

# Effect of Exposure to 900 MHz GSM Mobile Phone Radiofrequency Radiation on Estrogen Receptor Methylation Status in Colon Cells of Male Sprague Dawley Rats

Mokarram P.<sup>1</sup>, Sheikhi M.<sup>2</sup>, Mortazavi S. M. J.<sup>3\*</sup>, Saeb S.<sup>4</sup>, Shokrpour N.<sup>5</sup>

## ABSTRACT

**Background:** Over the past several years, the rapidly increasing use of mobile phones has raised global concerns about the biological effects of exposure to radiofrequency (RF) radiation. Numerous studies have shown that exposure to electromagnetic fields (EMFs) can be associated with effects on the nervous, endocrine, immune, cardiovascular, hematopoietic and ocular systems. In spite of genetic diversity, the onset and progression of cancer can be controlled by epigenetic mechanisms such as gene promoter methylation. There are extensive studies on the epigenetic changes of the tumor suppressor genes as well as the identification of methylation biomarkers in colorectal cancer. Some studies have revealed that genetic changes can be induced by exposure to RF radiation. However, whether or not RF radiation is capable of inducing epigenetic alteration has not been clarified yet. To date, no study has been conducted on the effect of radiation on epigenetic alterations in colorectal cancer (CRC). Several studies have also shown that methylation of estrogen receptor  $\alpha$  (ER $\alpha$ ), MYOD, MGMT, SFRP2 and P16 play an important role in CRC. It can be hypothesized that RF exposure can be a reason for the high incidence of CRC in Iran. This study aimed to investigate whether epigenetic pattern of ER $\alpha$  is susceptible to RF radiation and if RF radiation can induce radioadaptive response as epigenetic changes after receiving the challenge dose ( $\gamma$ -ray).

**Material and Method:** 40 male Sprague-Dawley rats were divided into 4 equal groups (Group I: exposure to RF radiation of a GSM cell phone for 4 hours and sacrificed after 24 hours; Group II: RF exposure for 4 hours, exposure to Co-60 gamma radiation (3 Gy) after 24 hours and sacrificed after 72 hrs; Group III: only 3Gy gamma radiation; Group 4: control group). DNA from colon tissues was extracted to evaluate the methylation status by methylation specific PCR.

**Results:** Our finding showed that exposure to GSM cell phone RF radiation was capable of altering the pattern of ER $\alpha$  gene methylation compared to that of non-exposed controls. Furthermore, no adaptive response phenomenon was induced in the pattern of ER $\alpha$  gene methylation after exposure to the challenging dose of Co-60  $\gamma$ -rays.

**Conclusion:** It can be concluded that exposure to RF radiation emitted by GSM mobile phones can lead to epigenetic detrimental changes in ER $\alpha$  promoter methylation pattern.

## Keywords

Radiofrequency (RF), DNA Methylation, Colon Cancer, Mobile Phone, Microwave

<sup>1</sup>Department of Biochemistry, Shiraz University of Medical Sciences, Shiraz, Iran

<sup>2</sup>Department of Radiobiology, School of Paramedical Sciences, Shiraz, Iran

<sup>3</sup>Ionizing and Non-ionizing Radiation Protection Research Center (INIR-PRC), Shiraz University of Medical Sciences, Shiraz, Iran

<sup>4</sup>Department of clinical biochemistry, school of medicine, Shiraz University of Medical Sciences, Shiraz, Iran

<sup>5</sup>Professor, School of Paramedical Sciences, Shiraz University of Medical Sciences, Shiraz, Iran

\*Corresponding author: S. M. J. Mortazavi, Ph.D. Medical Physics & Medical Engineering Department, The Head Ionizing and Non-ionizing Radiation Protection Research Center (INIRPRC), Shiraz University of Medical Sciences, Shiraz, Iran Shiraz University of Medical Sciences, Zand Street, Shiraz, Iran  
E-mail: mmortazavi@sums.ac.ir

Received: 6 June 2015  
Accepted: 12 June 2015

## Introduction

Over the past few years, the increasing use of mobile phones has led to a rise in the general community concerns about the possible risks of its use. In addition, the global system for mobile communications has provoked the researchers' attention on the biological effects of microwave radiation. Many studies have shown that health hazards can be triggered by cell phones [1-3].

