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Electromagnetic fields may act via calcineurin inhibition to suppress immunity, thereby increasing risk for opportunistic infection: Conceivable mechanisms of action

P.R. Doyon [a,*], O. Johansson [b]

[a] Doyon Independent Research, 1428 7th Ave., Santa Cruz, CA 95062, United States
[b] The Experimental Dermatology Unit, Department of Neuroscience, Karolinska Institute, 171 77 Stockholm, Sweden

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ABSTRACT

While a good number of studies have demonstrated that modern, man-made ambient electromagnetic fields can have both stimulatory and inhibitory effect on immune system function, the precise mechanisms have yet to be completely elucidated. It is hypothesized here that, depending on the parameters, one of the means by which long-term electromagnetic field exposure has the potential to eventually lead to immunosuppression is via downstream inhibition of the enzyme calcineurin — a protein phosphatase, which activates the T-cells of the immune system and can be blocked by pharmaceutical agents.

Calcineurin is the target of a class of pharmaceuticals called calcineurin inhibitors (e.g., cyclosporine, pimecrolimus and tacrolimus). When organ transplant recipients take such pharmaceuticals to prevent or suppress organ transplant rejection, one of the major side effects is immunosuppression leading to increased risk of opportunistic infection: e.g., fungal, viral (Epstein-Barr virus, cytomegalovirus), atypical bacterial (Nocardia, Listeria, mycobacterial, mycoplasma), and parasitic (e.g., toxoplasmosis) infections.

Frequent anecdotal reports, as well as a number of scientific studies, have shown that electromagnetic field exposures may indeed produce the same effect: a weakened immune system leading to an increase in the same or similar opportunistic infections: i.e., fungal, viral, atypical bacterial, and parasitic infections.

Furthermore, numerous research studies have shown that man-made electromagnetic fields have the potential to open voltage-gated calcium channels, which can in turn produce a pathological increase of intracellular calcium, leading downstream to the pathological production of a series of reactive oxygen species. Finally, there are a number of research studies demonstrating the inhibition of calcineurin by a pathological production of reactive oxygen species.

Hence, it is hypothesized here that exposures to electromagnetic fields have the potential to inhibit immune system response by means of an eventual pathological increase in the influx of calcium into the cytoplasm of the cell, which induces a pathological production of reactive oxygen species, which in turn can have an inhibitory effect on calcineurin. Calcineurin inhibition leads to immunosuppression, which in turn leads to a weakened immune system and an increase in opportunistic infection.

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Introduction

In the last thirty years we have seen a substantial increase in a number of disease states and functional impairments, many new or previously rare (e.g., autism spectrum disorder [ASD], chronic fatigue syndrome [CFS], attention deficit hyperactivity disorder [ADHD], etc.) [1–4]. Many of these tend not only to be coupled with a weakened immune system, but also to involve immune system disorders (e.g., allergies, food and chemical sensitivities, autoimmune disorders, etc.) (e.g. [5,6]). These disease states have paralleled major increases in ambient levels of man-made electromagnetic fields (EMFs) in our immediate environments. Furthermore, a number of experimental and epidemiological studies are continuing to link electromagnetic radiation (EMR) exposure with many of these disease states (e.g., [7–10]), their immune system dysfunctions, and their symptomologies.

Since calcium (Ca2+) is necessary for numerous enzymatic functions, a number of researchers have postulated that an EMF effect

* Corresponding author.
E-mail addresses: doyon.paul@gmail.com (P.R. Doyon), Olle.Johansson@ki.se (O. Johansson).

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may transpire via Ca2+ signaling transcription due to the influence of EMFs on Ca2+ cellular flux. While one such study by Manikonda et al. [11], for example, found that a 90-day extremely-low-frequency (ELF) 50 Hz magnetic field exposure (at 50 mT and 100 mT) induced an increase in calcineurin activity concomitant with an increase in intracellular Ca2+ ([Ca2+]i) levels in the hippocampal brain regions, Erkut et al. [12] found that with increasing radiofrequency (RF) EMF (1800 MHz) exposure duration (6, 12, and 24 h, respectively) of pregnant rats exposed for 20 days, "there was... [an increased] reduction in calcineurin activities" in both bone and muscle tissues of newborn rats. Hence, it is assumed here that, depending on the changing complexity of parameters (e.g., cell type; quality, duration, and intensity of exposure, etc.), EMFs can have a stimulatory, inhibitory, or no effect on intracellular calcineurin activity. It is further postulated here that while the influx of Ca2+ into the cell can initially have a stimulatory effect on the enzyme calcineurin, a pathological increase in Ca2+ can also stimulate the enzyme nitric oxide synthase to produce more nitric oxide (NO), leading to the production of peroxynitrite and other reactive oxygen species (ROS), which may have the downstream potential to inhibit the enzyme calcineurin.

An abundant number of studies have shown a substantial increase in ROS with EMF exposure. And while ROS, depending on concentration, can have both beneficial and deleterious effects, a recent review by Pall [13] has drawn attention to a process by which EMFs can induce the opening of voltage-gated calcium channels (VGCCs) in the plasma membrane via a change in its electric potential, triggering a pathological increase in [Ca2+]i via Ca2+ influx into cells (Fig. 1a). This in turn can trigger an increase in a number of ROS by means of a chain reaction initiated by the production of nitric oxide (NO) via Ca2+ stimulation of enzyme nitric oxide synthase (Figs. 1c–1f). Under normal circumstances, in a physiological context, one of the feedback-control mechanisms mediating Ca2+ entry into the cell through VGCCs is via Ca2+ binding proteins (one of which is the protein phosphatase enzyme, calcineurin), which help to control homeostasis of Ca2+ within the cell [14] (Fig. 1b). Nitric oxide is involved in a reverse feedback loop by which the enzyme guanylate cyclase is activated, inducing an increase in intracellular cyclic guanosine monophosphate (cGMP), which, in turn, again under normal circumstances, causes an inhibition of Ca2+ entry into the cell, thus decreasing intracellular concentrations [15]. However, with the advent of VGCC-opening EMFs into the equation, there is the real possibility that this feedback mechanism becomes impeded or stops working altogether, allowing the uncontrolled flow of Ca2+ into the cell.

Calcineurin, a serine-threonine phosphatase, found extensively in a variety of tissues with vital functions in neural, cardiac, skeletal, muscle, and immune cells, has not only been shown to play a central role in immunity, but it is also involved in a wide array of signaling pathways related to both cellular development and cell cycle progression.

Certain pharmaceutical agents known as calcineurin inhibitors, used mainly to prevent organ rejection of transplant recipients, also have an immunosuppressive side effect, known to lead to an increase in the following opportunistic infections: fungal/yeast (e.g., Cryptococcus neoformans); viral (esp. herpes-family viruses such as Epstein-Barr virus [EBV], cytomegalovirus [CMV]); atypical bacterial (e.g., mycoplasma, Nocardia, Listeria, mycobacteria); and parasitic (e.g., toxoplasmosis) infections [16–21].

Since ROS (e.g., superoxide [O2−], nitric oxide [NO], hydrogen peroxide [H2O2], and ROS-like singlet oxygen) have also been shown to inhibit calcineurin activity [22–28], it is hypothesized here that one possible mechanism by which EMFs inhibit immune system function is via a downstream pathological increase in Ca2+

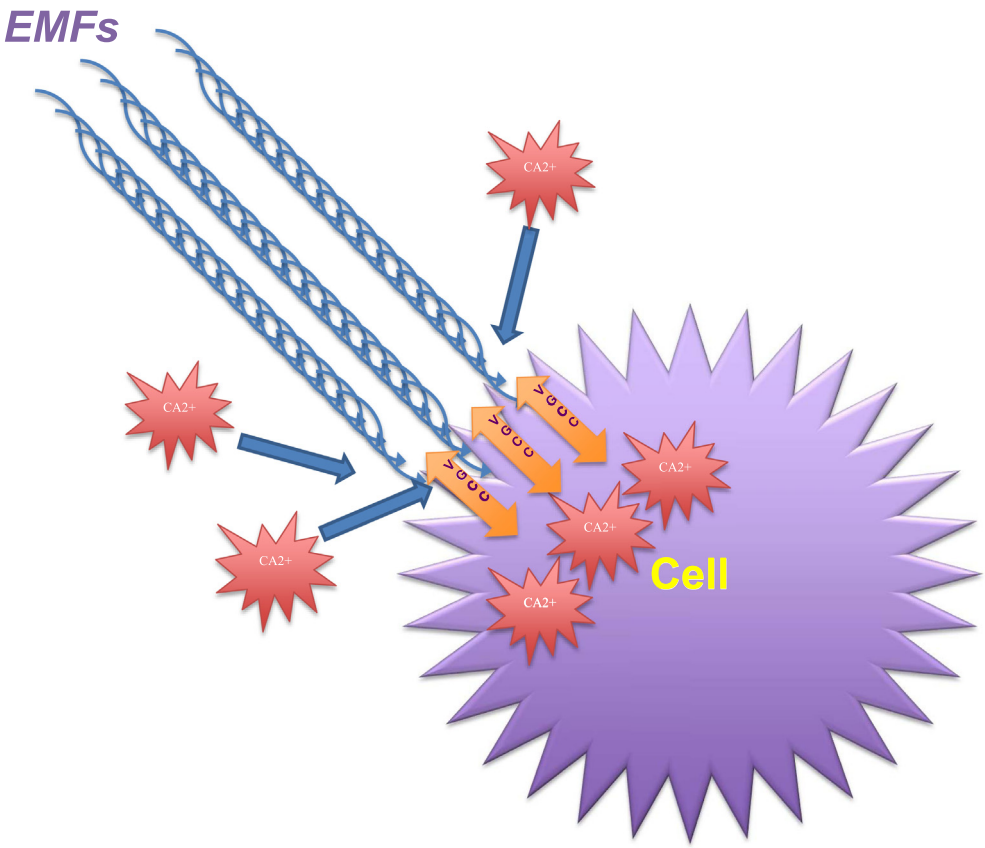

Fig. 1a. Electromagnetic fields (EMFs) open voltage-gated calcium channels (VGCCs) allowing an influx of extracellular calcium ions (Ca2+) into the cell.

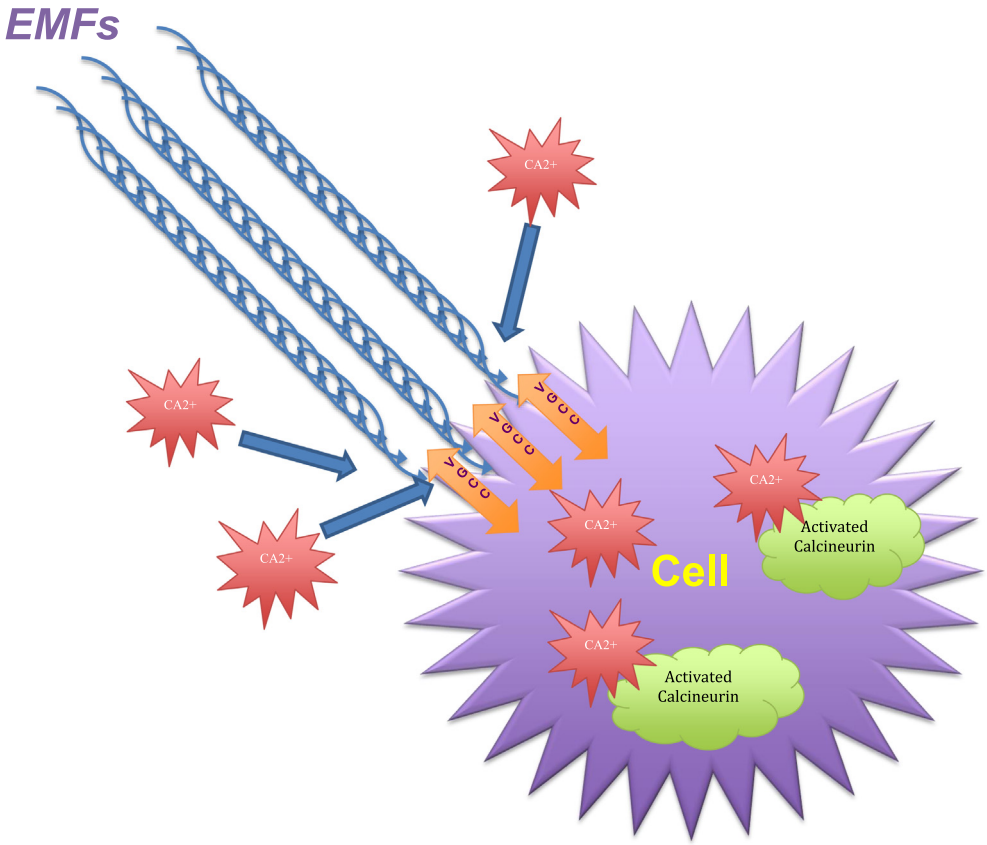

Fig. 1b. Increased levels of intracellular calcium ions (Ca2+) activate calcineurin (CN).

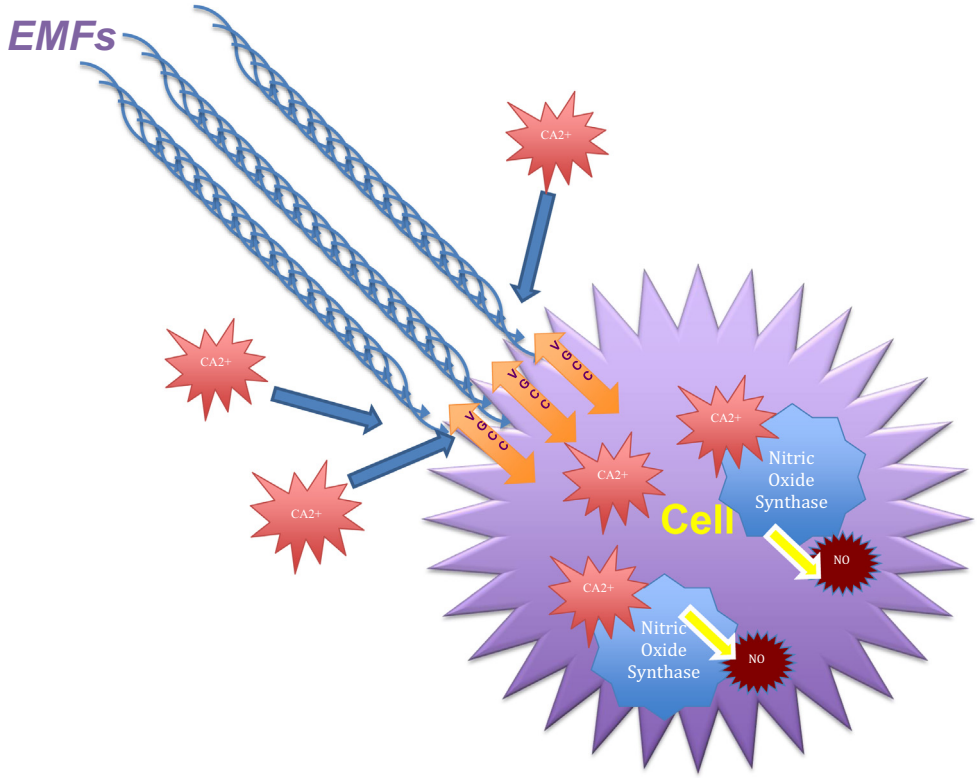

Fig. 1c. Increased levels of intracellular calcium ions (Ca2+) stimulate nitric oxide synthase to produce nitric oxide (NO).

