GENETICS

Dynamics of Chromosomal Aberrations in Male Mice of Various Strains during Aging

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We studied the incidence of chromosome aberrations in bone marrow cells and primary spermatocytes in various mouse strains. Experiments were performed on SAMP mice (accelerated aging), control SAMR mice, and long-living CBA and SHR mice. Experiments revealed a positive correlation between the age and the incidence of mutations in their somatic cells and gametes.

Key Words: *chromosomel aberrations; aging; interstrain differences; mice*

Somatic mutations play an important role in aging. The age-related dynamics of somatic mutations differs in various animal species and strains and probably determines lifetime [5,12]. It was reported that inbred mice differ in their lifetimes and rates of aging. Mutant SAMP mice are characterized by short lifetime (14 months) and more rapid aging compared to control SAMR mice [11]. It was hypothesized that uncompensated accumulation of reactive oxygen species underlies accelerated aging of SAMP mice [2,6]. Animals of these strains are characterized by normal development to the 4th month of life. Then the content of reactive oxygen species increases, which is accompanied by rapid aging [2]. SAMP mice carry a greater number of somatic mutations than SAMR mice [7,8]. We found no data on the age-related dynamics of this process in SAMP and SAMR mice compared to that in other strains of animals.

Here we compared the age-related dynamics of chromosomal aberrations (CA) in male SAMP and SAMR mice with that in CBA and SHR mice (long-living animals differing in the incidence of spontaneous neoplasms [9]).

MATERIALS AND METHODS

SAMP-1 and SAMR-1 mice were obtained from the Moscow State University and kept in the Department of Carcinogenesis and Oncogerontology (N. N. Petrov Institute of Oncology). Two-month-old CBA and SHR mice were obtained from the Rappolovo nursery. The animals were kept in plastic cages under natural light/dark regimen and *ad libitum* food and water supply. The incidence of CA in bone marrow cells and primary spermatocytes was studied in 3, 6, and 9-month-old animals [4]. Each group included 4 mice of the same age and strain. The data were processed statistically using methods for small samples. The significance of differences was estimated by Student's *t* test.

RESULTS

In all mouse strains the incidence of CA in bone marrow cells and primary spermatocytes increased during aging (Fig. 1, *a*, *b*). The incidence of CA in bone marrow cells in SAMP males was higher than in 3-, 6-, and 9-month-old SAMR, CBA, and SHR mice. The incidence of CA in gametes and somatic cells of 6- and

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9-month-old CBA mice was higher than in SHR males. This is consistent with higher incidence of spontaneous neoplasms in CBA mice, since mutations are known to contribute to tumor development. However, the incidence of CA in CBA and SHR mice was significantly lower than in SAMR and SAMP mice (except for somatic cells in 6-month-old animals, Fig. 1, *a*).

The increase in the incidence of CA in all mouse strains during aging attests to a positive correlation between these parameters and is consistent with published data [3,9,10,12]. Moreover, this is confirmed by the highest level of mutability in SAMP mice characterized by accelerated aging and short lifetime.

The causal relationship between studied parameters remains unclear. Since SAMP mice probably have hereditary defects of the antioxidant system [2], it can we assumed that the high incidence of CA in these animals results from the effects of reactive oxygen species on DNA molecule and DNA reparation and replication enzymes. This assumption is consistent with published data that normal aging is accompanied by suppression of antioxidant processes, while exogenous antioxidants decrease the rate of aging and the incidence of mutations [1]. Therefore, high content of reactive oxygen species is probably responsible for both rapid aging and high incidence of CA in male SAMP mice. It can not be excluded that high mutability is an additional factor accelerating aging associated with the defective antioxidant system in SAMP mice.

Our experiments demonstrated a positive correlation between the age and the incidence of mutations in gametes and somatic cells in mice. The causal relationship between studied parameters requires further investigations.

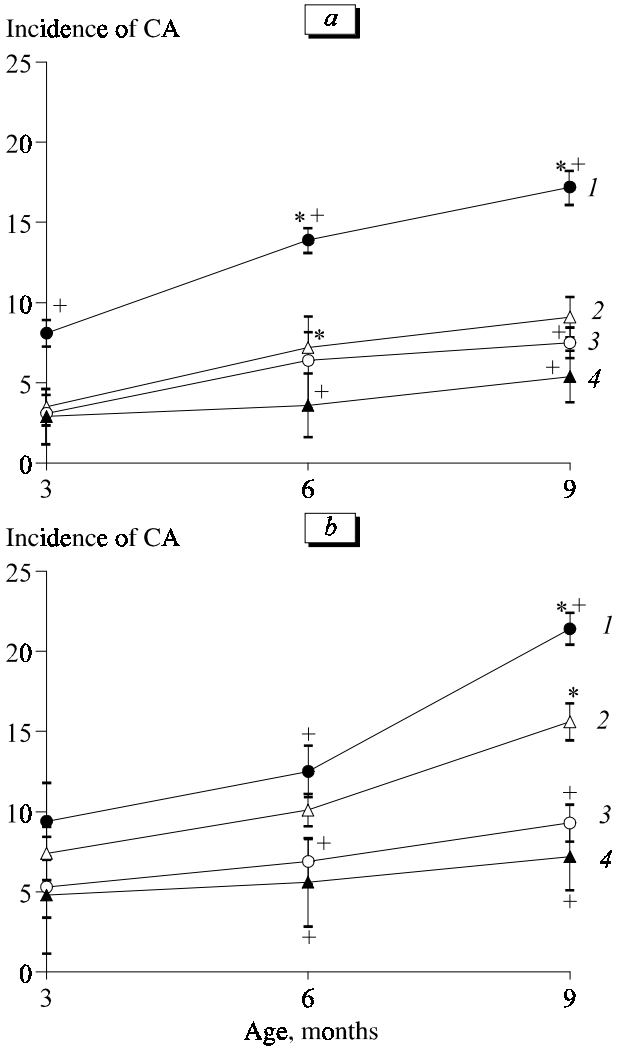

Fig. 1. Incidence of chromosome aberrations (CA) in bone marrow cells (*a*) and primary spermatocytes (*b*) in male SAMP (*1*), SAMR (*2*), CBA (*3*), and SHR (*4*) mice during aging. $p<0.05$: *compared to younger mice of the same strain, +compared to SAMR mice of the same age.

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