The adaptive response is an important effect of low dose radiation. Several factors including DNA repair, cell cycle regulation, antioxidant defense and the suppression of p53 accumulation may be involved in regulating the radiation response [4, 5].

Several studies have revealed that electromagnetic fields can lead to side effects in the nervous, endocrine, immune, cardiovascular, hematopoietic and ocular systems. Despite the increasing number of reports on the effects of electromagnetic radiation (EMR) in various biological systems, no satisfactory mechanism has been proposed to explain the effects of these exposures [2, 6-8]

Recently, the International Agency for Research on Cancer reported that RF exposure is a possible carcinogen. Furthermore, there are reports indicating higher risks of cancer in heavy mobile phone users [9]. In addition, a cohort study in Denmark showed some evidence of an increased risk of skin cancer among the users of mobile phones [10].

However, some recent studies have not shown an association between the risk of early childhood cancers and mother's exposure to mobile phone or living in the vicinity of base stations during pregnancy [4]. Moreover, this correlation was not detected in cancerous adults [3, 11].

In addition to genetic alteration, the onset and progression of cancer can be controlled by epigenetic mechanism such as gene promoter methylation. Epigenetic alterations are heritable changes in the structure and function of the genome that occur without changes in DNA

sequence. Epigenetic regulation has also been established for developing new approaches to cancer therapy [12].

Recently, many studies have reported the importance of DNA methylation as a biomarker for the early detection of cancer and a tool for monitoring patients with different types of cancer. In this regard, there are extensive studies on the biological significance of tumor suppressor genes as well as the identification of methylation biomarkers in colorectal cancer [12].

Studies have also shown that methylation of ER $\alpha$ , MYOD, MGMT, SFRP2, P16, APC, DCC, MINT, COX2, HLFT, SOCS1, and hMLH1 gene promoters play an important role in colorectal carcinogenesis [12, 13].

Estrogen receptor alpha (ER- $\alpha$ ), known as NR3A1 (nuclear receptor subfamily 3, group A, member 1), is encoded by the gene ESR1 (Estrogen Receptor 1), acts as ligand-activated transcription factors, and modulates gene expression by interactions with promoter response elements or other transcription factors via hormone binding, DNA binding and activation of transcription domains [14].

In spite of the fact that estrogen and its receptors are essential for sexual development and reproductive function, estrogen is involved in pathological processes including breast cancer, endometrial cancer and osteoporosis [15, 16]. ER promoter methylation seems to play a role in the early stages of carcinogenesis in several tumor sites including lymphoma, esophageal cancer and CRC [17].

Some studies have reported that CpG island methylation of the estrogen receptor (ER) is increased with age in non-neoplastic colorectal epithelium, and the same methylation occurred in most sporadic colorectal neoplasia [17]. In addition, the methylation level of the ER gene in UC patients with neoplasia was significantly higher than that in UC patients without neoplasia throughout the colorectum [18]. In addition to genetic alterations, the epigenetic modifications may be involved in

causing disruption of diseases such as autism [19] and cancer via an epigenomic side-effect of exposure to electromagnetic radiation.

On the other hand, numerous studies demonstrated that genetic changes are produced by radiofrequency (RF) radiation; however, the biological effects of RF radiation on the epigenetic factors are poorly understood. Several genes and environmental factors are involved in cancer, and electromagnetic fields may be one of these environmental factors. In this regard, colon cancer is a great model system for investigating the epigenetic mechanism of aberrant gene expression alteration [12]. Furthermore, the incidence of CRC increases due to changes in the lifestyle in Iran, and RF exposure could be a reason.