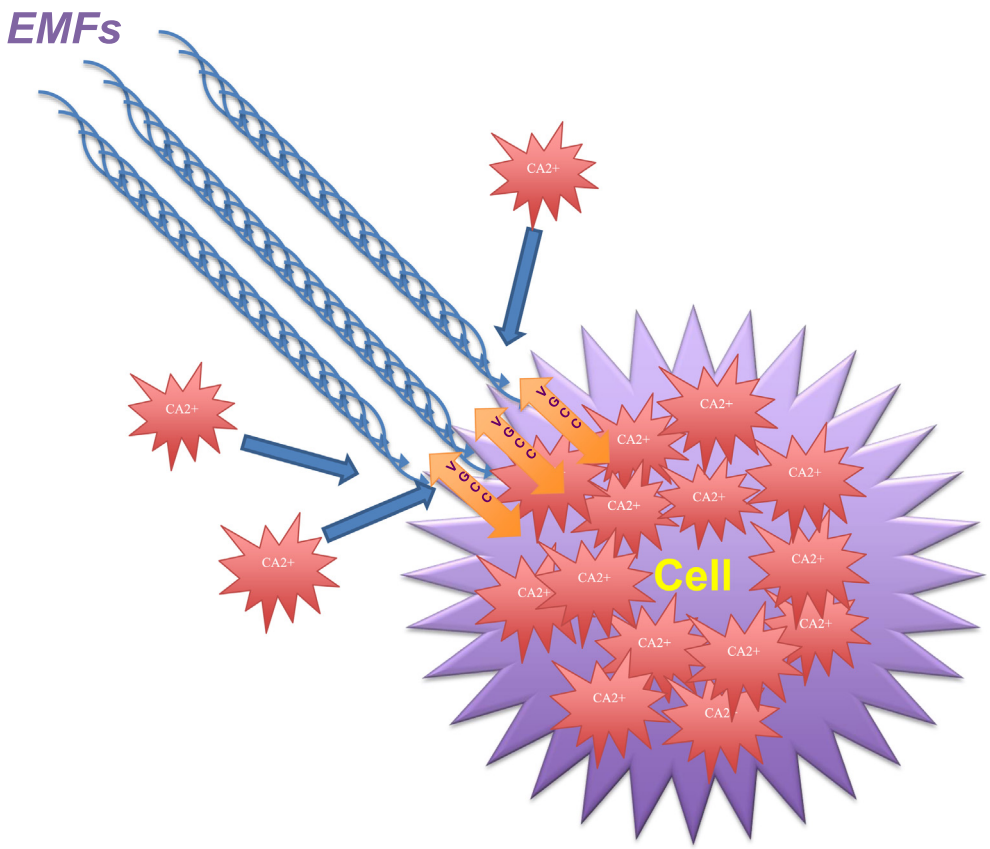

Fig. 1d. Electromagnetic fields (EMFs) can stimulate a pathological increase of calcium ions (Ca2+) within the cell.

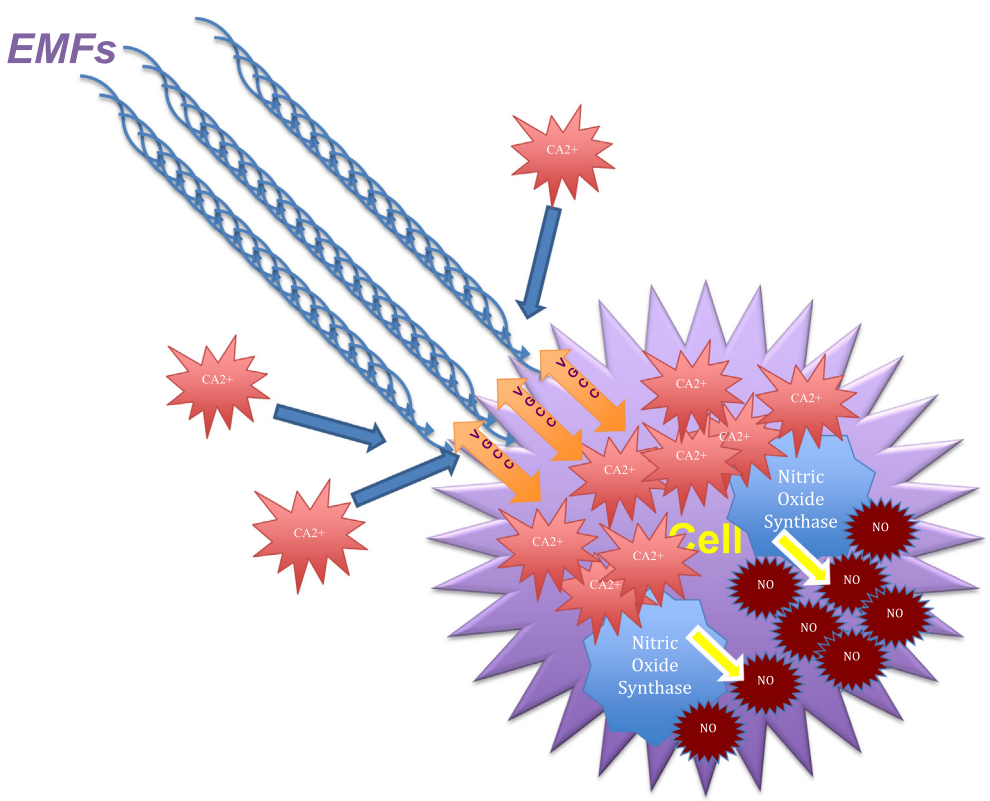

Fig. 1e. A pathological increase in calcium ions (Ca2+) can lead to a pathological increase in nitric oxide (NO).

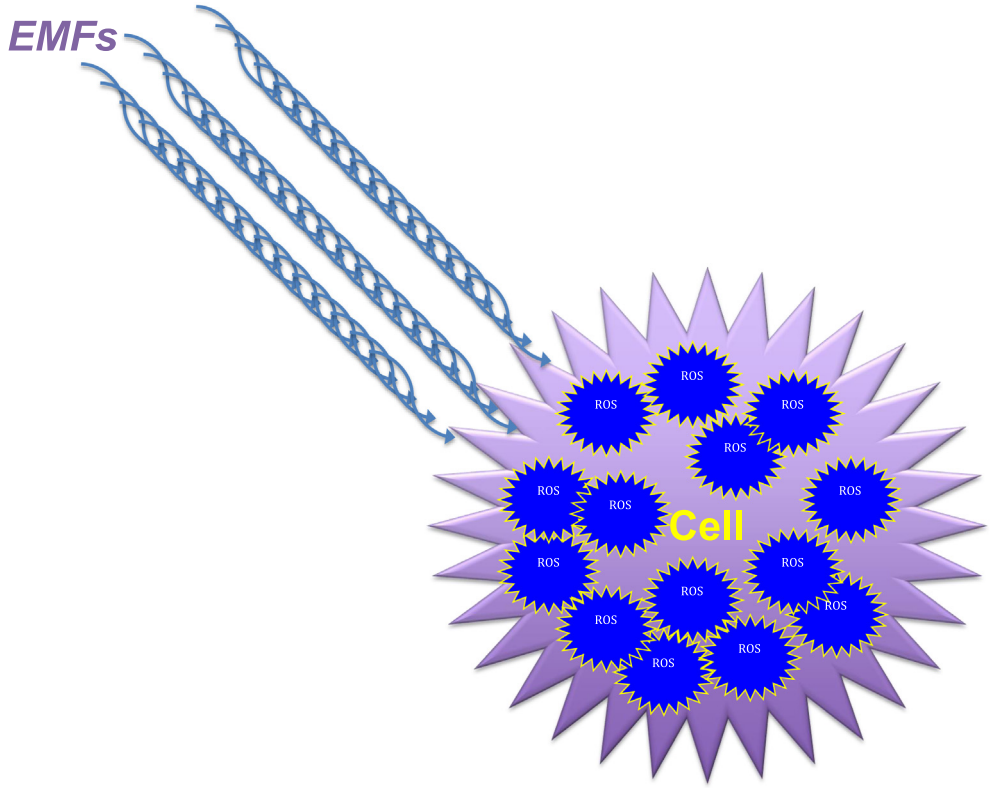

Fig. 1f. A pathological increase in nitric oxide (NO) can lead downstream to the formation of other reactive oxygen species (ROS), such as peroxynitrite.

in the cytoplasm of the cell (Fig. 1d), inducing a pathological production of ROS [13] and also possibly singlet oxygen [29] (Fig. 1f), which in turn has an inhibitory effect on calcineurin [22–28] (Fig. 1g). One other possible mechanism could be an EMF-induced blockage of Ca2+ uptake by T-lymphocytes, which might also prevent the activation of calcineurin [30,31]. Either

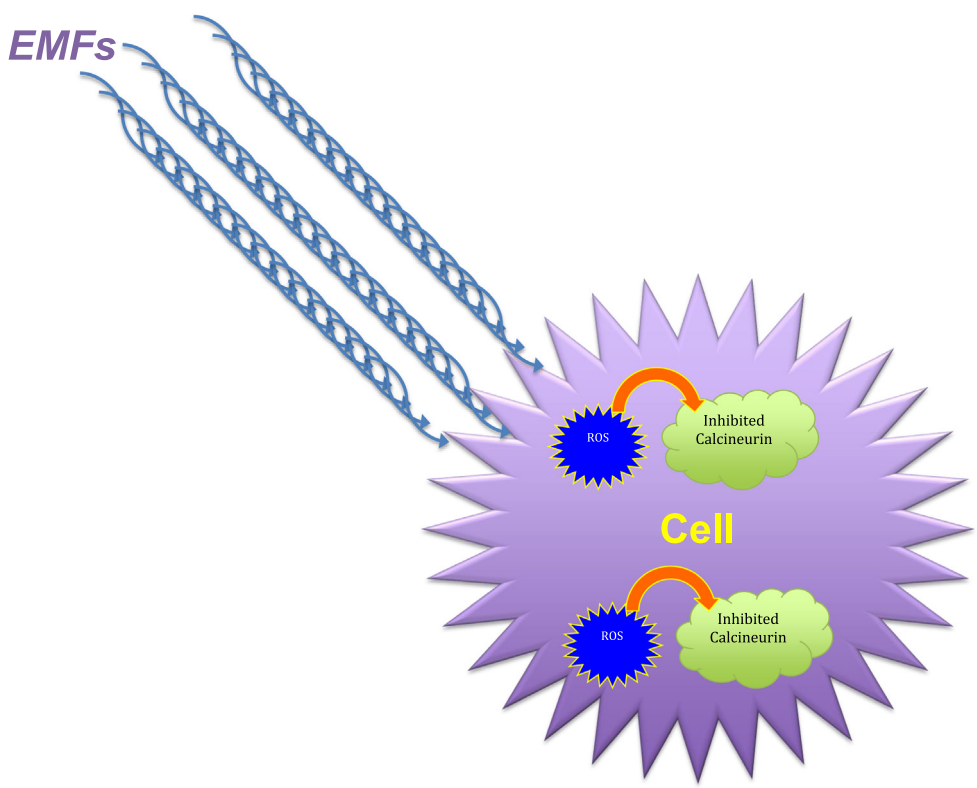

Fig. 1g. Reactive oxygen species (ROS) inhibit calcineurin.

way, calcineurin inhibition leads to immunosuppression, which in turn leads to a weakened immune system and an increase in opportunistic infections.

Calcineurin and T-lymphocytes

Calcineurin is a protein phosphatase enzyme, (named for its attraction to Ca2+ and affinity for neurons), which activates the T-lymphocytes involved in cell-mediated immunity (as opposed to humeral immunity). Calcineurin activated by Ca2+ thus generates nuclear factor of activated T-cells (NFAT), a transcription factor, via the process of dephosphorylation. The activated NFAT then moves into the nucleus binding to T-cell DNA stimulating production of interleukin 2 (IL-2), an important immune system cytokine. IL-2, in turn, enables the activation, proliferation, and differentiation of inactive or naive T-lymphocytes. (T-lymphocytes are one type of differentiated lymphocyte: the others being natural killer (NK) and B-cells. And it is important to note here that NK cells are also activated by IL-2 and thus would also be indirectly affected by calcineurin inhibition.) T-lymphocytes or T-cells are further differentiated into helper T-cell and cytotoxic T-cell subsets.

Calcineurin inhibitors

Calcineurin inhibitors are pharmaceutical agents (e.g., cyclosporine, tacrolimus, pimecrolimus) that act by inhibiting the function of calcineurin to produce NFAT, which in turn suppresses the ability of IL-2 to activate, differentiate, and proliferate T cells. They act pharmaceutically as immunosuppressants in order to prevent or suppress organ rejection in transplant patients — and also to suppress inflammation in psoriasis and rheumatoid arthritis. Consequential side-effects of taking calcineurin inhibitors are (1) an increased risk of infection, especially opportunistic infections such as fungal, yeast, viral (Epstein-Barr virus [EBV], cytomegalovirus [CMV]), and atypical bacterial infection (Nocardia, Listeria, mycobacterial, mycoplasma), and (2) an increased risk of neoplasms.

There is evidence which also suggests that calcineurin inhibitors act via increases in oxidative stress. Research by Hong et al. [22] has shown that at least one calcineurin inhibitor, cyclosporine (CsA), acts via the generation of high levels of ROS. Further research by Moreno et al. [23] showing increased oxidative stress markers in transplant recipients taking calcineurin inhibitors (cyclosporine and tacrolimus) vs. healthy subjects lends further evidence to this hypothesis.

EMF-induced calcium flux/uptake blockage

Specific frequency windows, power densities, modulations, and cellular states

Numerous studies [32–57] demonstrate EMF-induced Ca2+ flux and/or its possible related effects (Table 1), with the more recent of

Table 1
EMF Effect on Calcium Flux.

