CELLULAR AND MOLECULAR EFFECTS OF ELECTROMAGNETIC FIELDS

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Abstract

We designed and manufactured several equipments for exposure of cells to high-density (5 to 400 mT) ELF electromagnetic fields. This paper reviews our studies on genetic effects of ELF electromagnetic fields. There may be genotoxic activity due to exposure to high-density ELF electromagnetic field, such as 400 mT at 50 Hz. We observed significant increase in mutation at the HPRT gene and in expression of some genes in cultured cells after exposure to the 400 mT ELF electromagnetic field. Exposure of cells to the high-density 400 mT ELF electromagnetic field may affect the signal transduciton in the cells, resulting in the enhanced gene expression.

Introduction

The increased use of electrical energy in modern society has subjected the general and working population to unprecedented levels of exposure to ELF electromagnetic fields. There has been speculation that ELF electromagnetic fields can act as promoters or co-promoters of cancer. Some epidemiological studies have revealed a positive association between exposure to ELF electromagnetic fields and the incidence of several types of cancer, particularly leukemia and brain tumors. However, other studies have failed to discern any association between ELF electromagnetic fields and the incidence of cancer.

In *in vitro* studies, the existance of the effects of the electromagnetic fields at low flux densities has been contradictory among reports. We designed and manufactured several equipments for exposure of cells to high-density (5 to 400 mT) ELF electromagnetic fields [1〜3]. This paper reviews our studies on genetic effects of ELF electromagnetic fields.

Exposure units for ELF electromagnetic filelds and X-rays

Details of the exposure units for 400 mT, 50 mT and 5 mT ELF electromagnetic fields were described elsewhere [1〜3]. In brief, 5 mT (60 Hz ± 0.1 Hz) ELF electromagnetic field exposure unit consists of a CO_2 incubator with a built-in magnet generator using two Helmholtz coils. For 50 mT (60 Hz ± 0.1 Hz) ELF electromagnetic field exposure, the unit consists of a magnet generator using two Helmholtz coils with a built-in CO_2 incubator. For 400 mT exposure, the magnetic field oriented vertically is generated by a pair of magnetic cores. An acrylic CO_2 incubator is installed between the cores. The power source is AC 200 V, 50 Hz (± 0.1 Hz), three phase, and 35 kVA. The waveform of these ELF electromagnetic fields was sine-wave. The temperature in the exposure space in these units was kept at 37 ± 0.2 °C. The mean induced current intensity in the outer ring of the 15 cmφ annular culture plate was estimated to be 115, 1150 and 7660 mA/m^2 at 5, 50 and 400 mT, respectively. For the control experiments, a conventional incubator in a separate room was used. The measured ELF electromagnetic fields in the conventional incubator was < 0.5 μ T. X-irradiation was performed using a Hitachi MBR-1520 at 150 kVp, 20 mA with 0.5 mm Al and 0.1 mm Cu filters with a dose-rate of 0.98-1.02 Gy min^{-1} [4].

Gene expression

For the gene expression, the effect of 5 mT ELF electromagnetic field on *c-myc* mRNA expression was examined in Chinese hamster ovary (CHO) cells. No significant difference in the *c-myc* expression of CHO cells was observed with the ELF-field exposure, sham exposure and incubation in a conventional incubator [3]. Exposure of PC12-VG cells to 400 mT electromagnetic field enhanced the β -galactosidase gene expression stimulated by treatment of the cells with forskolin [5, 6]. The enhancing effect of the ELF electromagnetic field was inhibited by treatment of the cells with a specific inhibitor of PKC, calphostin C, as well as with the Ca^{2+} entry blockers nifedipin and dantrolen (Figure 1).

Enhanced expression of neuron derived orphan receptor (NOR-1) gene was also observed by exposure of CHO-K1 cells to 400 mT ELF electromagnetic field, but not to the 5 mT field [7]. The enhanced expression, reaching the maximum at 6 h, was transient and reduced to the control level after exposure to 400 mT ELF electromagnetic field for 24 h. The NOR-1 expression induced by treatment with forskolin and TPA was further enhanced by the simultaneous treatment with 400 mT ELF electromagnetic field, in which the maximum response was at 3 h.

Mutation

For the mutation induction, exposure to ELF electromagnetic field at 400 mT induced mutations in the hypoxanthine-guanine phosphoribosyl transferase (HPRT) gene of human melanoma MeWo cells [8 ~ 10]. The mutant frequency was enhanced both by increasing the exposure period and the induced current intensity. Mutations induced by X-rays were enhanced by the ELF electromagnetic field exposure. No significant increase in mutant frequency occurred when DNA replication was inhibited during ELF electromagnetic field exposure. Mutation induced by the ELF electromagnetic field increased during the DNA-synthesis phase in synchronously growing phase (Figure 2).

DNA replication error is suspected of causing the mutations produced by ELF electromagnetic field exposure.