Over the past several years, our laboratories have expanded their focus on studying the health effects of exposure to some common and/or occupational sources of electromagnetic fields (EMFs) such as cellular phones [20-27], mobile base stations [28], mobile phone jammers [29], laptop computers [30], radars [21], dentistry cavitrons [31] and MRI [32, 33]. To the best of our knowledge, there is no study on the effect of RF radiation on epigenetic alteration in CRC. Therefore, the present study is an attempt to investigate whether epigenetic pattern of ER $\alpha$  is sensitive to RF radiation and may be adapted to epigenetic changes after the challenge dose ( $\gamma$ -ray).

## Material and Methods

In this study, male Sprague-Dawley rats 3 weeks old weighing 200-250g were used.

The animals were purchased from the Experimental and Comparative Medicine Center at Shiraz University. Forty rats were randomly divided into 4 groups and kept in an animal care facility; food and water were supplied ad libitum. The animals in group I were exposed to cell phone radiation for 4 hours, (the rats were placed on a circle with a radius of 20 cm) and then sacrificed after 24hrs. Animals in group II were exposed to cell phone, after 24hrs irradiated by 3Gy  $\gamma$  (Co-60), and scarified after 72hrs. In group III, 10 rats were exposed to 3Gy  $\gamma$  radiation and group IV was used as control without exposure to RF.

A commercial mobile phone (Nokia, N70) with an average SAR of 0.95 W/kg was used to exposures. After exposure to radiation, the rats were sacrificed; the large bowel was removed and washed. The fresh samples were immediately snap frozen and stored at -80°C until processing. Then, genomic DNAs were extracted as described previously [34] and the purity of DNA was measured with Nano-drop.

## Methylation-specific PCR (MSP)

We determined ER promoter methylation status by chemical treatment with sodium bisulfite and subsequent MSP, as described in [34]. In brief, this technique uses bisulfite Modification to convert the unmethylated but not methylated cytosine to uracil. MSP utilizes this difference to amplify specifically either methylated or unmethylated DNA and primers. The sequences of primers used for amplification of the ER promoter are shown in Table 1.

**Table 1:** The Primer Sequences of ER Genes

Gene	Primer Sequence (5'-3')	Annealing Temperature, °C	Product Size, bp
Esr1 M-sense	TGAGTGTGTTTGTGTATTCGTATTC	50	M=137
Esr1 M-antisense	ATACTTCTCTACTCTCCACATCGTT	50	
Esr1 U-sense	GTGTGTTTGTGATTTGATTTGA	50	U=129
Esr1 U-antisense	ATACTTCTCTACTCTCCACATCATT	50	

The hot-start PCR reactions were performed in a 50 $\mu$ L reaction volume containing modified DNA in PCR buffer provided by Taq enzyme supplier. The reaction mixture was denatured at 95°C for 5 min, after which 1.5 U Taq polymerase was added; then, it was amplified by 40 cycles, each consisting of 30s denaturation at 95 °C, 45s annealing at 57°C for ER, and 30s polymerization at 72°C, followed by a single 10-min extension at 72°C. Negative controls were performed for each PCR set. 10  $\mu$ L of amplified PCR products was mixed with 5  $\mu$ L gel loading dye and electrophoresed on 2.5% agarose gel containing 0.5  $\mu$ g/ml gel red with TBE buffer and visualized under UV illumination. The universal methylated DNA (Zymo research) was used as positive control for methylated alleles of ER. The frequencies of the methylation status of ER promoter are summarized in Table 2.

## Results

As shown in Figure 1, the presence of ER methylated allele was 10/10 (100 %) for each group; whereas, the un-methylated band was variable between groups. Although un-methylated bands were detected in 100% of the control group, they disappeared in 10 rats exposed to cell phone and 3Gy gamma radiation.