Selected research studies	EMF type	Frequency	Power density, Field strength, or SAR	Biological effect/Conclusion
Kaczmarek LK, Adey WR. Weak electric gradients change ionic and transmitter fluxes in cortex. (1974) [32]	Electric field		20–60 mV/cm	Ca2+ and gamma aminobutyric acid (GABA) efflux in cat cerebral cortex.
Bawin SM, Adey WR. Sensitivity of calcium binding in cerebral tissue to weak environmental electric fields oscillating at low frequency. (1976) [33]	Weak sinusoidal electric fields	6 and 16 Hz	10 and 56 V/m	Inhibition of Ca2+ efflux in chick and cat cerebral tissue.
Blackman CF, et al. Induction of calcium-ion efflux from brain tissue by radio-frequency radiation: Effects of modulation frequency and field strength. (1979) [34]	Modulated RF field	147 MHz amplitude modulated by 16 Hz sine waves	0.75 mW/cm^{-2}	Ca2+ efflux from brain tissue, confirming the presence of the frequency "window" (previously described by Bawin et al.), and also a narrow power-density "window."
Joines WT, Blackman CF. Power density, field intensity, and carrier frequency determinants of RF-energy-induced calcium-ion efflux from brain tissue. (1980) [35]	Modulated RF field	50, 147, and 450 MHz carrier frequencies		The Ca2+ efflux from brain tissue obtained at three frequencies, when adjusted with incident power density (Pi) occur at the same average electric-field intensity within the sample.
Blackman CF, et al. Calcium-ion efflux from brain tissue: power-density versus internal field-intensity dependencies at 50-MHz RF radiation. (1980) [36]	Modulated RF field	50 MHz 147 MHz	1.44–1.67 mW/cm^2, 3.64 mW/cm^2 1.3 μW/g at 50 MHz, and 1.4 μW/g at 147 MHz	The enhancement of Ca2+ efflux from brain tissue is more dependent on the field intensity in the brain than on the power density of incident radiation.
Joines WT, Blackman CF. Equalizing the electric field intensity within chick brain immersed in buffer solution at different carrier frequencies. (1981) [37]	Modulated RF field	50, 147, and 450 MHz		Supports earlier conclusion that Ca2+ efflux results obtained at different carrier frequencies are in agreement when related by the electric field within the brain.
Joines WT, Blackman CF, Hollis MA. Broadening of the RF power-density window for calcium-ion efflux from brain tissue. (1981) [38]	Modulated RF field	50–147 MHz modulated sinusoidally at 16 Hz	0.83 mW/cm^2 0.55, 0.83, 1.11, and 1.38 mW/cm^2	Enhancement of Ca2 + efflux from brain tissue was induced by changing the spacing between sample tubes.
Blackman et al. Effects of ELF fields on calcium-ion efflux from brain tissue in vitro. (1982) [39]	ELF field	16 Hz sinusoidal	5–7.5 V/m and 35–50 V/m	A 16-Hz sinusoidal field without its carrier wave was found to induce Ca2+ efflux from brain tissue.
Blackman et al. Effects of ELF (1–120 Hz) and modulated (50 Hz) RF fields on the efflux of calcium ions from brain tissue in vitro. (1985) [40]	ELF (1–120 Hz) field Modulated RF (50 Hz) field	45, 50, and 60 Hz	40 Vp-p/m, 45–50 Vp-p/m, and 35–40 Vp-p/m	Demonstrated Ca2+ efflux from brain tissue at certain frequencies and power densities and not at others.
Blackman et al. A role for the magnetic field in the radiation-induced efflux of calcium ions from brain tissue in vitro. (1985) [41]	Local Geomagnetic Field [LGF]	15 and 45 Hz 1 and 30 Hz	38 μT, 19 μT, 25.3 μT, and 76 μT	Specific frequencies at specific field strengths induced change in calcium ion efflux from brain tissue in vitro, whereas others did not. These

Table 1 (*continued*)

Selected research studies	EMF type	Frequency	Power density, Field strength, or SAR	Biological effect/Conclusion
				effective frequencies could be rendered ineffective by altering the field strength whereas other ineffective frequencies could be made effective via the same means.
Conti P, et al. A role for Ca2+ in the effect of very low frequency electromagnetic field on the blastogenesis of human lymphocytes. (1985) [30]	Pulsed ELF field	3 Hz	6 mT	Field exposure caused DNA synthesis and Ca2+ uptake inhibition in mitogen-stimulated thymocytes, the effect being seemingly synergistic with calcium blocker agent, verapamil.
Conti P, et al. Mitogen dose-dependent effect of weak pulsed electromagnetic field on lymphocyte blastogenesis. (1986) [31]	Pulsed ELF field	3 Hz	50 G	Field exposure induced intense inhibition of DNA synthesis with use of optimal doses of mitogens, while opposite effects were induced with suboptimal concentration of mitogens.
Blackman et al. Influence of electromagnetic fields on the efflux of calcium ions from brain tissue in vitro: a three-model analysis consistent with the frequency response up to 510 Hz. (1988) [42]	ELF Field	15 Hz intervals over range 1–510 Hz	15 Vrms/m, 59 and 69 nTrms	"Hypothetical ordering of the frequency-response profile provides the basis for future experimental designs to test each possible interaction model and for their connection to the calcium-ion efflux endpoint."
Blackman et al. Effect of ambient levels of power-line-frequency electric fields on a developing vertebrate. (1988) [43]	Sinusoidal electric fields	Either 50 or 60 Hz	Average intensity of 10 Vrms/m	The brains of chicks born of eggs exposed to either 50 or 60 Hz for a 21-day incubation period had differing Ca2+ efflux reactions, demonstrating that the "exposure of a developing organism to ambient power-line-frequency electric fields at levels typically found inside buildings can alter the response of brain tissue to field-induced calcium-ion efflux."
Cadossi R, et al. Lymphocytes and pulsing magnetic fields. (1988) [47]	Pulsed magnetic field	75 Hz	1 mV/m	Exposure increased response of lymphocytes to suboptimal phytohemagglutinin (PHA) levels via the influx of Ca2+. Calcium blocker verapamil blocked PHA-stimulated Ca2+ influx while PEMF antagonized the verapamil block suggesting that the PEMF effect was on Ca2+ flux across the plasma membrane.
Blackman et al. Multiple power-density windows and their possible origin. (1989) [44]	Modulated RF field	50 MHz modulated sinusoidally at 16 Hz	1.75, 3.85, 5.57, 6.82, 7.65, 7.77, and 8.82 mW/cm2	Ca2+ efflux from brain tissue at a new set of power densities converted to specific absorption rate (SAR) by 0.36 mW/kg per mW/cm2.
Dutta SK, Ghosh B, Blackman CF. Radiofrequency radiation-induced calcium ion efflux enhancement from human and other neuroblastoma cells in culture. (1989) [45]	Modulated RF field	13–16 Hz and 57.5–60 Hz modulation ranges	SAR of 0.05 and 0.005 W/kg	Amplitude-modulated radiofrequency radiation can induce responses in cells of nervous tissue origin from widely different animal species, including humans.
Dutta SK, et al. Dose dependence of acetylcholinesterase activity in neuroblastoma cells exposed to modulated radio-frequency electromagnetic radiation. (1992) [46]	Modulated RF field	147 MHz sinusoidally modulated at 16 Hz		Exposed neuroblastoma cells (NG108) (30 min) showed increased AChE activity.
Walleczek J, Liburdy RP. Nonthermal 60 Hz sinusoidal magnetic-field exposure enhances 45Ca2+ uptake in rat thymocytes: dependence on mitogen activation. (1990) [63]	Sinusoidal magnetic field	60 Hz	1.0 mV/cm	A 60 min exposure enhanced 45Ca2+ uptake in lymphocytes activated with the mitogen Concanavalin A (Con A) while having no effect on 45Ca2+ uptake in resting lymphocytes. Furthermore, thymocytes with a reduced capacity to mobilize Ca2+ in response to Con A were most affected by the magnetic field.
Papatheofanis FJ. Use of calcium channel antagonists as magnetoprotective agents. (1990) [48]	Static magnetic field		0.1 T	Human polymorphonuclear leukocytes (PMNs) treated with the calcium channel antagonists diltiazem, nifedipine, and verapamil prior to being exposed to a magnetic field had no significant change in degranulation when compared to control and sham-exposed PMNs similarly treated.
Liburdy RP. Calcium signaling in lymphocytes and ELF fields. Evidence for an electric field metric and a site of interaction involving the calcium ion channel. (1992) [49]	ELF field	60 Hz magnetic	22 mT 1.7 mV/cm	Calcium influx increased during mitogen-activated signal transduction in thymic lymphocytes exposed for 60 min.
Walleczek J, Budinger TF. Pulsed magnetic field effects on calcium signaling in lymphocytes: dependence on cell status and field intensity. (1992) [62]	Pulsed Magnetic ELF field	3 Hz	Bpeak = 6.5 mT, Emax = 0.69 mV/cm, Jmax = 2.6 microA/cm^2	Various field effects were observed in response to a pulsed magnetic ELF field in lymphocytes: (1) stimulation, (2) inhibition, and (3) no effect. These were dependent on Ca2+ signal transduction activation, which was in turn dependent on lymphocyte responsiveness to the mitogen ConA. Furthermore, the magnitude of field response increased in line with increasing field flux densities.
Fitzsimmons RJ, et al. Combined magnetic fields increased net calcium flux in bone cells. (1994) [56]	Combined magnetic field (CMF)	Between 15.3 and 16.3 Hz	10(-5) V/m	Ca2+ flux enhanced in human osteoblast-like cells

(*continued on next page*)

Table 1 (*continued*)

Selected research studies	EMF type	Frequency	Power density, Field strength, or SAR	Biological effect/Conclusion
Kenny JS, et al. Quantitative study of calcium uptake by tumorigenic bone (TE-85) and neuroblastoma x glioma (NG108-15) cells exposed to extremely-low-frequency (ELF) electric fields. (1997) [57]	Capacitively coupled electric fields (CCEF)	16 Hz	18.3 mV/cm	45Ca2+ uptake enhanced in tumorigenic bone [TE-85] and neuroblastoma x glioma [NG108-15]) cells at frequency-specific 16 Hz also increasing TE-85 [Ca2+]i from 140 to 189–210 nM and NG108-15 [Ca2+]i from 67 to 189–210 nM.
Fanelli C, et al. Magnetic fields increase cell survival by inhibiting apoptosis via modulation of Ca2 + influx. (1999) [50]	Magnetic field		6 G	Magnetic fields were show to increase cell survival via the inhibition of apoptosis via their modulation of Ca2+ influx.
Cho MR, et al. Transmembrane calcium influx induced by ac electric fields. (1999) [51]	Electric field	1 or 10 Hz	10 V/cm	A continuous 30 min. electric field applied to human hepatoma (Hep3B) cells prompted a fourfold increase in [Ca2+]i. This [Ca2+]i increase was inhibited by a depletion in extracellular Ca2 +, and also partially by cation channel inhibitor $GdCl_3$ or the nonspecific calcium channel blocker $CoCl_2$, with simultaneous treatment of both $GdCl_3$ and $CoCl_2$ completely inhibiting the increase in $[Ca2+]_i$.
Grassi C, et al. Effects of 50 Hz electromagnetic fields on voltage-gated Ca2+ channels and their role in modulation of neuroendocrine cell proliferation and death. (2004) [52]	ELF	50 Hz		Proliferation of human neuroblastoma IMR32 (+40%) and rat pituitary GH3 cells (+38%) was significantly enhanced by exposure to ELF EMFs. Furthermore, puromycin- and H(2)O(2)-induced apoptosis in IMR32 cells was also inhibited by field exposure. Ca(2+) channel blockade counteracted the field exposure effects on both proliferation and apoptosis.
Craviso GL, et al. Nanosecond electric pulses: a novel stimulus for triggering Ca2+ influx into chromaffin cells via voltage-gated Ca2+ channels [53]	Pulsed electric field		5 MV/m	A single 5 ns, high-voltage electric pulse exposure stimulated Ca(2+) entry into bovine chromaffin cells via the opening of L-type voltage-gated Ca(2+) channels (VGCC) while VGCC blockers inhibited this response.
Craviso GL, et al. Modulation of intracellular Ca2+ levels in chromaffin cells by nanoelectropulses. (2011) [54]	Pulsed electric field	1 Hz, 10 Hz, and 1 kHz.	5 MV/m	A single 5 ns pulse exposure induced Ca(2+) influx and a rapid, transient increase in intracellular calcium concentration ([Ca(2+)](i) in chromaffin cells. A temperature sensitivity was also noted with a number of cellular responses.
Morotomi-Yano K, Akiyama H, Yano K. Different involvement of extracellular calcium in two modes of cell death induced by nanosecond pulsed electric fields. (2014) [55]	Pulsed electric field			Various cellular responses (e.g., Ca2+ influx and cell death) were induced by nanosecond pulsed electric fields (nsPEFs). Necrosis was enhanced with the presence of extracellular Ca2+ in HeLa S3 cells. The presence of a Ca2+ ionophore boosted necrosis while the absence of extracellular Ca2+ made HeLa S3 cells less susceptible to nsPEFs. It was concluded that cell death induced by nsPEFs is cell-type dependent and that extracellular Ca2+ is essential for nsPEF-induced necrosis.

these studies [47–57] implicating the EMF effect of opening of VGCCs as being responsible for this flux. These have predominantly shown not only an influx of Ca2+ with EMF exposures, but also that both calcium channel blockers and a reduction in extracellular Ca2 + can impede this effect. Furthermore, EMF stimulation of Ca2+ flux occurs dependent on specific frequency windows, specific power densities, specific modulations, (but not in others lying between them), and the specific biological parameters of the cell. A limited number of studies [30,31] have also shown blockage of Ca2+ uptake by cells — similar to the effect of the voltage-gated calcium channel (VGCC) blocker verapamil — along with inhibition of lymphocyte blastogenesis when a 3-Hz (6 mT) EMF was used.

(It should be noted that with Ca2+ influx and efflux, both processes are induced via VGCC activation. Ca2+ efflux has been studied via the loading of cells with radioactively labeled 45Ca2+. When VGCCs are activated raising intracellular Ca2+ levels via non-radioactive Ca2+ influx, 45Ca2+ efflux ensues.)

In summary, ELF EMFs can induce calcium influx via the opening of VGCCs at specific frequencies coupled with specific field strengths and not at others. A change in frequency can stimulate VGCC openings at different field strengths and vice versa: i.e., specific frequencies can be made ineffective with a change in field strength, while, conversely, also rendering previously ineffective signals effective with, for example, the same change in the field strength. Radiofrequency (RF) EMFs at specific frequencies can also cause Ca2+ influx via the opening of VGCCs, but at only a specific range of intensities and only when they are amplitude-modulated with low frequencies. While continuous wave ELFs have been shown to induce Ca2+ influx, unmodulated RF EMFs have so far shown no effect on Ca2+ influx. Furthermore, biological effects induced by Ca2+ influx are also dependent on the qualitative state of the cell (e.g., whether or not blastogenesis is taking place).

EMF effect on immune system cells

T-lymphocytes and VGCCs

While by 1985, calcium channels had yet to be uncovered in T-lymphocytes [58], it is now well established that T-lymphocyte activation is associated with both antigen receptor — or mitogen — stimulation and a continuous increase in free [Ca2+]i levels via heightened transmembrane Ca2+ influx via both VGCCs [59] and

also a non-voltage-gated calcium channel (nVGCC) influx [60,61], the latter of which is most likely opening in response to T-cell activating mitogens, and facilitated by inositol trisphosphate (InsP3) — a secondary messenger molecule used in signal transduction and lipid signaling.

Qualitatively different field responses: inhibition, stimulation or no field effect

Walleczek and Budinger [62], in investigating the effects of pulsed magnetic fields on Ca2+ signaling in T-lymphocytes, found that magnetic fields at 3 Hz inhibited Ca2+ uptake (i.e., influx) in mitogen-stimulated thymocytes (immature T-lymphocytes) and that this inhibition increased with increasing magnetic flux densities, noting that variations in both physical field exposure characteristics as well as biological parameters (e.g., the state of the cell) can determine the outcome of cellular EMF exposure experiments. Inhibition, stimulation, or no field effect can be observed in direct dependence on physical and biological boundary conditions [62].

This is in line with the Conti et al. [28] experiment also applying a 3-Hz (6-mT) pulsed magnetic field on mitogen-dependent human lymphocytes and finding a reduction in uptake of Ca2+.

In an earlier study, however, Walleczek and Liburdy [63], this time looking at 60-Hz sinusoidal magnetic field (22-mT) effect on thymocytes, found that Ca2+ uptake (i.e., influx) under the same experimental conditions was enhanced, and not reduced as with the case of the 3-Hz model, further highlighting the fact that varying EMF frequency differentials can induce field responses that are qualitatively different. This is in line with the conclusion of Blackman et al. [41] that there are specific frequency windows that can change in accordance with changes in power density.

Over the past 35 years, a large number of papers [64–108] have addressed effects — often contradictory — on immune system function with exposures to EMF of both extremely low frequency (ELF) and modulated radiofrequency (RF). Outcomes have been both stimulatory and inhibitory, with both pathological and — some — potentially therapeutic effects. Contradictory EMF effect can be attributed to the fact that the immune system will show varied responses based on the interactions of a number of parameters: (1) EMF exposure quality, (2) EMF exposure duration, (3) EMF exposure frequency, (4) EMF exposure power density, and (5) the specific state of the cell. And this is seemingly closely related to changes in Ca2+ ion flux.

