GENETICS

Nuclear Weapons Tests and Human Germline Mutation Rate

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The population around the Semipalatinsk nuclear test site in Kazakhstan provides an unparalleled opportunity for the analysis of the genetic risk of ionizing radiation to humans. The Semipalatinsk nuclear test site has been the site for 470 nuclear tests performed by the Soviet Union during the period 1949–89, including atmospheric and surface explosions from 1949 to 1963 and underground tests from 1963 to 1989 (*1*). The surrounding population was mainly exposed to the fresh radioactive fallout from four surface explosions conducted between 1949 and 1956, and currently the radioactive contamination outside the test zone is low (*2*).

Blood samples were collected from 40 three-generation families inhabiting the rural areas of the Beskaragai district of Kazakhstan around the Semipalatinsk nuclear test site. These areas are characterized by the highest effective doses of exposure to ionizing radiation (> 1 Sv) (*2*). The control group was composed of 28 three-generation nonirradiated families from the geographically similar noncontaminated rural area of the Taldy Kurgan district of Kazakhstan. Both groups were matched by ethnicity, year of birth, parental age, occupation, and and whether or not they were smokers. All parents and offspring were profiled with eight hypervariable minisatellite probes CEB1, CEB15, CEB25, CEB36, MS1, MS31, MS32, and B6.7 previously used for the analysis of human families from Belarus exposed to the post-Chernobyl radioactive fallout (*3*, *4*).

The frequency of minisatellite mutation was established in the F_1 and F_2 control and exposed offspring, which yielded germline mutation rates in the P_0 and F_1 generations, respectively. Spontaneous minisatellite mutation rates in the P_0 and F_1 generations of control group were similar ($P = 1$; Fisher's exact test). We therefore combined data for these two generations to produce a single estimate of mutation rate for the control group, which was subsequently compared with the corresponding values in the exposed population. A statistically significant 1.8-fold increase in mutation rate was found in the P_0 generation, and a less marked 1.5-fold increase was also found in the F_1 generation (Fig. 1A).

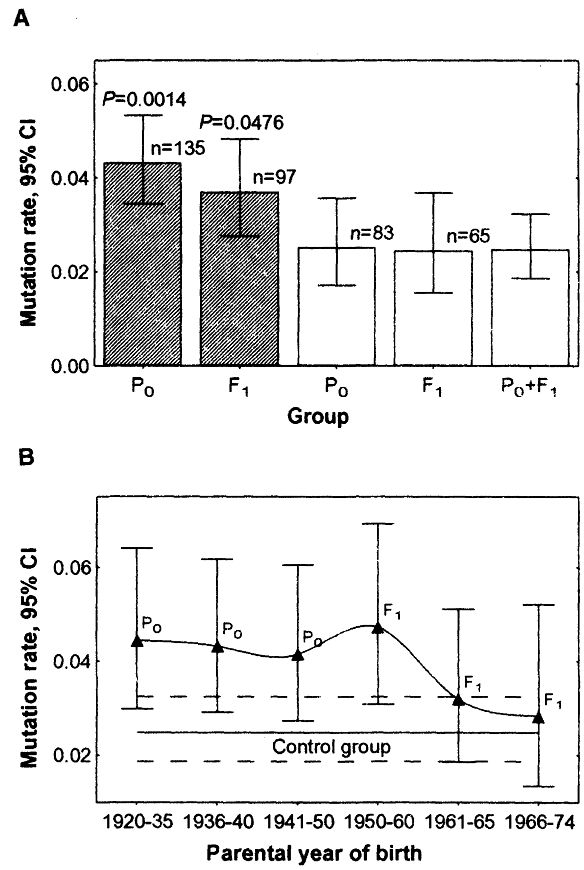

Fig. 1. (**A**) Germline mutation rates [±95% confidence intervals (CI)] in the control (open boxes) and exposed (hatched boxes) groups. Probabilities of difference from the whole control group and the number of offspring in each cohort are given. (**B**) Germline mutation rate in the exposed parents grouped according to year of birth. The solid line represents mutation rate (±95% CI) for the whole control group.

Up to 85% of the collective effective dose for the population around the Semipalatinsk nuclear test site was attributed to just four surface explosions carried out in 1949, 1951, 1953, and 1956 (*1*). All P_0 parents born between 1926 and 1948 were therefore directly exposed to relatively high levels of ionizing radiation after these tests. Some F_1 parents (born between 1950 and 1956) were also exposed over this crucial period, whereas those born later were likely to receive considerably smaller doses (*2*). This heterogeneity in the parental exposure could explain a relatively moderate 1.5-fold increase in the mutation rate in the F_1 generation. Thus, for all cohorts of P_0 parents from the Semipalatinsk district, the germline mutation rate remains stable and significantly exceeds that for the control group, apparently reflecting a relatively uniform high-dose exposure during the late 1940s to early 1950s. (Fig. 1B). Meanwhile, germline mutation rate in the exposed F_1 generation shows a negative correlation with the parental year of birth, with the highest mutation rate in the most exposed cohort of parents born before 1960, similar to that in the P_0 families. This negative correlation may therefore reflect the decreased exposure after the decay of radioisotopes in the late 1950s and after the cessation of surface and atmospheric nuclear tests, thus suggesting that an elevated mutation rate in the affected families is indeed radiation induced.

In conclusion, this study shows that the exposure to radioactive fallout from the nuclear weapons tests carried out at the Semipalatinsk nuclear test site in the late 1940s to early 1950s roughly doubled germline mutation rate in the affected population. Most importantly, the negative correlation between mutation rate and the parental year of birth found in the heterogeneously exposed F_1 families provides experimental evidence for change in human germline mutation rate with declining exposure to ionizing radiation and therefore shows that the Moscow treaty banning nuclear weapon tests in the atmosphere (August 1963) has been effective in reducing genetic risk to the affected population.

References and Notes

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