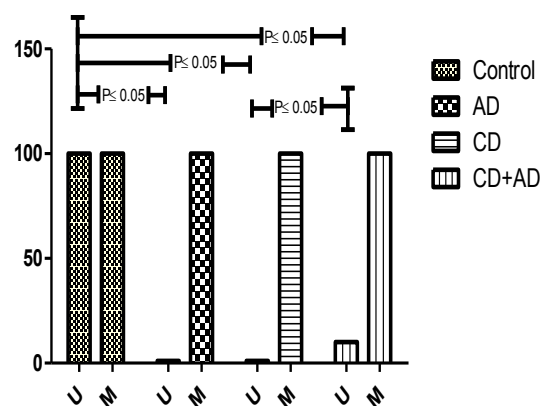
In addition, rats in group II which were exposed to cell phone and then after 24hrs irradiated with 3Gy gamma (Co-60) could not

compensate for the epigenetic damage and un-methylated bands were detected in 10% of the rats. Some examples of ER methylation in different treated groups are shown in Figure 2.

## Discussion

In the current study, we clarified that methylation pattern of ER $\alpha$  is sensitive to RF radiation which may not be adapted to epigenetic changes after the challenge dose ( $\gamma$ -ray).

The data indicated that the rat colon epithelium appears to behave differently as compared to the human epithelium tissue in the case of ER methylation. Normal cells are completely semi-methylated and only a subset of rats exposed to radiation showed un-methylated ER allele. This marked difference between the colonic epithelium in rats and human may

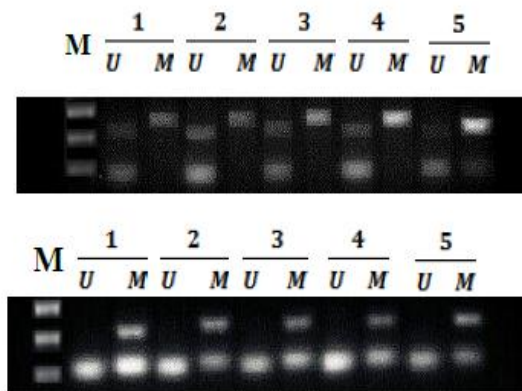


**Figure 1:** Methylation Status in Different Groups

**Table 2:** The Frequencies of Methylation Status of ER Promoter

GROUP	Methylation Status (%)	
	Methylated allele	Unmethylated allele
Group I (AD)	100%	0%
Group II (AD+CD)	100%	10%
Group III (CD)	100%	0%
Group IV (Control)	100%	100%

Group I: Rats were exposed to cell phone radiation for 4 hours, Group II: the rats were exposed to cell phone radiation, then after 24hrs irradiated with 3Gy gamma radiation. Group III: the rats were exposed 3Gy $\gamma$ . Group iv: control group. M, U shows the presence of methylated or unmethylated allele.



**Figure 2:** Examples of MSP reactions for promoter methylation analysis of ER in the control group and irradiated sample by cell phone. U indicates the presence of un-methylated allele, and M indicates the presence of methylated allele.

be related either to differential effects of ER expression on cellular proliferation or to differences in carcinogenic exposures in the two species.

Recently, DNA methylation and its role in tumorigenesis have become one of the hotly debated issues in molecular oncology. More recently, total hypomethylation with specific hypermethylation at individual loci was observed in cancer. More studies suggest that DNA hypomethylation may also control the gene expression and chromosomal stability [35].

Many researchers have proposed some candidate genes which are hyper-methylated in several cancers including colorectal cancer (CRC) [36].

ER alpha and MYOD, p53 the cell cycle regulatory genes, cyclin A1, UDP-glucuronosyltransferase (UGT1A1) and retinoic acid receptor (RAR) are hypermethylated in colorectal cancer. This type of change in methylation appeared in an early phase of colon carcinogenesis [35]. Treatment with either the inhibitors of histone deacetylase or demethylating agents restore the normal expression of hypermethylated cells [35]. Among these genes,

the methylation status of ER promoter in the lymph nodes of stage I and II CRC patients may be a useful marker for the identification of patients at a high risk for local recurrence [37].

Nowadays, the correlation of environmental chemicals and radiation with alterations of the epigenome which potentially contribute to cancer and other diseases has been proved.