Based on accumulated evidence showing that nonthermal exposure of ELF-EMF can elicit changes in immune cells, in 1992, Walleczek [64] had hypothesized that EMFs indirectly affect the immune system via cell membrane-mediated Ca2+ signaling processes. Eichwald and Walleczek [65], in 1996, further noting that in studies of immune system cellular Ca2+ -uptake regulation, depending on the degree of cellular activation, various field effects — stimulatory, inhibitory, or no field effect — have been observed under identical field parameters. They hypothesized that cellular biochemical stimulation results in specific signaling pathway activation, which regulates cellular Ca2+ dynamics (the release of Ca2+ from [Ca2+]i stores and capacitative Ca2+ entry), hypothesizing that a specific EMF-sensitive enzyme may be activating a feedback control loop on signaling processes, which in turn would modulate entry of Ca2+ into the cell, and affect other Ca2+ -dependent cellular processes (e.g., DNA synthesis). More recent studies, detailed in a review by Nejabakhsh and Feng [14], have established that this is indeed the case. Nejabakhsh and Feng state that calcium ion entry through voltage-gated calcium channels is essential for cellular signaling in a wide variety of cells and multiple physiological processes. Perturbations of voltage-gated calcium channel function can lead to pathophysiological consequences. Calcium binding proteins serve as calcium sensors and regulate the calcium channel properties via feedback mechanisms [14].

Pall [13], in a review of the literature, has described how EMFs may produce — what is usually — a pathological increase in [Ca2+]i via the opening of VGCCs that trigger an influx of Ca2+ from extracellular medium, leading downstream to the production of nitric oxide and peroxynitrite and consequent oxidative stress, and further that a wide range of these EMF effects have been shown to be blocked by calcium channel blockers, concluding that "voltage-gated calcium channels are essential to the responses produced by extremely low frequency (including 50/60 Hz) EMFs and also to microwave frequency range EMFs, nanosecond EMF pulses, and static electrical and magnetic fields [13]."

EMFs and ROS

Over the past 10 years there has been an exponential increase in studies [109–211] showing increased ROS activity with EMF exposure at power density levels more in line with what people are now receiving in their daily lives. Increased intracellular ROS activity has been found to increase lipid peroxidation and protein oxidation, impair antioxidant enzyme function, and is correlated with DNA damage, reduced cell membrane integrity, and reduced mitochondrial function. The majority of these studies show increased levels in markers for oxidative stress, e.g., malondialdehyde (MDA) and nitric oxide (NO), and decreases in levels of the antioxidant enzymes, e.g., superoxide dismutase (SOD), glutathione peroxidase (GSH-px), and catalase (CAT) — with a number of studies showing a protective and ameliorative effect of these induced by certain antioxidant nutritional substances like *Ginkgo biloba*, caffeic acid phenethyl ester (CAPE), garlic, ginseng, lotus seedpod procyanidins (LSPCs), β-glucan, L-carnitine, melatonin, vitamin E, C, zinc, and selenium. In a recent review by Yakymenko et al. [211] (and the only one of its kind at present), 100 peer-reviewed studies were surveyed examining the oxidative effects of low-intensity RF EMF with 93 confirming RF EMF-induced oxidative stress in biological systems.

ROS and calcineurin inhibition

Sommer et al. [24] found that the ROS — superoxide (O2−), nitric oxide (NO), and hydrogen peroxide (H2O2) — all had a potent inhibitory effect on calcineurin, concluding that ROS and reactive nitrogen species (RNS) have an inhibitory effect on calcineurin via the oxidation of both catalytic metals and critical thiols.

Lee et al. [25], in noting a correlation in increased ROS with calcineurin inactivity, describe the inactivation of calcineurin by hydrogen peroxide triggering the proteolytic cleavage and decreased enzymatic activity of calcineurin, with the cleaved form of calcineurin having no enzymatic ability to dephosphorylate NFATc.

Smit et al. [212] found — in noting similarities in the immunosuppressive effect of UV radiation with calcineurin inhibitors, when they investigated the UV effect on calcineurin in skin — a significant reduction in calcineurin activity in skin with exposure to UV radiation, along with a reduction in production of cytokines IL-2, gamma-interferon, IL-4, and IL-10, all controlled by the Ca2+ -calcineurin pathway — indicating that UV radiation can result in calcineurin inactivation in skin, suppressing skin immunity in a manner similar to calcineurin inhibitors. Musson et al. [26], in noting that calcineurin is a target of modulation by ROS, were able to show, both in vivo and in vitro, that UVA1 radiation suppresses calcineurin activity via the production of singlet oxygen and superoxide. Musson et al. [27], also further emphasizing calcineurin's documented sensitivity to oxidative stress, assessed and contrasted the influences of UVA1 and arsenite on calcineurin, showing that these two agents had a strong inhibitory effect on calcineurin activity in Jurkat and skin cells with a reduction in

NFAT nuclear translocation in Jurkat cells, and that these effects could be partially ameliorated with an increase in the dismutation of superoxide in Jurkat and skin cells.

EMFs and immune system dysfunction/suppression

While a diverse number of studies [66–108] show nonthermal EMF effect on the immune system function, many of these studies find effect with short-term exposure to EMFs at power densities many times more powerful than we would at present expect to encounter in our everyday lives. Notwithstanding, it has been proposed that long-term low-level non-ionizing radiation exposures may be equivalent to short-term high-intensity ionizing radiation exposures [101], and similarly that long-term low-level non-ionizing radiation effects to what are considered "low" power densities can also be equivalent to effects produced by short-term high-intensity non-ionizing radiation exposures at what are considered "high" power densities [102]. In other words, many of the biological effects produced in many of these short-term exposure conditions using power densities at levels higher than we would normally experience in everyday life may very well be mimicked by present-day long-term exposures to lower power densities many of us are currently encountering.

Experimental immunological research studies have demonstrated that nonthermal EMF exposures can affect immune-specific organs [66–70], innate and adaptive immune cell activity [30,31,68,69,71–73,77–79], antibodies [69,82,83], cytokines [87–89,95], and enzymes [65,131], with other research studies showing effects on the autoimmune system [86,91], cellular Ca2+ uptake [30,31], augmentation of chemical toxicity [84], food sensitivities [92], and increased free-radical production [109–211].

The same opportunistic infections induced as side effects in transplant recipients taking immunosuppressant calcineurin inhibitors to prevent organ rejection — reactivated viral (EBV, CMV, Coxsackie, etc.), candida, mold, bacterial (mycoplasma), and parasitic (toxoplasmosis) infections — have also been uncovered in a number of what have been described as neuro-immune dysfunction syndromes (NIDS)[213]: e.g., CFS, ASD, ADHD, and Alzheimer's disease [AD], [214–264] etc.

For example, Nicholson and Haier [214,215] have uncovered various systemic and central nervous system bacterial and viral infections (e.g., Mycoplasma species, Chlamydia pneumonia, Borrelia burgdorferi, human herpes virus-1, -6, and -7, and other bacterial and viral infections) in patients with amyotrophic lateral sclerosis (ALS), multiple sclerosis (MS), Alzheimer's disease (AD), Parkinson's disease (PD), autism spectrum disorders (ASD), a number of psychiatric disorders (paranoia, dementia, schizophrenia, bipolar disorder, panic attacks, major depression, anorexia nervosa, and obsessive-compulsive disorder), neuropsychiatric movement disorders (e.g., Giles de la Tourette's syndrome), autoimmune diseases (Guillain-Barré syndrome, paediatric autoimmune neuropsychiatric disorders associated with Streptococci ["PANDAS"]), fatiguing illnesses (CFS/myalgic encephalomyelitis [ME]), Gulf War Syndrome, and Lyme disease — with many of these showing cytokine changes, increases in ROS with its resulting oxidative stress, changes in neurotransmitter levels, and decreased NK cell activity.

Many of these mysterious disease states of unknown etiology have increased exponentially in the last thirty years in proportion with increases in ambient man-made electromagnetic fields. And with this correlation, the question "Is there causation?" begs to be asked. There is more research that suggests there is. For example, Grimaldi et al. [104] found that a 50-Hz EMF exposure could activate the Epstein-Barr virus genome in latently infected human lymphoid cells, and Canseven et al. [105] further found that a 50-Hz magnetic field could suppress NK cell activity on candida stellatoidea — and as noted earlier, NK activation is dependent on IL-2 production by T-cells.

Nageswari [106–108], for example, in several experiments, found that chronic low-power microwave radiation exposure (2.1 GHz @ 5 mW/cm^2 3 h daily, 6 days a week for 3 months) on the immunological systems of rabbits produced significant suppression of T-lymphocyte numbers; lymphoid cell depletion in lymph node, spleen, and appendix; recurrent infections; an increased susceptibility to bacterial infection; an increase in the number of large leukocytes; a decrease in the number of small leukocytes, neutrophils, and erythrocytes; leukocytosis; cataracts; and weight loss, etc.

In addition to the number of experimental studies showing immunological effects, long-term epidemiological — especially residential and occupational — studies have indicated a host of symptoms and biological markers associated with long-term EMF exposures. For example, residential studies on people living in the vicinity of cellular base stations report the following symptoms: fatigue; headache; sleep disturbances; discomfort; irritability; anxiety; depression; memory loss; concentration difficulties, dizziness; vertigo; nausea; loss of appetite; decreased libido; visual perturbations; blurred vision; tremors; skin rashes; elevated blood pressure; motor, memory, and learning impairment in children; cold hands and feet; and cardiovascular symptoms [102,265–275].

Interesting to note here is that many of these symptoms are also found in the above-mentioned neuro-immune dysfunction syndromes, especially CFS. For example, even the CDC lists on its CFS website the following (strikingly similar to the above) symptoms: increased malaise, headache, problems with sleep, depression or mood problems (irritability, mood swings, anxiety, panic attacks), difficulties with memory and concentration, brain fog, dizziness, and visual disturbances (sensitivity to light, blurring, eye pain) [276].

Also found in the vicinity of base stations were increased rates of suicide, increased risk of cancer, elevated brain tumor incidence, and decreased lung function in children [102]. With regard to biological markers associated with occupational exposures, there have been reductions in total lymphocytes [277,279]; in T-lymphocyte subsets, T8 [79], CD4 and CD3 [277,279] counts; NK cell [277,278,280,281] counts; interferon gamma (IFNγ) [277]; ornithine decarboxylase (ODC) activity [278]; PHA-stimulated IFNγ release from PBMC [280]; and blood cytotoxic activity of NK lymphocytes [280] found in workers occupationally exposed to a variety of EMFs.

Summary and discussion

Planetary life is incessantly exposed on a daily basis to an increasingly thickening soup of invisible EMF frequencies at a variety of power densities, pulse modulations, and durations. It has been estimated that we are now being exposed to between one quadrillion (10^{15}) to one quintillion (10^{18}) times the amount of EMR we would normally receive from natural background sources. Health effects reported in the literature include opening of the blood-brain barrier, genotoxicity, cancer, and infertility, and involve neurological, neurodegenerative, immune system, allergic, inflammatory, and cardiovascular effects [152].

Calcineurin inhibitors act by preventing calcineurin from activating the transcription factor NFAT to move into the T-cell nuclear DNA and to stimulate production of IL-2, in order to enable the activation, proliferation, and differentiation of inactive T lymphocytes. There is evidence to suggest that some calcineurin inhibitors themselves produce this inhibition via the actuation of ROS — as do EMFs via Ca2+ influx, leading to pathological levels of [Ca2+]i. A number of studies [141,173,174] further indicate that Ca2+ influx

can occur with everyday wireless (e.g., cell phone and WiFi) radiation exposures.

The ROS nitric oxide, superoxide, hydrogen peroxide, and singlet oxygen have been shown in a number of studies to inhibit calcineurin. EMFs have been shown to induce an intracellular increase in nitric oxide [112,118,121,132,144,181] and changes in superoxide dismutase [109,121,126,132,133,144,158,163,194,198,208], the latter strongly suggesting an increase in superoxide. Both nitric oxide and superoxide are known calcineurin inhibitors. Furthermore, superoxide can dismutate into hydrogen peroxide, another known calcineurin inhibitor. Finally, there is evidence to suggest that nitric oxide and hydrogen peroxide react to produce singlet oxygen [29]. Hence, it is hypothesized that EMFs have the potential to indirectly inhibit calcineurin via the downstream production of any one or more of the following ROS or ROS-like molecules — nitric oxide, superoxide, hydrogen peroxide, and singlet oxygen — as a result of a pathological influx of Ca2+ into the cell.

Electromagnetic fields have been shown to induce either stimulatory, inhibitory, or no effect on the immune system in relationship to how specific EMF frequencies, specific EMF power densities, and specific EMF durations interact with specific field parameters of the cell — especially with regard to either Ca2+ flux into or blockage of Ca2+ uptake by the cell. While the research seems to suggest that at specific frequencies and certain power densities, nonthermal EMF exposures can have an initially stimulating effect on the immune system, at higher power densities and/or with longer durations, this effect can be or become inhibitory — most likely due to increases in intracellular ROS and singlet oxygen, with the research also suggesting certain antioxidant substances ameliorating these effects.

Johansson [282], in a recent review of the literature, concluded that EMFs disturb immune function through stimulation of various allergic and inflammatory responses, as well as having effects on tissue repair processes, which may potentially lead to an underlying cause for cellular damage and tissue repair reduction. Such disturbances increase the risks for various diseases and functional impairments, including cancer and electrohypersensitivity (EHS).

Besides leaving the organism open to opportunistic infection, calcineurin inhibition has been correlated with an increase in neoplasms and skin cancer — and it has also been shown that UV radiation can inhibit calcineurin via the production of singlet oxygen and superoxide [26]. The fact that a number of ROS and singlet oxygen can be produced via means other than UV radiation — i.e., downstream effects of pathological increases in intracellular Ca2+ levels [e.g. 29] — supports the hypothesis that these can also inhibit calcineurin. The hypothesis that EMFs also inhibit calcineurin via the production of ROS furthermore adds support to research by Hallberg and Johansson [283–286], finding increases in skin cancers in correlation with increasing exposures to ambient man-made EMFs.

In summary, there has been a significant rise in a number of disease states (autism spectrum disorder, chronic fatigue syndrome, etc.) over the last thirty years, and these have coupled increases in levels of artificial electromagnetic pollution. Many of these disease states are paired with a weakened immune system, not to mention immune system disorders. Moreover, an increasing number of experimental and epidemiological studies are connecting many of these disease states, and their symptomologies, with electromagnetic radiation exposures. Calcium (Ca2+) is necessary for a number of enzymatic functions, and numerous researchers have proposed an EMF effect due to Ca2+ influx and Ca2+ signaling transcription. Two studies to date have found an EMF effect on calcineurin: one finding ELF to have a stimulatory effect and the other finding RF to have an inhibitory effect. While this paper proposes that depending on the complexity of parameters, EMF exposures can have stimulatory, inhibitory, or no effect on calcineurin activity, it also proposes that a pathophysiological increase in intracellular Ca2+ levels due to EMF activation of VGCCs can stimulate the production of ROS, which may lead downstream to calcineurin inhibition and a weakened immunity — as ROS have been shown in a number of studies to inhibit calcineurin. The infections induced by patients taking calcineurin inhibitors have interestingly also been found in a number of disease states termed neuro-immune system disorders (NIDS), (e.g., CFS, ASD, ADHD, and AD).

