EFFECTS OF RADIO-FREQUENCY ELECTROMAGNETIC FIELD RADIATION ON CELL SIGNALING[1]

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Numerous in vivo and in vitro studies have been performed to investigate the biological and health effects of radio-frequency electromagnetic field (RF) from mobile phone, but the reports of possible effects are contradictory and the mechanism behind the effects are still unclear. For elucidation, it's important to know whether and how a weak RF physical factor transfers into a biological signal and affects on cell signaling. A multicellular organism is a complex interactive entity with the processes of growth, development, and differentiation dependent on the endogenous and exogenous signals between and within various cells. There are three classes of cell communication [1]: extracellular communication, intracellular communication, and intercellular communication.

EXTRACELLULAR COMMUNICATION

That RFs have their targets on cells and may act as ligands to some specific receptors was supposed and epidermal growth factor (EGF) receptor, as one of the specific receptors was identified in our lab. Chinese hamster lung (CHL) cells were exposed to GSM 1800 MHz microwave modulated by 217 Hz pulses for 15 min at SARs of 4.0, 2.0, 1.0, 0.5, and 0.1 W/kg with their sham exposure control each, respectively. The clustering of EGF receptors was examined by indirect immunofluorescence with a conforcal microscope. Cells treated with 100 ng/ml EGF were served as positive control. The results showed that the RF exposure, except 0.1 W/kg, induced obviously clustering of EGF receptors on cell surface (Fig. 1), just like the ligand EGF. However, there was no effect for unmodulated 1800 MHz exposure at the above SARs. The occurrence of clustering of EGF receptor was also observed in HaCaT human keratinocytes following the modulated microwave exposure. Thus, the physical signal may couple from some surface receptors to the cell interior.

INTRACELLULAR COMMUNICATION

There are some reports indicating that RF exposure may activate intracellular signal transduction pathways. Activity of total non-cAMP-dependent protein kinase in human tonsil lymphocytes was decreased to half of control levels after exposure to a modulated RF field at a peak intensity of 1 mW/cm^2 [2]. Consistently, a significant decrease in protein kinase C activity was observed in developing brain of chronically exposed rats to a modulated RF at 1.48 W/kg [3]. The results indicate that the exposure could affect membrane bound enzymes associated with cell signaling. It was also reported that 900MHz GSM microwave radiation at a SAR of 2.4 W/kg activates P38 mitogen-activated protein kinase stress signaling pathway in human endothelial cell line, leading to phosphorytation of Hsp27 [4]. Recently, it was reported that exposure of human epidermoid cancer cells to non-thermal 1.95 GHz microwave decreased the expression of ras and Raf-1 and the activity of

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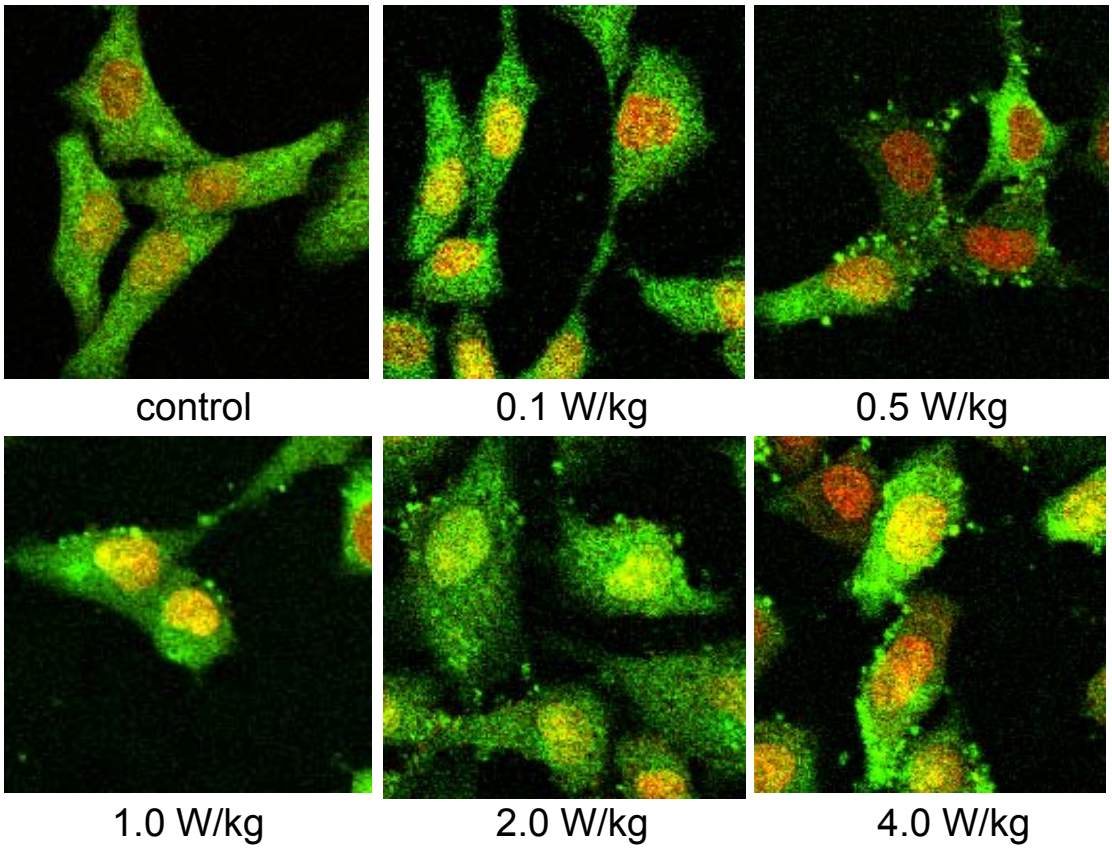

Fig. 1 RF (different SAR) induces the clustering of EGFR

ras and Erk-1/2. However, addition of proteasome inhibitor counteracted the effects of the microwave on ras and Raf-1 expression [5].

INTERCELLULAR COMMUNICATION

A series of experiments conducted in our lab showed that extremely low frequency (ELF) magnetic fields may inhibit gap junctional intercellular communication (GJIC), and due to hyperphosphorylation of connexin 43 (Cx43) and internalization of Cx43, a structural and junctional protein of gap junction, from plasma membrane to cytoplasm [6]. For RF, as a different frequency band electromagnetic field, may also modulate GJIC. It has been reported that the GJIC was significantly inhibited in rabbit lens epithelial cells after the rabbits were irradiated with 2450 MHz for 3 hours. In the experiment, one eye of a rabbit served as experiment eye while the other eye shielded with copper grid cloth served as control. The power densities at the location of the rabbit's eyes were 5 or 10 mW/cm^2. They reported that there were significant differences in GJIC function between control and exposure groups and between the two different exposure groups. Moreover, they also found the gap junction proteins (Cx43), detected by indirect immunofluorescence analysis, in the exposure groups displayed less bright labeled spots in the regions of intercellular junction than the control cells, and most of Cx43 labeled spots occurred in the cytoplasm [7]. An in vitro study on the effects of modulated microwave with precise dosimetry on GJIC will be conducted in our lab. The effects of EMF on GJIC seem to be dependent on the frequency band, as they are very different for ELF, RF and

millimeter wave exposure.

Collectively, it may be suggested that the RF radiation, as a physical extracellular factor, may couple the signal from surface receptor sites to the cell interior. That the cell membrane is the primary site of interaction with RF is supported. The initial events lead to the activation of certain intracellular signal transduction pathways and finally affect the function of GJIC. Modulation of cell signaling may interfere in homeostatic regulations of the body. However, there have no many works on this field so far. Further researches are needed.

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