Evidence indicates that exposure to different sources of electromagnetic fields (EMFs) decreases the human sperm motility and also the visual reaction time in university students and radar worker [1, 30]. However, it is not known whether non-ionizing radiation directly induces changes in the epigenome of irradiated cells to increase the risk of cancer.

There is only one study that indicated the electromagnetic fields do not have enough energy to cause DNA alterations directly; however, they are able to induce epigenetic modifications in several diseases in the nervous system such as autism [19].

Therefore, our aim in current study was to investigate the ER methylation status in the colon tissue after exposure to RF.

Based on our results, exposure to mobile radiation might be dangerous due to the decrease in the content of U-allele which causes ER expression compared to non-exposure control.

Although we considered the fact that gene hypermethylation is a hallmark for cancer, it seems that the harmful epigenetic alteration could increase in M-allele or decrease in U-allele of the target gene.

For the first time, our data showed that the effect of exposure to mobile phone radiation and 3Gy gamma radiation are the same and both of them could decrease U-allele in the treated colon tissues of rats compared to the controls ( $p=.000$ ). In addition, these epigenetic changes via cell phone could not be protected by challenging gamma radiation. In this regard, there is a controversy between the effects of radiation on the epigenetic alteration. In one study, researchers showed that

acute gamma radiation treatment of two types of human cells had no appreciable direct effect on DNA cytosine methylation patterns in the exposed cells. However, another study demonstrated that radiation induces epigenetic changes and the degree of differential methylation of these pathways varied with radiation dose and time post-irradiation which is consistent with our study. We used 3Gy radiation compared to 10 Gy that was used in Lahtaz's study. Therefore, our results are in line with those of Antwih et al. [38] showing that lower radiation differs in epigenetic alteration compared to higher doses. Herein, we could not detect adaptive response (AR) in epigenetic alterations in our treated groups. Our results were not in the same line with those of other studies that showed the DNA methylation contributes to AR to ionizing radiation or Cd in Human B lymphoblast cells. They showed that long-term low-dose radiation (LDR) or long-term low-dose Cd exposure induced AR against challenging doses of Cd and irradiation, respectively [39].

However, it seems that RF radiation could not protect the effect of 3 Gy radiation in the colon tissue. The reason for this discrepancy might be time, dose of radiation exposure and type of tissue that were evaluated. Since the epigenetic alterations are tissue-specific, the data from B-cell will be different in comparison to the colon tissue [39].

In conclusion, DNA methylation changes suggest an epigenetic role in the cellular response to RF radiation. However, more investigations should be conducted to clarify the epigenetic side effects of RF radiation as an influential risk factor for cancer and claim that RF radiation might be considered as dangerous as ionizing agent in the case of epigenetic alterations.

## Acknowledgement

This study was supported by the Ionizing and Non-ionizing Radiation Protection Research Center (INIRPRC), Shiraz University

of Medical Sciences (SUMS), Shiraz, Iran.