In conclusion, this hypothesis proposes that one means by which man-made electromagnetic fields have the potential to disturb immune system homeostasis is by opening VGCCs (Fig. 1a) and pathologically increasing intracellular Ca2+ levels (Fig. 1d), leading to pathological intracellular levels of ROS (Figs. 1e and 1f), which in turn have the potential to inhibit calcineurin (Fig. 1g), leaving the body increasingly susceptible to opportunistic infection. Given this possibility, while it can be said that candida, mold, mycoplasma, EBV, CMV, and other opportunistic pathogens are certainly part of the etiological conundrum of many unexplained disease states, perhaps the root of the problem may have more to do with an overlooked invisible environmental factor potentially weakening immune systems and making many more susceptible to these pathogens. While there is much research showing that EMFs alter immune system function, original experimental research demonstrating whether or not long-term low-level EMF exposure may indeed lead to immunosuppression and increase in opportunistic infection is required. Furthermore, original experimental research needs to be undertaken to determine for certain whether or not long-term exposure to EMFs (especially RF) can effect a decrease in calcineurin levels within immune cells, as was found with calcineurin in muscle and bone cells exposed to RF EMFs. This would determine a clear mechanism by which EMF exposure can in fact lead to immunosuppression.

Conflict of interest statement

The authors confirm that there are no conflicts of interest.

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References

[1] Ashwood P, Van de Water J. A review of autism and the immune response. Clin Dev Immunol 2004;11(2):165–74. http://dx.doi.org/10.1080/10446670410001722096.
[2] Brurberg KG, Fonhus MS, Larun L, Flottorp S, Malterud K. Case definitions for chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME): a systematic review. BMJ Open 2014;4(2):e003973. http://dx.doi.org/10.1136/bmjopen-2013-003973 [Published online 2014 Feb 7].
[3] Bierl C, Nisenbaum R, Hoaglin DC, et al. Regional distribution of fatiguing illnesses in the United States: a pilot study. Popul Health Metrics 2004;2:1. http://dx.doi.org/10.1186/1478-7954-2-1.
[4] Wang KY. Updated findings on neurodevelopmental disorders in Taiwan: impact of the institutionalized national healthcare system on prevalence and health outcomes. Curr Opin Psychiatry 2016;29(2):144–8. http://dx.doi.org/10.1097/YCO.0000000000000229.
[5] Matsumoto Y, Ninomiya S. Allergy among Japanese patients with chronic fatigue syndrome. Arerugi 1992;41(12):1722–5 [Japanese].
[6] Bakkaloglu B, Anlar B, Anlar FY, et al. Atopic features in early childhood autism. Eur J Paediatr Neurol 2008;12(6):476–9. http://dx.doi.org/10.1016/j.ejpn.2007.12.008 [Epub 2008 Feb 12].
[7] Herbert MR, Sage C. Autism and EMF? Plausibility of a pathophysiological link – Part I. Pathophysiology 2013;20(3):191–209. http://dx.doi.org/10.1016/j.pathophys.2013.08.001 [Epub 2013 Oct 4].
[8] Herbert MR, Sage C. Autism and EMF? Plausibility of a pathophysiological link part II. Pathophysiology 2013;20(3):211–34. http://dx.doi.org/10.1016/j.pathophys.2013.08.002 [Epub 2013 Oct 8].

[9] Maisch D, Rapley B, Rowland RE, Podd J. Chronic fatigue syndrome (CFS) – is prolonged exposure to environmental level powerline frequency magnetic fields a co-factor to consider in treatment? ACNEM J 1998;17(2):29–35.
[10] Maisch D, Podd J, Rapley B. Changes in health status in a group of CFS and CF patients following removal of excessive 50 Hz magnetic field exposure. ACNEM J 2002;21(1):15–9.
[11] Manikonda PK, Rajendra P, Devendranath D, Gunasekaran B, Channakeshava, Aradhya RS, et al. Influence of extremely low frequency magnetic fields on Ca2+ signaling and NMDA receptor functions in rat hippocampus. Neurosci Lett 2007;413(2):145–9 [Epub 2006 Dec 28].
[12] Erkut A, Tumkaya L, Balik MS, et al. The effect of prenatal exposure to 1800 MHz electromagnetic field on calcineurin and bone development in rats. Acta Cir. Bras 2016;31(2):74–83. http://dx.doi.org/10.1590/S0102-865020160020000001.
[13] Pall ML. Electromagnetic fields act via activation of voltage-gated calcium channels to produce beneficial or adverse effects. J Cell Mol Med 2013;17(8):958–65. http://dx.doi.org/10.1111/jcmm.12088 [Epub 2013 Jun 26].
[14] Nejatbakhsh N, Feng ZP. Calcium binding protein-mediated regulation of voltage-gated calcium channels linked to human diseases. Acta Pharmacol Sin 2011;32(6):741–8. http://dx.doi.org/10.1038/aps.2011.64.
[15] Zolle O, Lawrie AM, Simpson AW. Activation of the particulate and not the soluble guanylate cyclase leads to the inhibition of Ca2+ extrusion through localized elevation of cGMP. J Biol Chem 2000;275(34):25892–9.
[16] Bardal SK, Waechter JE, Martin DS. Calcineurin Inhibitors. Appl Pharmacol 1st ed. [Internet]. 2010 [cited 2014 July 16]. Available from: https://www.inkling.com/read/applied-pharmacology-bardal-waechter-martin-1st/chapter-17/calcineurin-inhibitors.
[17] Greenberg A, editor. Primer on kidney diseases. Philadelphia: Elsevier Health Sciences; 2005.
[18] Singh N, Alexander BD, et al. Cryptococcus neoformans in organ transplant recipients: impact of calcineurin-inhibitor agents on mortality. J Infect Dis 2007;195(5):756–64 [Epub 2007 Jan 23].
[19] Yusuf S, Cairns J, Camm J, Fallen EL, Gersh BJ. Evidence-Based Cardiology (Google eBook) [Internet]. Oxford, UK: Wiley-Blackwell; 2011 [cited 2015 Feb 1]. Available from Wiley: http://www.wiley.com/WileyCDA/WileyTitle/productCd-1405159251.html.
[20] Mian AN, Farney AC, Mendley SR. Mycoplasma hominis septic arthritis in a pediatric renal transplant recipient: case report and review of the literature. Am J Transplant 2005;5(1):183–8.
[21] Loupy A, Join-Lambert OF, Bebear CM, Legendre C, Anglicheau D. Urogenital mycoplasma: an emerging cause of deep wound infection after kidney transplantation? NDT Plus 2008;1(4):239.
[22] Hong F, Lee J, Song JW, et al. Cyclosporin A blocks muscle differentiation by inducing oxidative stress and inhibiting the peptidyl-prolyl-cis-trans isomerase activity of cyclophilin A: cyclophilin A protects myoblasts from cyclosporin A-induced cytotoxicity. FASEB J 2002;16(12):1633–5 [Epub 2002 Aug 7].
[23] Moreno JM, Ruiz MC, Ruiz N, et al. Modulation factors of oxidative status in stable renal transplantation. Transplant Proc 2005;37(3):1428–30.
[24] Sommer D, Coleman S, Swanson SA, Stemmer PM. Differential susceptibilities of serine/threonine phosphatases to oxidative and nitrosative stress. Arch Biochem Biophys 2002;404(2):271–8.
[25] Lee JE, Kim H, Jang H, Cho EJ, Youn HD. Hydrogen peroxide triggers the proteolytic cleavage and the inactivation of calcineurin. J Neurochem 2007;100(6):1703–12 [Epub 2007 Jan 8].
[26] Musson RE, Hensbergen PJ, Westphal AH, et al. UVA1 radiation inhibits calcineurin through oxidative damage mediated by photosensitization. Free Radic Biol Med 2011;50(10):1392–9. http://dx.doi.org/10.1016/j.freeradbiomed.2011.02.019 [Epub 2011 Feb 24].
[27] Musson RE, Mullenders LH, Smit NP. Effects of arsenite and UVA-1 radiation on calcineurin signaling. Mutat Res 2012;735(1–2):32–8. http://dx.doi.org/10.1016/j.mrfmmm.2012.04.007 [Epub 2012 May 4].
[28] Ullrich V, Namgaladze D, Frein D. Superoxide as inhibitor of calcineurin and mediator of redox regulation. Toxicol Lett 2003;139(2–3):107–10.
[29] Noronha-Dutra AA, Epperlein MM, Woolf N. Reaction of nitric oxide with hydrogen peroxide to produce potentially cytotoxic singlet oxygen as a model for nitric oxide-mediated killing. FEBS Lett 1993;321(1):59–62.
[30] Conti P, Gigante GE, Alesse E, et al. A role for Ca2+ in the effect of very low frequency electromagnetic field on the blastogenesis of human lymphocytes. FEBS Lett 1985;181(1):28–32.
[31] Conti P, Gigante GE, Cifone MG, et al. Mitogen dose-dependent effect of weak pulsed electromagnetic field on lymphocyte blastogenesis. FEBS Lett 1986;199(1):130–4.
[32] Kaczmarek LK, Adey WR. Weak electric gradients change ionic and transmitter fluxes in cortex. Brain Res 1974;66(3):537–40.
[33] Bawin SM, Adey WR. Sensitivity of calcium binding in cerebral tissue to weak environmental electric fields oscillating at low frequency. Proc Natl Acad Sci USA 1976;73(6):1999–2003.
[34] Blackman CF, Elder JA, Weil CM, Benane SG, Eichinger DC, House DE. Induction of calcium-ion efflux from brain tissue by radio-frequency radiation: effects of modulation frequency and field strength. Radio Sci 1979;14(6S):93–8. http://dx.doi.org/10.1029/RS014i06Sp00093.
[35] Joines WT, Blackman CF. Power density, field intensity, and carrier frequency determinants of RF-energy-induced calcium-ion efflux from brain tissue. Bioelectromagnetics 1980;1(3):271–5.
[36] Blackman CF, Benane SG, Joines WT, Hollis MA, House DE. Calcium-ion efflux from brain tissue: power-density versus internal field-intensity dependencies at 50-MHz RF radiation. Bioelectromagnetics 1980;1(3):277–83.
[37] Joines WT, Blackman CF. Equalizing the electric field intensity within chick brain immersed in buffer solution at different carrier frequencies. Bioelectromagnetics 1981;2(4):411–3.
[38] Joines WT, Blackman CF, Hollis MA. Broadening of the RF power-density window for calcium-ion efflux from brain tissue. IEEE Trans Biomed Eng 1981;28(8):568–73.
[39] Blackman CF, Benane SG, Kinney LS, Joines WT, House DE. Effects of ELF fields on calcium-ion efflux from brain tissue in vitro. Radiat Res 1982;92(3):510–20.
[40] Blackman CF, Benane SG, House DE, Joines WT. Effects of ELF (1–120 Hz) and modulated (50 Hz) RF fields on the efflux of calcium ions from brain tissue in vitro. Bioelectromagnetics 1985;6(1):1–11.
[41] Blackman CF, Benane SG, Rabinowitz JR, House DE, Joines WT. A role for the magnetic field in the radiation-induced efflux of calcium ions from brain tissue in vitro. Bioelectromagnetics 1985;6(4):327–37.
[42] Blackman CF, Benane SG, Elliott DJ, House DE, Pollock MM. Influence of electromagnetic fields on the efflux of calcium ions from brain tissue in vitro: a three-model analysis consistent with the frequency response up to 510 Hz. Bioelectromagnetics 1988;9(3):215–27.
[43] Blackman CF, House DE, Benane SG, Joines WT, Spiegel RJ. Effect of ambient levels of power-line-frequency electric fields on a developing vertebrate. Bioelectromagnetics 1988;9(2):129–40.
[44] Blackman CF, Kinney LS, House DE, Joines WT. Multiple power-density windows and their possible origin. Bioelectromagnetics 1989;10(2):115–28.
[45] Dutta SK, Ghosh B, Blackman CF. Radiofrequency radiation-induced calcium ion efflux enhancement from human and other neuroblastoma cells in culture. Bioelectromagnetics 1989;10(2):197–202.
[46] Dutta SK, Das K, Ghosh B, Blackman CF. Dose dependence of acetylcholinesterase activity in neuroblastoma cells exposed to modulated radio-frequency electromagnetic radiation. Bioelectromagnetics 1992;13(4):317–22.
[47] Cadossi R, Emilia G, Ceccherelli G, et al. Lymphocytes and pulsing magnetic fields. In: Marino EE, editor. Modern Bioelectricity. New York: Dekker; 1998. p. 451–96.
[48] Papatheofanis FJ. Use of calcium channel antagonists as magnetoprotective agents. Radiat Res 1990;122:24–8.
[49] Liburdy RP. Calcium signaling in lymphocytes and ELF fields. Evidence for an electric field metric and a site of interaction involving the calcium ion channel. FEBS Lett 1992;301(1):53–9.
[50] Fanelli C, Coppola S, Barone R, et al. Magnetic fields increase cell survival by inhibiting apoptosis via modulation of Ca2+ influx. FASEB J 1999;13(1):95–102.
[51] Cho MR, Thatte HS, Silvia MT, Golan DE. Transmembrane calcium influx induced by ac electric fields. FASEB J 1999;13(6):677–83.
[52] Grassi C, D'Ascenzo M, Torsello A, et al. Effects of 50 Hz electromagnetic fields on voltage-gated Ca2+ channels and their role in modulation of neuroendocrine cell proliferation and death. Cell Calcium 2004;35(4):307–15.
[53] Craviso GL, Choe S, Chatterjee P, Chatterjee I, Vernier PT. Nanosecond electric pulses: a novel stimulus for triggering Ca2+ influx into chromaffin cells via voltage-gated Ca2+ channels. Cell Mol Neurobiol 2010;30(8):1259–65. http://dx.doi.org/10.1007/s10571-010-9573-1 [Epub 2010 Nov 16].
[54] Craviso GL, Choe S, Chatterjee I, Vernier PT. Modulation of intracellular Ca2+ levels in chromaffin cells by nanoelectropulses. Bioelectrochemistry 2012;87:244–52. http://dx.doi.org/10.1016/j.bioelechem.2011.11.016 [Epub 2011 Dec 8].
[55] Morotomi-Yano K, Akiyama H, Yano K. Different involvement of extracellular calcium in two modes of cell death induced by nanosecond pulsed electric fields. Arch Biochem Biophys 2014;555–556:47–54. http://dx.doi.org/10.1016/j.abb.2014.05.020 [Epub 2014 Jun 2].
[56] Fitzsimmons RJ, Ryaby JT, Magee FP, Baylink DJ. Combined magnetic fields increased net calcium flux in bone cells. Calcif Tissue Int 1994;55(5):376–80.
[57] Kenny JS, Kisaalita WS, Rowland G, Thai C, Foutz T. Quantitative study of calcium uptake by tumorigenic bone (TE-85) and neuroblastoma x glioma (NG108-15) cells exposed to extremely-low-frequency (ELF) electric fields. FEBS Lett 1997;414(2):343.
[58] DeCoursey TE, Chandy KG, Gupta S, Cahalan MD. Voltage-dependent ion channels in T-lymphocytes. J Neuroimmunol 1985;10(1):71–95.
[59] Gomes B, Savignac M, Moreau M, et al. Lymphocyte calcium signaling involves dihydropyridine-sensitive L-type calcium channels: facts and controversies. Crit Rev Immunol 2004;24(6):425–47.
[60] Gardner P. Calcium and T lymphocyte activation. Cell 1989;59(1):15–20.
[61] Gardner P. Patch clamp studies of lymphocyte activation. Annu Rev Immunol 1990;8:231–52. http://dx.doi.org/10.1146/annurev.iy.08.040190.001311.
[62] Walleczek J, Budinger TF. Pulsed magnetic field effects on calcium signaling in lymphocytes: dependence on cell status and field intensity. FEBS Lett 1992;314(3):351–5.
[63] Walleczek J, Liburdy RP. Nonthermal 60 Hz sinusoidal magnetic-field exposure enhances 45Ca2+ uptake in rat thymocytes: dependence on mitogen activation. FEBS Lett 1990;271(1–2):157–60.
[64] Walleczek J. Electromagnetic field effects on cells of the immune system: the role of calcium signaling. FASEB J 1992;6(13):3177–85.

