumulation of various forms of unrepaired cellular damage produced by endogenous and exogenous stresses. The basic cell stress response is DNA damage resulted in mutational changes in the genome [3]. Unrepaired damages result in disturbances in the genetic apparatus at the karyotype level. A debate topic is a genetic stability of *in vitro* expanded MSC [4]. The genetic stability at various cultivation steps can be monitored with chromosome analysis. It was proposed that MSC long-term cultivation

and aging may be accompanied with karyotypic abnormalities. We examined the karyotype with molecular and morphological karyotyping in a number of MSC lines. On the first steps cells in most lines had normal karyotype. The frequency of random chromosomal aberrations increased during cultivation. They were evident mostly as aneuploidy and chromosomal rearrangements [5]. Until recently, an undeservedly little attention has been paid to apply chromosome analysis for aging assessment. Nowadays, the karyotyping is thought to be a very informative parameter for evaluation of aging cells. Collectively, our findings show that aging *in vitro* is accompanied with genetic instability. They apparently shed light on the events that takes place in stem cells in aging human organism [6]. Current medicine is broadly focused in developing cell therapies based on mesenchymal stem cells (MSC), with applications to aging-associated diseases and rejuvenescence. Extensive *ex vivo* cell expansion is required to accumulate a substantial cell mass needed for cell therapy. However, it is quite likely that long-term culture evokes genetic instability which should be carefully monitored before cell application in the cell therapy.

### References

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