## Conflict of Interest

None Declared

## References

1. Mortazavi SM, Ahmadi J, Shariati M. Prevalence of subjective poor health symptoms associated with exposure to electromagnetic fields among university students. *Bioelectromagnetics*. 2007;**28**:326-30. doi.org/10.1002/bem.20305. PubMed PMID: 17330851.
2. Mortazavi SMJ, Habib A, Ganj-Karimi AH, Samimi-Doost R, Pour-Abedi A, Babaie A. Alterations in TSH and Thyroid Hormones Following Mobile Phone Use. *Oman Med J*. 2009; **24**(4): 274-278. doi: 10.5001/omj.2009.56. PMID: PMC3243874.
3. Agarwal A, Deepinder F, Sharma RK, Ranga G, Li J. Effect of cell phone usage on semen analysis in men attending infertility clinic: an observational study. *Fertil Steril*. 2008;**89**(1):124-8. Epub 2007 May 4. PubMed PMID: 17482179.
4. Cao Y, Tong J. Adaptive response in animals exposed to non-ionizing radiofrequency fields: some underlying mechanisms. *Int J Environ Res Public Health*. 2014; **11**(4):4441-8. doi: 10.3390/ijerph110404441. Review. PubMed PMID: 24758897; PubMed Central PMCID: PMC4025035.
5. Dimova EG, Bryant PE, Chankova SG. Adaptive response: some underlying mechanisms and open questions. *Genetics and Molecular Biology*. 2008;**31**(2):396-408.
6. Benson VS, Pirie K, Schuz J, Reeves GK, Beral V, Green J. Mobile phone use and risk of brain neoplasms and other cancers: prospective study. *Int J Epidemiol*. 2013;**42**:792-802. doi.org/10.1093/ije/dyt072. PubMed PMID: 23657200.
7. Akan Z, Aksu B, Tulunay A, Bilsel S, Inhan-Garip A. Extremely low-frequency electromagnetic fields affect the immune response of monocyte-derived macrophages to pathogens. *Bioelectromagnetics*. 2010;**31**(8):603-12. doi: 10.1002/bem.20607. Epub 2010 Aug 31. PubMed PMID: 20809504.
8. Aydin B, Akar A. Effects of a 900-MHz electromagnetic field on oxidative stress parameters in rat lymphoid organs, polymorphonuclear leukocytes and plasma. *Arch Med Res*. 2011;**42**(4):261-7. doi: 10.1016/j.arcmed.2011.06.001. PubMed PMID: 21820603.
9. Hardell L, Carlberg M, Soderqvist F, Mild KH. Case-control study of the association between malignant brain tumours diagnosed between 2007 and 2009