[65] Eichwald C, Walleczek J. Activation-dependent and biphasic electromagnetic field effects: model based on cooperative enzyme kinetics in cellular signaling. Bioelectromagnetics 1996;17(6):427–35.
[66] Pershin SB, Frenkel' ID, Galenchik AI, Korovkina EG. The immune and hormonal effects of the local action of microwaves of different intensities. Vopr Kurortol Fizioter Lech Fiz Kult 1989;1:16–21 [Russian].
[67] Arafa HM, Abd-Allah AR, El-Mahdy MA, Ramadan LA, Hamada FM. Immunomodulatory effects of L-carnitine and q10 in mouse spleen exposed to low-frequency high-intensity magnetic field. Toxicology 2003;187(2–3):171–81.
[68] Yang HK, Cain CA, Lockwood J, Tompkins WA. Effects of microwave exposure on the hamster immune system. I. Natural killer cell activity. Bioelectromagnetics 1983;4(2):123–39.
[69] Rama Rao GV, Cain CA, Tompkins WA. Effects of microwave exposure on the hamster immune system. IV. Spleen cell IgM hemolytic plaque formation. Bioelectromagnetics 1985;6(1):41–52.
[70] Wilson BW, Stevens RG, Anderson LE. Neuroendocrine mediated effects of electromagnetic-field exposure: possible role of the pineal gland. Life Sci 1989;45(15):1319–32.
[71] Stankiewicz W, Dabrowski MP, Kubacki R, Sobiczewska E, Szmigielski S. Immunotropic influence of 900 MHz microwave GSM signal on human blood immune cells activated in vitro. Electromagn Biol Med 2006;25(1):45–51.
[72] Dumanskiĭ IuD, Nogachevskaia SI. Changes in the immune status under the influence of high-frequency electromagnetic radiation. Lik Sprava 1993;1:65–9 [Russian].
[73] Li YZ, Chen SH, Zhao KF, et al. Effects of electromagnetic radiation on health and immune function of operators. Zhonghua Lao Dong Wei Sheng Zhi Ye Bing Za Zhi 2013;31(8):602–5 [Chinese].
[74] Rama Rao G, Cain CA, Lockwood J, Tompkins WA. Effects of microwave exposure on the hamster immune system. II. Peritoneal macrophage function. Bioelectromagnetics 1983;4(2):141–55.
[75] Rao GR, Cain CA, Tompkins WA. Effects of microwave exposure on the hamster immune system. III. Macrophage resistance to vesicular stomatitis virus infection. Bioelectromagnetics 1984;5(4):377–88.
[76] Zafra C, Peña J, de la Fuente M. Effect of microwaves on the activity of murine macrophages in vitro. Int Arch Allergy Appl Immunol 1988;85(4):478–82.
[77] Simko M, Mattsson MO. Extremely low frequency electromagnetic fields as effectors of cellular responses in vitro: possible immune cell activation. J Cell Biochem 2004;93(1):83–92.
[78] Budd RA, Czerski P. Modulation of mammalian immunity by electromagnetic radiation. J Microw Power Electromagn Energy 1985;20(4):217–31.
[79] Moszczynski P, Lisiewicz J, Dmoch A. The effect of various occupational exposures to microwave radiation on the concentrations of immunoglobulins and T lymphocyte subsets. Wiad Lek 1999;52(1-2):30–4 [Polish].
[80] Smialowicz RJ, Rogers RR, Garner RJ, Riddle MM, Luebke RW, Rowe DG. Microwaves (2,450 MHz) suppress murine natural killer cell activity. Bioelectromagnetics 1983;4(4):371–81.
[81] Makar VR, Logani MK, Bhanushali A, Kataoka M, Ziskin MC. Effect of millimeter waves on natural killer cell activation. Bioelectromagnetics 2005;26(1):10–9.
[82] Veyret B, Bouthet C, Deschaux P, et al. Antibody responses of mice exposed to low-power microwaves under combined, pulse-and-amplitude modulation. Bioelectromagnetics 1991;12(1):47–56.
[83] Elekes E, Thuroczy G, Szabo LD. Effect on the immune system of mice exposed chronically to 50 Hz amplitude-modulated 2.45 GHz microwaves. Bioelectromagnetics 1996;17(3):246–8.
[84] Chernykh AM. Hygienic evaluation of the combined effect of electromagnetic fields and pesticides in experimental conditions. Gig Sanit 2003 Mar-Apr (2):56–8 [in Russian].
[85] Grigoriev YG, Grigoriev OA, Ivanov AA, et al. Confirmation studies of Soviet research on immunological effects of microwaves: Russian immunology results. Bioelectromagnetics 2010;31(8):589–602. http://dx.doi.org/10.1002/bem.20605 [Epub 2010 Sep 20].
[86] Grigoriev IuG, Shafirkin AV, Nosocskii AM. New data for proving the presence of significant effects of electromagnetic exposure (to autoimmune changes in rats). Radiats Biol Radioecol 2011;51(6):721–30 [in Russian].
[87] Chuian OM, Temur'iants NA, Makhonina MM, Zaiachnikova TV. Effect of hypokinetic stress and low intensity electromagnetic field of extremely high frequency on changes of cytokine concentration in rat blood. Fiziol Zh 2005;51(6):70–8 [Ukrainian].
[88] Salehi I, Sani KG, Zamani A. Exposure of rats to extremely low-frequency electromagnetic fields (ELF-EMF) alters cytokines production. Electromagn Biol Med 2013;32(1):1–8. http://dx.doi.org/10.3109/15368378.2012.692343 [Epub 2012 Oct 9].
[89] He GL, Liu Y, Li M, et al. The amelioration of phagocytic ability in microglial cells by curcumin through the inhibition of EMF-induced pro-inflammatory responses. J Neuroinflammation 2014;19(11):49. http://dx.doi.org/10.1186/1742-2094-11-49.
[90] Yuan ZQ, Li F, Wang DG, Wang Y, Zhang P. [Effect of low intensity and very high frequency electromagnetic radiation on occupationally exposed personnel]. Zhonghua Lao Dong Wei Sheng Zhi Ye Bing Za Zhi. 2004; 22(4):267–269 [in Chinese].
[91] Vinogradov GI, Batanov GV, Naumenko GM, Levin AD, Trifonov SI. Effect of nonionizing microwave radiation on autoimmune reactions and antigenic structure of serum proteins. Radiobiologiia 1985;25(6):840–3 [in Russian].
[92] Monro JA, Puri BK. The effect of pulsed electromagnetic field therapy on food sensitivity. Electromagn Biol Med. 2014. [Epub ahead of print].
[93] Conti P, Gigante GE, Cifone MG, et al. Reduced mitogenic stimulation of human lymphocytes by extremely low frequency electromagnetic fields. FEBS Lett 1983;162(1):156–60.
[94] Cossarizza A, Monti D, Bersani F, et al. Extremely low frequency pulsed electromagnetic fields increase cell proliferation in lymphocytes from young and aged subjects. Biochem Biophys Res Commun 1989;160(2):692–8.
[95] Cossarizza A, Monti D, Bersani F, et al. Extremely low frequency pulsed electromagnetic fields increase interleukin-2 (IL-2) utilization and IL-2 receptor expression in mitogen-stimulated human lymphocytes from old subjects. FEBS Lett 1989;248(1–2):141–4.
[96] Kolomytseva MP, Gapeev AB, Sadovnikov VB, Chemeris NK. Suppression of nonspecific resistance of the body under the effect of extremely high frequency electromagnetic radiation of low intensity. Biofizika 2002;47(1):71–7 [in Russian].
[97] Sambucci M, Laudisi F, Nasta F, et al. Early life exposure to 2.45 GHz WiFi-like signals: effects on development and maturation of the immune system. Prog Biophys Mol Biol 2011;107(3):393–8. http://dx.doi.org/10.1016/j.pbiomolbio.2011.08.012 [Epub 2011 Sep 9].
[98] Goldberg RB, Creasey WA. A review of cancer induction by extremely low frequency electromagnetic fields. Is there a plausible mechanism? Med Hypotheses 1991;35(3):265–74.
[99] Shandala MG, Dumanskii UD, Rudnev MI, Ershova LK, Los IP. Study of nonionizing microwave radiation effects upon the central nervous system and behavior reactions. Environ Health Perspect 1979;30:115–21.
[100] Cleary SF, Liu LM, Merchant RE. In vitro lymphocyte proliferation induced by radio-frequency electromagnetic radiation under isothermal conditions. Bioelectromagnetics 1990;11(1):47–56.
[101] Levitt BB, Morrow T. Electrosmog: What Price Convenience? WestView [Internet]. 2007 July. [cited 2015 Feb 17]. Available from: http://emfsafetynetwork.org/wp-content/uploads/2009/11/Revised-ElectroSmog-Piece-West-View-July-07.pdf.
[102] Levitt BB, Lai H. Biological effects from exposure to electromagnetic radiation emitted by cell tower base stations and other antenna arrays. Environ Rev 2010;18(NA):369–95. http://dx.doi.org/10.1139/A10-018 [Internet].
[103] Szudzinski A, Pietraszek A, Janiak M, Wrembel J, Kałczak M, Szmigielski S. Acceleration of the development of benzopyrene-induced skin cancer in mice by microwave radiation. Arch Dermatol Res 1982;274(3–4):303–12.
[104] Grimaldi S, Pasquali E, Barbatano L, et al. Exposure to a 50 Hz electromagnetic field induces activation of the Epstein-Barr virus genome in latently infected human lymphoid cells. J Environ Pathol Toxicol Oncol 1997;16(2–3):205–7.
[105] Canseven AG, Seyhan N, Mirshahidi S, Imir T. Suppression of natural killer cell activity on *Candida stellatoidea* by a 50 Hz magnetic field. Electromagn Biol Med 2006;25(2):79–85.
[106] Nageswari KS, Sarma KR, Rajvanshi VS, et al. Effect of chronic microwave radiation on T cell-mediated immunity in the rabbit. Int J Biometeorol 1991;35(2):92–7.
[107] Nageswari KS, Tandon HC, Varma S, Bhatnagar VM. Effect of prolonged low power microwave radiation on peripheral leucocyte counts in rabbits. Indian J Med Res 1982;75:453–9.
[108] Nageswari KS, Tandon HC, Varma S, Bhatnagar VM. Effect of chronic microwave radiation on rabbit erythrocytes. Indian J Exp Biol 1982;20(1):13–5.
[109] Abu Khadra KM, Khalil AM, Abu Samak M, Aljaberi A. Evaluation of selected biochemical parameters in the saliva of young males using mobile phones. Electromagn Biol Med 2014 [Epub ahead of print].
[110] Agarwal A, Desai NR, Makker K, et al. Effects of radiofrequency electromagnetic waves (RF-EMW) from cellular phones on human ejaculated semen: an in vitro pilot study. Fertil Steril 2009;92(4):1318–25. http://dx.doi.org/10.1016/j.fertnstert.2008.08.022 [Epub 2008 Sep 20].
[111] Al-Damegh MA. Rat testicular impairment induced by electromagnetic radiation from a conventional cellular telephone and the protective effects of the antioxidants vitamins C and E. Clinics (Sao Paulo). 2012;67(7):785–92.
[112] Avci B, Akar A, Bilgici B, Tuncel OK. Oxidative stress induced by 1.8 GHz radio frequency electromagnetic radiation and effects of garlic extract in rats. Int J Radiat Biol 2012 Nov;88(11):799–805. http://dx.doi.org/10.3109/09553002.2012.711504 [Epub 2012 Aug 8].
[113] Aynali G, Nazıroglu M, Celik O, Dogan M, Yarıktas M, Yasan H. Modulation of wireless (2.45 GHz)-induced oxidative toxicity in laryngotracheal mucosa of rat by melatonin. Eur Arch Otorhinolaryngol 2013;270(5):1695–700. http://dx.doi.org/10.1007/s00405-013-2425-0 [Epub 2013 Mar 12].
[114] Ayse IG, Zafer A, Sule O, Isil IT, Kalkan T. Differentiation of K562 cells under ELF-EMF applied at different time courses. Electromagn Biol Med 2010;29(3):122–30. http://dx.doi.org/10.3109/15368378.2010.502451.
[115] Bediz CS, Baltaci AK, Mogulkoc R, Oztekin E. Zinc supplementation ameliorates electromagnetic field-induced lipid peroxidation in the rat brain. Tohoku J Exp Med 2006;208(2):133–40.
[116] Bekhite MM, Finkensieper A, Abou-Zaid FA, et al. Static electromagnetic fields induce vasculogenesis and chondro-osteogenesis of mouse embryonic stem cells by reactive oxygen species-mediated up-regulation of vascular endothelial growth factor. Stem Cells Dev 2010;19(5):731–43. http://dx.doi.org/10.1089/scd.2008.0266.
[117] Belova NA, Potselueva MM, Skrebnitskaia LK, Znobishcheva AV, Lednev VV. Effects of weak magnetic fields on the production of reactive oxygen species in peritoneal neutrophils in mice. Biofizika 2010;55(4):657–63 [in Russian].