Whether exposure to ELF electromagnetic fields at low flux densities induces mutations is debatable. We investigated the effect of long-term exposure to 5 mT ELF electromagnetic field at 60 Hz on mutant frequency. CHO-K1 cells were exposed or sham-exposed to the 5 mT ELF electromagnetic field for up to 6 weeks with or without X-irradiation (3 Gy), and the mutant frequency of the HPRT gene was analyzed [11]. Long-term exposure to 5 mT ELF electromagnetic

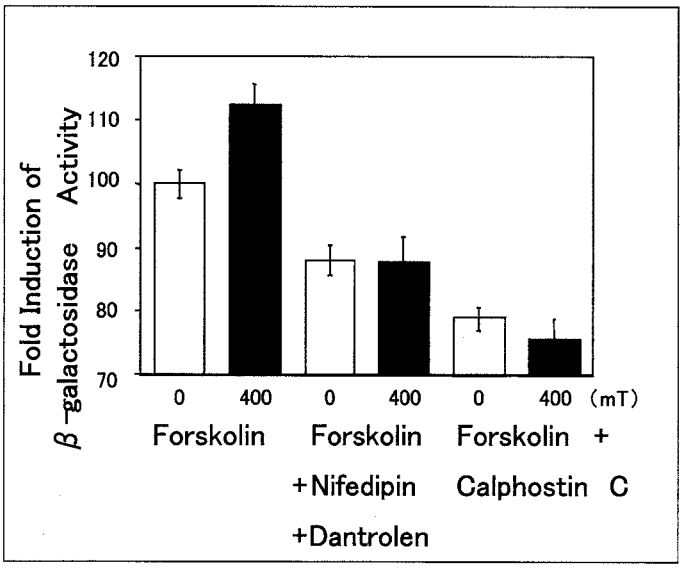

Fig. 1 ELFMF effects on β -galactosidase activity in PC12-VG cells treated with forskolin and the calcium entry blockers, nifedipin and dantrolen, or with forskolin and calphostin C, a specific inhibitor of PKC. Asterisks (*) show the statistic significance ($p<0.01$) in comparison to treatment with forskolin alone.

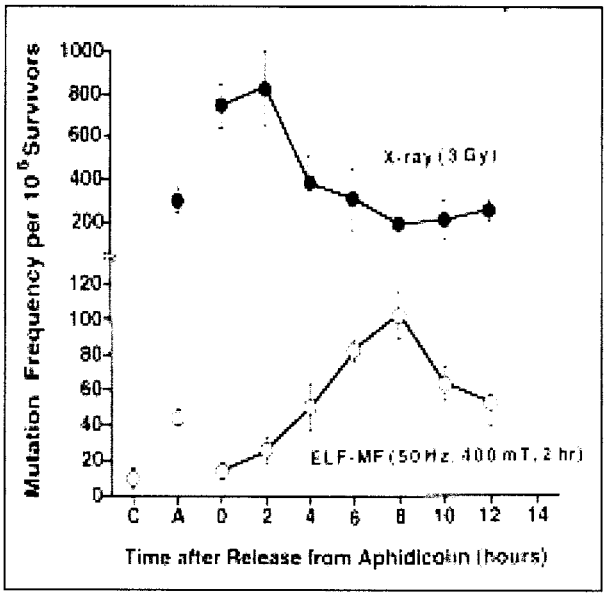

Fig. 2 6+TG^r mutations in synchronously growing MeWo cells induced by exposure or sham-exposure to ELF-MF (400mT at 50 Hz) for 2 h or X-ray irradiation (3 Gy) at various times after release from aphidicolin treatment.

field did not increase mutations, suggesting a threshold for mutation induction greater than a magnetic density of 5 mT. However, enhancement of the X ray-induced mutation rate was observed after treatment with X-irradiation followed by long term exposure to 5 mT ELF electromagnetic field (Figure 3).

These results suggest thtat exposre to more than 5 mT ELF electromagnetic field may promote X-ray-induced mutations.

Conclusion

Most of the published experimental results suggest that very low-density ELF electromagnetic fields do not have a clearly demonstrated potential to cause genotoxic effects. However, there may be genotoxic activity due to exposure to high-density ELF electromagnetic field, such as 400 mT at 50 Hz. We observed significant increase in mutation at the HPRT gene and in expression of some genes in cultured cells after exposure to the 400 mT ELF

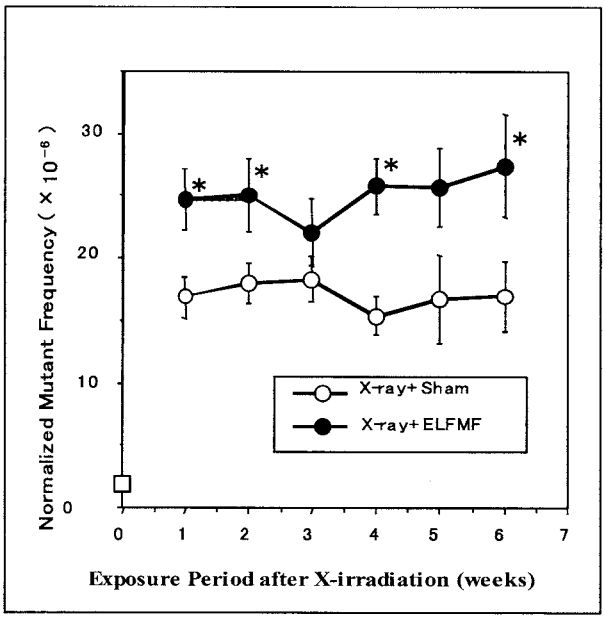

Fig. 3 The normalized mutant frequency of *HPRT*gene in CHO-K1 cells treated with X-irradiation with 3 Gy followed by long-term exposures to ELFMF (5mT at 60Hz) or sham exposure for up to 6 weeks.

electromagnetic field. Exposure of cells to the high-density 400 mT ELF electromagnetic field may affect the signal transduciton in the cells, resulting in the enhanced gene expression. These positive effects of the ELF electromagnetic field were not observed at lower density ELF electromagnetic field, such as 5 mT. There may be a threshold for mutation induction and gene expression, at least over the magnetic density of 5 mT.

Acknowledgement

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