- and mobile and cordless phone use. *Int J Oncol*. 2013;**43**:1833-45. doi.org/10.3892/ijo.2013.2111. PubMed PMID: 24064953. PubMed PMCID: 3834325.
10. Poulsen AH, Friis S, Johansen C, Jensen A, Frei P, Kjaear SK, et al. Mobile phone use and the risk of skin cancer: a nationwide cohort study in Denmark. *Am J Epidemiol*. 2013;**178**:190-7. doi.org/10.1093/aje/kws426. PubMed PMID: 23788669.
  11. Elliott P, Toledano MB, Bennett J, Beale L, de Hoogh K, Best N, et al. Mobile phone base stations and early childhood cancers: case-control study. *BMJ*. 2010;**340**:c3077. doi.org/10.1136/bmj.c3077. PubMed PMID: 20570865. PubMed PMCID: 3191724.
  12. Kim JG, Park MT, Heo K, Yang KM, Yi JM. Epigenetics meets radiation biology as a new approach in cancer treatment. *Int J Mol Sci*. 2013;**14**:15059-73. doi.org/10.3390/ijms140715059. PubMed PMID: 23873297. PubMed PMCID: 3742287.
  13. Nagasaka T, Goel A, Notohara K, Takahata T, Sasamoto H, Uchida T, et al. Methylation pattern of the O6-methylguanine-DNA methyltransferase gene in colon during progressive colorectal tumorigenesis. *Int J Cancer*. 2008;**122**:2429-36. doi.org/10.1002/ijc.23398. PubMed PMID: 18240147. PubMed PMCID: 2851179.
  14. Campbell-Thompson M, Lynch IJ, Bhardwaj B. Expression of estrogen receptor (ER) subtypes and ERbeta isoforms in colon cancer. *Cancer Res*. 2001;**61**:632-40. PubMed PMID: 11212261.
  15. Gustafsson JA. Estrogen receptor beta--a new dimension in estrogen mechanism of action. *J Endocrinol*. 1999;**163**(3):379-83. Review. PubMed PMID: 10588810.
  16. Vladusic EA, Hornby AE, Guerra-Vladusic FK, Lalkins J, Lupu R. Expression and regulation of estrogen receptor beta in human breast tumors and cell lines. *Oncol Rep*. 2000;**7**(1):157-67. PubMed PMID: 10601611.
  17. Issa JP, Ottaviano YL, Celano P, Hamilton SR, Davidson NE, Baylin SB. Methylation of the oestrogen receptor CpG island links ageing and neoplasia in human colon. *Nat Genet*. 1994;**7**:536-40. doi.org/10.1038/ng0894-536. PubMed PMID: 7951326.
  18. Tominaga K, Fujii S, Mukawa K, Fujita M, Ichikawa K, Tomita S, et al. Prediction of colorectal neoplasia by quantitative methylation analysis of estrogen receptor gene in nonneoplastic epithelium from patients with ulcerative colitis. *Clin Cancer Res*. 2005;**11**:8880-5. doi.org/10.1158/1078-0432.CCR-05-1309. PubMed PMID: 16361578.
  19. Ahuja YR, Sharma S, Bahadur B. Autism: An epigenomic side-effect of excessive exposure to electromagnetic fields. *Medicine and Medical Sciences*. 2013;**5**:171-7.
  20. Mortazavi SM, Motamedifar M, Namdari G, Taheri M, Mortazavi AR, Shokrpour N. Non-linear adaptive phenomena which decrease the risk of infection after pre-exposure to radiofrequency radiation. *Dose Response*. 2013;**12**(2):233-45. doi: 10.2203/dose-response.12-055.Mortazavi. eCollection 2014 May. PubMed PMID: 24910582; PubMed Central PMCID: PMC4036396.
  21. Mortazavi SMJ, Taeb S, Dehghan N. Alterations of Visual Reaction Time and Short Term Memory in Military Radar Personnel. *Iran J Public Health*. 2013; **42**(4): 428-435. Published online 2013 April 1. PMCID: PMC3684731.
  22. Mortazavi SM, Rouintan MS, Taeb S, Dehghan N, Ghaffarpanah AA, Sadeghi Z, Ghafouri F. Human short-term exposure to electromagnetic fields emitted by mobile phones decreases computer-assisted visual reaction time. *Acta Neurol Belg*. 2012;**112**(2):171-5. doi: 10.1007/s13760-012-0044-y. Epub 2012 Feb 10. PubMed PMID:22426673.
  23. Mortazavi S, Mosleh-Shirazi M, Tavassoli A, Taheri M, Mehdizadeh A, Namazi S, et al. Increased Radioreistance to Lethal Doses of Gamma Rays in Mice and Rats after Exposure to Microwave Radiation Emitted by a GSM Mobile Phone Simulator. *Dose Response*. 2013;**11**:281-92. doi.org/10.2203/dose-response.12-010.Mortazavi. PubMed PMID: 23930107. PubMed PMCID: 3682203.
  24. Mortazavi S, Mosleh-Shirazi M, Tavassoli A, Taheri M, Bagheri Z, Ghalandari R, et al . A comparative study on the increased radioreistance to lethal doses of gamma rays after exposure to microwave radiation and oral intake of flaxseed oil. *IJRR*. 2011; **9**(1) :9-14.
  25. Mortazavi SM, Daiee E, Yazdi A, Khiabani K, Kavousi A, Vazirinejad R, Behnejad B, Ghasemi M, Mood MB. Mercury release from dental amalgam restorations after magnetic resonance imaging and following mobile phone use. *Pak J Biol Sci*. 2008;**11**(8):1142-6. PubMed PMID: 18819554.
  26. Mortazavi SM, Mahbudi A, Atefi M, Bagheri Sh, Bahaedini N, Besharati A. An old issue and a new look: electromagnetic hypersensitivity caused by radiations emitted by GSM mobile phones. *Technol Health Care*. 2011;**19**(6):435-43. doi: 10.3233/THC-2011-0641. PubMed PMID: 22129944.
  27. Mortazavi SMJ, Motamedifar M, Namdari G, Taheri M, Mortazavi AR. Counterbalancing immunosup-