[118] Bilgici B, Akar A, Avci B, Tuncel OK. Effect of 900 MHz radiofrequency radiation on oxidative stress in rat brain and serum. Electromagn Biol Med 2013;32(1):20–9. http://dx.doi.org/10.3109/15368378.2012.699012 [Epub 2013 Jan 9].
[119] Bodera P, Stankiewicz W, Zawada K, et al. Changes in antioxidant capacity of blood due to mutual action of electromagnetic field (1800 MHz) and opioid drug (tramadol) in animal model of persistent inflammatory state. Pharmacol Rep 2013;65(2):421–8.
[120] Bułdak RJ, Polaniak R, Bułdak L, et al. Short-term exposure to 50 Hz ELF-EMF alters the cisplatin-induced oxidative response in AT478 murine squamous cell carcinoma cells. Bioelectromagnetics 2012;33(8):641–51. http://dx.doi.org/10.1002/bem.21732 [Epub 2012 Apr 25].
[121] Burlaka A, Tsybulin O, Sidorik E, et al. Overproduction of free radical species in embryonal cells exposed to low intensity radiofrequency radiation. Exp Oncol 2013;35(3):219–25.
[122] Calabrò E, Condello S, Currò M, et al. Effects of low intensity static magnetic field on FTIR spectra and ROS production in SH-SY5Y neuronal-like cells. Bioelectromagnetics 2013;34(8):618–29. http://dx.doi.org/10.1002/bem.21815 [Epub 2013 Sep 25].
[123] Calabrò E, Condello S, Currò M. 50 Hz Electromagnetic field produced changes in FTIR spectroscopy associated with mitochondrial transmembrane potential reduction in neuronal-Like SH-SY5Y cells. Oxid Med Cell Longevity 2013;2013:8. http://dx.doi.org/10.1155/2013/414393 [Article ID 414393].
[124] Campisi A, Gulino M, Acquaviva R, et al. Reactive oxygen species levels and DNA fragmentation on astrocytes in primary culture after acute exposure to low intensity microwave electromagnetic field. Neurosci Lett 2010;473(1):52–5. http://dx.doi.org/10.1016/j.neulet.2010.02.018 [Epub 2010 Feb 13].
[125] Cetin H, Nazıroglu M, Celik O, Yuksel M, Pastaci N, Ozkaya MO. Liver antioxidant stores protect the brain from electromagnetic radiation (900 and 1800 MHz)-induced oxidative stress in rats during pregnancy and the development of offspring. J Matern Fetal Neonatal Med 2014;27(18):1915–21. http://dx.doi.org/10.3109/14767058.2014.898056 [Epub 2014 Apr 9].
[126] Ceyhan AM, Akkaya VB, Gulecol SC, Ceyhan BM, Ozguner F, Chen W. Protective effects of β-glucan against oxidative injury induced by 2.45-GHz electromagnetic radiation in the skin tissue of rats. Arch Dermatol Res 2012;304(7):521–7. http://dx.doi.org/10.1007/s00403-012-1205-9 [Epub 2012 Jan 12].
[127] De Iuliis GN, Newey RJ, King BV, Aitken RJ. Mobile phone radiation induces reactive oxygen species production and DNA damage in human spermatozoa in vitro. PLoS One 2009;4(7):e6446. http://dx.doi.org/10.1371/journal.pone.0006446.
[128] Desai NR, Kesari KK, Agarwal A. Pathophysiology of cell phone radiation: oxidative stress and carcinogenesis with focus on male reproductive system. Reprod Biol Endocrinol 2009;22(7):114. http://dx.doi.org/10.1186/1477-7827-7-114.
[129] Deshmukh PS, Banerjee BD, Abegaonkar MP, et al. Effect of low level microwave radiation exposure on cognitive function and oxidative stress in rats. Indian J Biochem Biophys 2013;50(2):114–9.
[130] Devrim E, Erguder IB, Kilicoglu B, Yaykasli E, Cetin R, Durak I. Effects of electromagnetic radiation use on oxidant/antioxidant status and DNA turnover enzyme activities in erythrocytes and heart, kidney, liver, and ovary tissues from rats: possible protective role of vitamin C. Toxicol Mech Methods 2008;18(9):679–83. http://dx.doi.org/10.1080/15376510701380182.
[131] Di Loreto S, Falone S, Caracciolo V, et al. Fifty hertz extremely low-frequency magnetic field exposure elicits redox and trophic response in rat-cortical neurons. J Cell Physiol 2009;219(2):334–43. http://dx.doi.org/10.1002/jcp.21674.
[132] Duan Y, Wang Z, Zhang H, et al. The preventive effect of lotus seedpod procyanidins on cognitive impairment and oxidative damage induced by extremely low frequency electromagnetic field exposure. Food Funct 2013;4(8):1252–62. http://dx.doi.org/10.1039/c3fo60116a.
[133] Elhag MA, Nabil GM, Attia AM. Effects of electromagnetic field produced by mobile phones on the oxidant and antioxidant status of rats. Pak J Biol Sci 2007;10(23):4271–4.
[134] El-Helaly M, Abu-Hashem E. Oxidative stress, melatonin level, and sleep insufficiency among electronic equipment repairers. Indian J Occup Environ Med 2010;14(3):66–70. http://dx.doi.org/10.4103/0019-5278.75692.
[135] Eser O, Songur A, Aktas C, et al. The effect of electromagnetic radiation on the rat brain: an experimental study. Turk Neurosurg 2013;23(6):707–15. http://dx.doi.org/10.5137/1019-5149.JTN.7088-12.2.
[136] Ferreira AR, Knakievicz T, Pasquali MA, et al. Ultra high frequency-electromagnetic field irradiation during pregnancy leads to an increase in erythrocytes micronuclei incidence in rat offspring. Life Sci 2006;80(1):43–50 [Epub 2006 Aug 23].
[137] Frahm J, Mattsson MO, Simkó M. Exposure to ELF magnetic fields modulate redox related protein expression in mouse macrophages. Toxicol Lett 2010;192(3):330–6. http://dx.doi.org/10.1016/j.toxlet.2009.11.010 [Epub 2009 Nov 12].
[138] Friedman J, Kraus S, Hauptman Y, Schiff Y, Seger R. Mechanism of short-term ERK activation by electromagnetic fields at mobile phone frequencies. Biochem J 2007;405(3):559–68.
[139] Garaj-Vrhovac V, Gajski G, Pažanin S, et al. Assessment of cytogenetic damage and oxidative stress in personnel occupationally exposed to the pulsed microwave radiation of marine radar equipment. Int J Hyg Environ Health 2011;214(1):59–65. http://dx.doi.org/10.1016/j.ijheh.2010.08.003 [Epub 2010 Sep 15].
[140] Garip AI, Akan Z. Effect of ELF-EMF on number of apoptotic cells; correlation with reactive oxygen species and HSP. Acta Biol Hung 2010;61(2):158–67. http://dx.doi.org/10.1556/ABiol.61.2010.2.4.
[141] Ghazizadeh V, Nazıroglu M. Electromagnetic radiation (Wi-Fi) and epilepsy induce calcium entry and apoptosis through activation of TRPV1 channel in hippocampus and dorsal root ganglion of rats. Metab Brain Dis 2014;29(3):787–99. http://dx.doi.org/10.1007/s11011-014-9549-9 [Epub 2014 May 3].
[142] Goraca A, Ciejka E, Piechota A. Effects of extremely low frequency magnetic field on the parameters of oxidative stress in heart. J Physiol Pharmacol 2010;61(3):333–8.
[143] Gumral N, Naziroglu M, Koyu A, et al. Effects of selenium and L-carnitine on oxidative stress in blood of rat induced by 2.45-GHz radiation from wireless devices. Biol Trace Elem Res 2009;132(1–3):153–63. http://dx.doi.org/10.1007/s12011-009-8372-3.
[144] Guney M, Ozguner F, Oral B, Karahan N, Mungan T. 900 MHz radiofrequency-induced histopathologic changes and oxidative stress in rat endometrium: protection by vitamins E and C. Toxicol Ind Health 2007;23(7):411–20.
[145] Gurler HS, Bilgici B, Akar AK, Tomak L, Bedir A. Increased DNA oxidation (8-OHdG) and protein oxidation (AOPP) by low level electromagnetic field (2.45 GHz) in rat brain and protective effect of garlic. Int J Radiat Biol 2014;90(10):892–6. http://dx.doi.org/10.3109/09553002.2014.922717 [Epub 2014 Jun 25].
[146] Hamzany Y, Feinmesser R, Shpitzer T, et al. Is human saliva an indicator of the adverse health effects of using mobile phones? Antioxid Redox Signal 2013;18(6):622–7. http://dx.doi.org/10.1089/ars.2012.4751 [Epub 2012 Oct 9].
[147] Hou Q, Wang M, Wu S, et al. Oxidative changes and apoptosis induced by 1800-MHz electromagnetic radiation in NIH/3T3 cells. Electromagn Biol Med 2014 [Epub ahead of print].
[148] Ilhan A, Gurel A, Armutcu F, et al. Ginkgo biloba prevents mobile phone-induced oxidative stress in rat brain. Clin Chim Acta 2004;340(1–2):153–62.
[149] Irmak MK, Fadillioglu E, Gulec M, Erdogan H, Yagmurca M, Akyol O. Effects of electromagnetic radiation from a cellular telephone on the oxidant and antioxidant levels in rabbits. Cell Biochem Funct 2002;20(4):279–83.
[150] Kahya MC, Nazıroglu M, Cig B. Selenium reduces mobile phone (900 MHz)-induced oxidative stress, mitochondrial function, and apoptosis in breast cancer cells. Biol Trace Elem Res 2014;160(2):285–93. http://dx.doi.org/10.1007/s12011-014-0032-6 [Epub 2014 Jun 27].
[151] Kesari KK, Kumar S, Nirala J, Siddiqui MH, Behari J. Biophysical evaluation of radiofrequency electromagnetic field effects on male reproductive pattern. Cell Biochem Biophys 2013;65(2):85–96. http://dx.doi.org/10.1007/s12013-012-9414-6.
[152] Kesari KK, Siddiqui MH, Meena R, Verma HN, Kumar S. Cell phone radiation exposure on brain and associated biological systems. Indian J Exp Biol 2013;51(3):187–200.
[153] Kesari KK, Behari J. Evidence for mobile phone radiation exposure effects on reproductive pattern of male rats: role of ROS. Electromagn Biol Med 2012;31(3):213–22. http://dx.doi.org/10.3109/15368378.2012.700292.
[154] Kesari KK, Kumar S, Behari J. 900-MHz microwave radiation promotes oxidation in rat brain. Electromagn Biol Med 2011;30(4):219–34. http://dx.doi.org/10.3109/15368378.2011.587930.
[155] Kovacic P, Somanathan R. Electromagnetic fields: mechanism, cell signaling, other bioprocesses, toxicity, radicals, antioxidants and beneficial effects. J Recept Signal Transduction Res 2010;30(4):214–26. http://dx.doi.org/10.3109/10799893.2010.488650.
[156] Kovacic P, Pozos RS. Cell signaling (mechanism and reproductive toxicity): redox chains, radicals, electrons, relays, conduit, electrochemistry, and other medical implications. Birth Defects Res C Embryo Today 2006;78(4):333–44.
[157] Koylu H, Mollaoglu H, Ozguner F, Naziroglu M, Delibas N. Melatonin modulates 900 MHz microwave-induced lipid peroxidation changes in rat brain. Toxicol Ind Health 2006;22(5):211–6.
[158] Koyu A, Ozguner F, Yilmaz H, Uz E, Cesur G, Ozcelik N. The protective effect of caffeic acid phenethyl ester (CAPE) on oxidative stress in rat liver exposed to the 900 MHz electromagnetic field. Toxicol Ind Health 2009;25(6):429–34. http://dx.doi.org/10.1177/0748233709106821.
[159] Liu C, Duan W, Xu S, et al. Exposure to 1800 MHz radiofrequency electromagnetic radiation induces oxidative DNA base damage in a mouse spermatocyte-derived cell line. Toxicol Lett 2013;218(1):2–9. http://dx.doi.org/10.1016/j.toxlet.2013.01.003 [Epub 2013 Jan 18].
[160] Liu DD, Ren Z, Yang G, Zhao QR, Mei YA. Melatonin protects rat cerebellar granule cells against electromagnetic field-induced increases in Na(+) currents through intracellular Ca(2+) release. J Cell Mol Med 2014;18(6):1060–70. http://dx.doi.org/10.1111/jcmm.12250 [Epub 2014 Feb 18].
[161] Liu K, Zhang G, Wang Z, et al. The protective effect of autophagy on mouse spermatocyte derived cells exposure to 1800 MHz radiofrequency electromagnetic radiation. Toxicol Lett 2014;228(3):216–24. http://dx.doi.org/10.1016/j.toxlet. 2014.05.004 [Epub 2014 May 9].
[162] Lu YS, Huang BT, Huang YX. Reactive oxygen species formation and apoptosis in human peripheral blood mononuclear cell induced by 900 MHz mobile phone radiation. Oxid Med Cell Longevity 2012;2012:740280. http://dx.doi.org/10.1155/2012/740280 [Epub 2012 Jun 14].