- pression-induced infections during long-term stay of humans in space. *J Med Hypotheses and Ideas*. 2013;**7**(1):8-10. doi:10.1016/j.jmhi.2012.12.001
28. Mortazavi SMJ. Safety Issue of Mobile Phone Base Stations. *J biomed physics & engineering*. 2013;**3**(1):1-2.
29. Mortazavi SMJ. Adaptive responses after exposure to cosmic and natural terrestrial radiation. *Indian J Rad Res*. 2004;**1**(1):104-12.
30. Mortazavi SMJ, Tavassoli A, Ranjbari F, Moammajee P. Effects of laptop computers' electromagnetic field on sperm quality. *Journal of Reproduction & Infertility*. 2011;**11**(4):251-8.
31. Mortazavi SM, Vazife-Doost S, Yaghooti M, Mehdizadeh S, Rajaie-Far A. Occupational exposure of dentists to electromagnetic fields produced by magnetostrictive cavitrans alters the serum cortisol level. *J Nat Sci Biol Med*. 2012;**3**(1):60-4. doi: 10.4103/0976-9668.95958. PubMed PMID: 22690053; PubMed Central PMCID: PMC3361780.
32. In: FC News (Federal Communications Commission). Document: Enforcement bureau steps up education and enforcement efforts against cellphone and GPS jamming. [February 9, 2011]. Available from: [https://transition.fcc.gov/eb/News\\_Releases/DOC-304575A1.html](https://transition.fcc.gov/eb/News_Releases/DOC-304575A1.html).
33. Mortazavi SM, Neghab M, Anoosheh SM, Bahaedini N, Mortazavi G, Neghab P, Rajaeifard A. High-field MRI and mercury release from dental amalgam fillings. *Int J Occup Environ Med*. 2014;**5**(2):101-5. PubMed PMID: 24748001.
34. Mokarram P, Zamani M, Kavousipour S, Naghibalhossaini F, Irajie C, Moradi Sarabi M, et al. Different patterns of DNA methylation of the two distinct O6-methylguanine-DNA methyltransferase (O6-MGMT) promoter regions in colorectal cancer. *Mol Biol Rep*. 2013;**40**:3851-7. doi.org/10.1007/s11033-012-2465-3. PubMed PMID: 23271133.
35. Agrawal A, Murphy RF, Agrawal DK. DNA methylation in breast and colorectal cancers. *Mod Pathol*. 2007;**20**:711-21. doi.org/10.1038/modpathol.3800822. PubMed PMID: 17464311.
36. Nagaraju GP, El-Rayes BF. SPARC and DNA methylation: possible diagnostic and therapeutic implications in gastrointestinal cancers. *Cancer Lett*. 2013;**328**:10-7. doi.org/10.1016/j.canlet.2012.08.028. PubMed PMID: 22939997.
37. Harder J, Engelstaedter V, Usadel H, Lassmann S, Werner M, Baier P, et al. CpG-island methylation of the ER promoter in colorectal cancer: analysis of micrometastases in lymph nodes from UICC stage I and II patients. *Br J Cancer*. 2009;**100**:360-5. doi.org/10.1038/sj.bjc.6604859. PubMed PMID: 19142184. PubMed PMCID: 2634714.
38. Antwi DA, Gabbara KM, Lancaster WD, Ruden DM, Zielske SP. Radiation-induced epigenetic DNA methylation modification of radiation-response pathways. *Epigenetics*. 2013;**8**(8):839-48. doi: 10.4161/epi.25498. Epub 2013 Jun 27. PubMed PMID: 23880508; PubMed Central PMCID: PMC3883787.
39. Ye S, Yuan D, Xie Y, Pan Y, Shao C. Role of DNA methylation in the adaptive responses induced in a human B lymphoblast cell line by long-term low-dose exposures to gamma-rays and cadmium. *Mutat Res Genet Toxicol Environ Mutagen*. 2014;**773**:34-8. doi.org/10.1016/j.mrgentox.2014.08.004. PubMed PMID: 25308704.