[163] Luo YP, Ma HR, Chen JW, Li JJ, Li CX. Effect of American Ginseng Capsule on the liver oxidative injury and the Nrf2 protein expression in rats exposed by electromagnetic radiation of frequency of cell phone. Zhongguo Zhong Xi Yi Jie He Za Zhi 2014;34(5):575–80 [Chinese].
[164] Lupke M, Rollwitz J, Simko M. Cell activating capacity of 50 Hz magnetic fields to release reactive oxygen intermediates in human umbilical cord blood-derived monocytes and in Mono Mac 6 cells. Free Radic Res 2004;38 (9):985–93.
[165] Maaroufi K, Had-Aissouni L, Melon C, et al. Spatial learning, monoamines and oxidative stress in rats exposed to 900 MHz electromagnetic field in combination with iron overload. Behav Brain Res 2014;258:80–9. http://dx.doi.org/10.1016/j.bbr.2013.10.016 [Epub 2013 Oct 18].
[166] Maaroufi K, Save E, Poucet B, Sakly M, Abdelmelek H, Had-Aissouni L. Oxidative stress and prevention of the adaptive response to chronic iron overload in the brain of young adult rats exposed to a 150-kilohertz electromagnetic field. Neuroscience 2011;186:39–47. http://dx.doi.org/10.1016/j.neuroscience.2011.04.003 [Epub 2011 Apr 12].
[167] Mailankot M, Kunnath AP, Jayalekshmi H, Koduru B, Valsalan R. Radio frequency electromagnetic radiation (RF-EMR) from GSM (0.9/1.8 GHz) mobile phones induces oxidative stress and reduces sperm motility in rats. Clinics (Sao Paulo) 2009;64(6):561–5.
[168] Marjanovic AM, Pavicic I, Trosic I. Cell oxidation-reduction imbalance after modulated radiofrequency radiation. Electromagn Biol Med 2014:1–6 [Epub ahead of print].
[169] Marjanovic AM, Pavicic I, Trosic I. Biological indicators in response to radiofrequency/microwave exposure. Arh Hig Rada Toksikol 2012;63 (3):407–16. http://dx.doi.org/10.2478/10004-1254-63-2012-2215.
[170] Meral I, Mert H, Mert N, et al. Effects of 900-MHz electromagnetic field emitted from cellular phone on brain oxidative stress and some vitamin levels of guinea pigs. Brain Res 2007;1169:120–4 [Epub 2007 Jul 17].
[171] Morabito C, Guarnieri S, Fano G, Mariggio MA. Effects of acute and chronic low frequency electromagnetic field exposure on PC12 cells during neuronal differentiation. Cell Physiol Biochem 2010;26(6):947–58. http://dx.doi.org/10.1159/000324003 [Epub 2011 Jan 4].
[172] Nazıroglu M, Gumral N. Modulator effects of selenium and L-carnitine on wireless devices (2.45 GHz) induced oxidative stress and electroencephalography records in brain of rat. Int J Radiat Biol 2009;85 (8):680–9. http://dx.doi.org/10.1080/09553000903009530.
[173] Nazıroglu M, Cig B, Dogan S, Uguz AC, Dilek S, Faouzi D. 2.45 GHz wireless devices induce oxidative stress and proliferation through cytosolic Ca2+ influx in human leukemia cancer cells. Int J Radiat Biol 2012;88(6):449–56. http://dx.doi.org/10.3109/09553002.2012.682192 [Epub 2012 May 2]. CrossRef.
[174] Nazıroglu M, Celik O, Ozgul C, et al. Melatonin modulates wireless (2.45 GHz)-induced oxidative injury through TRPM2 and voltage gated Ca(2+) channels in brain and dorsal root ganglion in rat. Physiol Behav 2012;105 (3):683–92. http://dx.doi.org/10.1016/j.physbeh.2011.10.005 [Epub 2011 Oct 12]. CrossRef.
[175] Nazıroglu M, Tokat S, Demirci S. Role of melatonin on electromagnetic radiation-induced oxidative stress and Ca2 + signaling molecular pathways in breast cancer. J Recept Signal Transduction Res 2012;32(6):290–7. http://dx.doi.org/10.3109/10799893.2012.737002.
[176] Odaci E, Unal D, Mercantepe T, et al. Pathological effects of prenatal exposure to a 900 MHz electromagnetic field on the 21-day-old male rat kidney. Biotech Histochem 2014:1–9 [Epub ahead of print].
[177] Okano H. Effects of static magnetic fields in biology: role of free radicals. Front Biosci 2008;13:6106–25.
[178] Oksay T, Naziroglu M, Dogan S, Guzel A, Gumral N, Kosar PA. Protective effects of melatonin against oxidative injury in rat testis induced by wireless (2.45 GHz) devices. Andrologia 2012. http://dx.doi.org/10.1111/and.12044 [Epub ahead of print].
[179] Oktem F, Ozguner F, Mollaoglu H, Koyu A, Uz E. Oxidative damage in the kidney induced by 900-MHz-emitted mobile phone: protection by melatonin. Arch Med Res 2005;36(4):350–5.
[180] Oral B, Guney M, Ozguner F, et al. Endometrial apoptosis induced by a 900-MHz mobile phone: preventive effects of vitamins E and C. Adv Ther 2006;23 (6):957–73.
[181] Ozguner F, Bardak Y, Comlekci S. Protective effects of melatonin and caffeic acid phenethyl ester against retinal oxidative stress in long-term use of mobile phone: a comparative study. Mol Cell Biochem 2006;282(1–2):83–8.
[182] Ozguner F, Altinbas A, Ozaydin M, et al. Mobile phone-induced myocardial oxidative stress: protection by a novel antioxidant agent caffeic acid phenethyl ester. Toxicol Ind Health 2005;21(9):223–30.
[183] Ozguner F, Oktem F, Ayata A, Koyu A, Yilmaz HR. A novel antioxidant agent caffeic acid phenethyl ester prevents long-term mobile phone exposure-induced renal impairment in rat. Prognostic value of malondialdehyde, N-acetyl-beta-D-glucosaminidase and nitric oxide determination. Mol Cell Biochem 2005;277(1–2):73–80.
[184] Ozguner F, Oktem F, Armagan A, Yilmaz R, Koyu A, Demirel R, et al. Comparative analysis of the protective effects of melatonin and caffeic acid phenethyl ester (CAPE) on mobile phone-induced renal impairment in rat. Mol Cell Biochem 2005;276(1–2):31–7.
[185] Ozorak A, Nazıroglu M, Celik O, et al. Wi-Fi (2.45 GHz)- and mobile phone (900 and 1800 MHz)-induced risks on oxidative stress and elements in kidney and testis of rats during pregnancy and the development of offspring. Biol Trace Elem Res 2013;156(1–3):221–9. http://dx.doi.org/10.1007/s12011-013-9836-z [Epub 2013 Oct 8].
[186] Politanski P, Rajkowska E, Pawlaczyk-Łuszczyńska M, et al. Static magnetic field affects oxidative stress in mouse cochlea. Int J Occup Med Environ Health 2010;23(4):377–84. http://dx.doi.org/10.2478/v10001-010-0041-4.
[187] Poniedzialek B, Rzymski P, Nawrocka-Bogusz H, Jaroszyk F, Wiktorowicz K. The effect of electromagnetic field on reactive oxygen species production in human neutrophils in vitro. Electromagn Biol Med 2013;32(3):333–41. http://dx.doi.org/10.3109/ 15368378.2012.721845 [Epub 2012 Nov 8].
[188] Ragy MM. Effect of exposure and withdrawal of 900-MHz-electromagnetic waves on brain, kidney and liver oxidative stress and some biochemical parameters in male rats. Electromagn Biol Med 2014 [Epub ahead of print].
[189] Reale M, Kamal MA, Patruno A, et al. Neuronal cellular responses to extremely low frequency electromagnetic field exposure: implications regarding oxidative stress and neurodegeneration. PLoS One 2014;9(8): e104973. http://dx.doi.org/10.1371/journal.pone.0104973 eCollection.
[190] Sadeghipour R, Ahmadian S, Bolouri B, Pazhang Y, Shafiezadeh M. Effects of extremely low-frequency pulsed electromagnetic fields on morphological and biochemical properties of human breast carcinoma cells (T47D). Electromagn Biol Med 2012;31(4):425–35. http://dx.doi.org/10.3109/15368378.2012.683844 [Epub 2012 Jun 7].
[191] Safronova VG, Gapeev AB, Alovskaia AA, Gabdulkhakova AG, Chemeris NK, Fesenko EE. Millemetre waves inhibit the synergistic effect of calcium ionophore A23187 and phorbol ester in neutrophil respiratory burst. Biofizika 1997;42(6):1267–73 [in Russian].
[192] Sangun O, Dundar B, Darici H, Comlekci S, Doguc DK, Celik S. The effects of long-term exposure to a 2450 MHz electromagnetic field on growth and pubertal development in female Wistar rats. Electromagn Biol Med 2014 [Epub ahead of print].
[193] Seifirad S, Farzampour S, Nourbakhsh M, Amoli MM, Razzaghy-Azar M, Larijani B. Effects of extremely low frequency electromagnetic fields on paraoxonase serum activity and lipid peroxidation metabolites in rat. J Diabetes Metab Disord 2014;13(1):85. http://dx.doi.org/10.1186/s40200-014-0085-2 eCollection.
[194] Sefidbakht Y, Moosavi-Movahedi AA, Hosseinkhani S, et al. Effects of 940 MHz EMF on bioluminescence and oxidative response of stable luciferase producing HEK cells. Photochem Photobiol Sci 2014;13 (7):1082–92. http://dx.doi.org/10.1039/ c3 pp50451d [Epub 2014 Jun 2].
[195] Stopczyk D, Gnitecki W, Buczynski A, Kowalski W, Buczynska M, Kroc A. Effect of electromagnetic field produced by mobile phones on the activity of superoxide dismutase (SOD-1)–in vitro researches. Ann Acad Med Stetin 2005;51(Suppl. 1):125–8 [Polish].
[196] Stopczyk D, Gnitecki W, Buczynski A, Markuszewski L, Buczynski J. Effect of electromagnetic field produced by mobile phones on the activity of superoxide dismutase (SOD-1) and the level of malonyldialdehyde (MDA) — in vitro study. Med Pr 2002;53(4):311–4 [Polish].
[197] Tok L, Nazıroglu M, Dogan S, Kahya MC, Tok O. Effects of melatonin on Wi-Fi-induced oxidative stress in lens of rats. Indian J Ophthalmol 2014;62 (1):12–5. http://dx.doi.org/10.4103/0301-4738.126166.
[198] Turedi S, Hanci H, Topal Z, et al. The effects of prenatal exposure to a 900-MHz electromagnetic field on the 21-day-old male rat heart. Electromagn Biol Med 2014:1–8 [Epub ahead of print].
[199] Turker Y, Nazıroglu M, Gumral N, et al. Selenium and L-carnitine reduce oxidative stress in the heart of rat induced by 2.45-GHz radiation from wireless devices. Biol Trace Elem Res 2011;143(3):1640–50. http://dx.doi.org/10.1007/s12011-011-8994-0 [Epub 2011 Mar 1].
[200] Wartenberg M, Wirtz N, Grob A, et al. Direct current electrical fields induce apoptosis in oral mucosa cancer cells by NADPH oxidase-derived reactive oxygen species. Bioelectromagnetics 2008;29(1):47–54.
[201] Wartenberg M, Hescheler J, Sauer H. Electrical fields enhance growth of cancer spheroids by reactive oxygen species and intracellular Ca2+. Am J Physiol 1997;272(5):R1677–83.
[202] Wu W, Yao K, Wang KJ, et al. Blocking 1800 MHz mobile phone radiation-induced reactive oxygen species production and DNA damage in lens epithelial cells by noise magnetic fields. Zhejiang Da Xue Xue Bao Yi Xue Ban 2008;37(1):34–8 [Chinese].
[203] Yang LL, Zhou Y, Li HJ, et al. Effects of electromagnetic pulse exposure on the morphological change and excretion function of BV-2 cells and possible mechanism. Zhonghua Lao Dong Wei Sheng Zhi Ye Bing Za Zhi 2012;30 (3):163–7 [Chinese].
[204] Yao K, Wu W, Yu Y, et al. Effect of superposed electromagnetic noise on DNA damage of lens epithelial cells induced by microwave radiation. Invest Ophthalmol Vis Sci 2008;49(5):2009–15. http://dx.doi.org/10.1167/iovs.07-1333.
[205] Yao K, Wu W, Wang K, et al. Electromagnetic noise inhibits radiofrequency radiation-induced DNA damage and reactive oxygen species increase in human lens epithelial cells. Mol Vis 2008;14:964–9.
[206] Yokus B, Cakir DU, Akdag MZ, Sert C, Mete N. Oxidative DNA damage in rats exposed to extremely low frequency electro magnetic fields. Free Radic Res 2005;39(3):317–23.
[207] Yoshikawa T, Tanigawa M, Tanigawa T, Imai A, Hongo H, Kondo M. Enhancement of nitric oxide generation by low frequency electromagnetic field. Pathophysiology 2000;7(2):131–5.
[208] Yurekli AI, Ozkan M, Kalkan T, et al. GSM base station electromagnetic radiation and oxidative stress in rats. Electromagn Biol Med 2006;25 (3):177–88.

[209] Zhang QJ, Wu K. Biological oxidative stress induced by electromagnetic irradiation. Space Med Med Eng (Beijing) 2004;17(2):152–6 [Chinese].
[210] Zmyślony M, Politanski P, Rajkowska E, Szymczak W, Jajte J. Acute exposure to 930 MHz CW electromagnetic radiation in vitro affects reactive oxygen species level in rat lymphocytes treated by iron ions. Bioelectromagnetics 2004;25(5):324–8.
[211] Yakymenko I, Tsybulin O, Sidorik E, Henshel D, Kyrylenko O, Kyrylenko S. Oxidative mechanisms of biological activity of low-intensity radiofrequency radiation. Electromagn Biol Med 2016;35(2):186–202. http://dx.doi.org/10.3109/15368378.2015.1043557 [Epub 2015 Jul 7].
[212] Smit N, Musson R, Romijn F, van Rossum H, van Pelt J. Effects of ultraviolet A-1 radiation on calcineurin activity and cytokine production in (skin) cell cultures. Photochem Photobiol 2010;86(2):360–6. http://dx.doi.org/10.1111/j.1751-1097.2009.00650.x [Epub 2009 Nov 18].
[213] Neuro-Immune Dysfunction Syndrome (NIDS) [Internet]. [place unknown] Neuro Immune Dysfunction Syndromes (NIDS) Research and Treatment Institute; [date unknown] [cited 2015 Feb 19]. Available from: http://www.nids.net.
[214] Nicolson GL, Haier J. Role of chronic bacterial and viral infections in neurodegenerative, neurobehavioral, psychiatric, autoimmune and fatiguing illnesses: part 1. BJMP 2009;2(4):20–8.
[215] Nicolson GL, Haier J. Role of chronic bacterial and viral infections in neurodegenerative, neurobehavioral, psychiatric, autoimmune and fatiguing illnesses: part 2. BJMP 2010;3(1):301.
[216] Komaroff AL. Chronic fatigue syndromes: relationship to chronic viral infections. J Virol Methods 1988;21(1–4):3–10.
[217] Jones JF. Epstein-Barr virus and the chronic fatigue syndrome: a short review. Microbiol Sci 1988;5(12):366–9.
[218] Kawai K, Kawai A. Studies on the relationship between chronic fatigue syndrome and Epstein-Barr virus in Japan. Inter Med 1992;31(3):313–8.
[219] Artsimovich NG, Chugunov VS, Kornev AV, Ivanova TM, Chugunov AV, Oprishchenko MA. The chronic fatigue syndrome. Zh Nevrol Psikhiatr Im S S Korsakova 1994;94(5):47–50 [in Russian].
[220] Glover DM. Chronic fatigue syndrome. Adolesc Med 1995;6(1):101–14.
[221] Wallace 2nd HL, Natelson B, Gause W, Hay J. Human herpes viruses in chronic fatigue syndrome. Clin Diagn Lab Immunol 1999;6(2):216–23.
[222] Ewig S, Dengler HJ. Chronic fatigue syndrome. Klin Wochenschr 1990;68(16):789–96 [in German].
[223] Hilgers A, Frank J. Chronic fatigue syndrome: immune dysfunction, role of pathogens and toxic agents and neurological and cardial changes. Wien Med Wochenschr 1994;144(16):399–406 [in German].
[224] Cater 2nd RE. Chronic intestinal candidiasis as a possible etiological factor in the chronic fatigue syndrome. Med Hypotheses 1995;44(6):507–15.
[225] Scheurlen M. Pathogenicity of fungi in the intestines–current status of the discussion. Fortschr Med 1996;114(26):319–21 [German].
[226] Brunet JL, Fatoohi F, Liaudet AP, Cozon GJ. Role of pathological delayed-type hypersensitivity in chronic fatigue syndrome: importance of the evaluation of lymphocyte activation by flow cytometry and the measurement of urinary neopterin. Allerg Immunol (Paris) 2002;34(2):38–44 [French].
[227] Auger PL, Gourdeau P, Miller JD. Clinical experience with patients suffering from a chronic fatigue-like syndrome and repeated upper respiratory infections in relation to airborne molds. Am J Ind Med 1994;25(1):41–2.
[228] Sorenson WG. Fungal spores: hazardous to health? Environ Health Perspect 1999;107(Suppl 3):469–72.
[229] Anyanwu E, Campbell AW, Jones J, Ehiri JE, Akpan AI. The neurological significance of abnormal natural killer cell activity in chronic toxigenic mold exposures. Sci World J 2003;3:1128–37.
[230] Gharibzadeh S, Hoseini SS. Is there any relation between moldy building exposure and chronic fatigue syndrome? Med Hypotheses 2006;66(6):1243–4 [Epub 2006 Mar 9].
[231] Empting LD. Neurologic and neuropsychiatric syndrome features of mold and mycotoxin exposure. Toxicol Ind Health 2009;5(9–10):577–81.
[232] Brewer JH, Thrasher JD, Straus DC, Madison RA, Hooper D. Detection of mycotoxins in patients with chronic fatigue syndrome. Toxins (Basel) 2013;5(4):605–17. http://dx.doi.org/10.3390/toxins5040605.
[233] Brewer JH, Thrasher JD, Hooper D. Chronic illness associated with mold and mycotoxins: is naso-sinus fungal biofilm the culprit? Toxins (Basel) 2013;6(1):66–80. http://dx.doi.org/10.3390/toxins6010066.
[234] Choppa PC, Vojdani A, Tagle C, Andrin R, Magtoto L. Multiplex PCR for the detection of Mycoplasma fermentans, M. hominis and M. penetrans in cell cultures and blood samples of patients with chronic fatigue syndrome. Mol Cell Probes 1998;12(5):301–8.
[235] Vojdani A, Choppa PC, Tagle C, Andrin R, Samimi B, Lapp CW. Detection of Mycoplasma genus and Mycoplasma fermentans by PCR in patients with chronic fatigue syndrome. FEMS Immunol Med Microbiol 1998;22(4):355–65.
[236] Nasralla M, Haier J, Nicolson GL. Multiple mycoplasmal infections detected in blood of patients with chronic fatigue syndrome and/or fibromyalgia syndrome. Eur J Clin Microbiol Infect Dis 1999;18(12):859–65.
[237] Nijs J, Nicolson GL, De Becker P, Coomans D, De Meirleir K. High prevalence of Mycoplasma infections among European chronic fatigue syndrome patients. Examination of four Mycoplasma species in blood of chronic fatigue syndrome patients. FEMS Immunol Med Microbiol 2002;34(3):209–14.
[238] Endresen GK. Mycoplasma blood infection in chronic fatigue and fibromyalgia syndromes. Rheumatol Int 2003;23(5):211–5 [Epub 2003 Jul 16].
[239] Gentile I, Zappulo E, Bonavolta R, et al. Prevalence and titre of antibodies to cytomegalovirus and epstein-barr virus in patients with autism spectrum disorder. Vivo 2014;28(4):621–6.
[240] Mora M, Quintero L, Cardenas R, Suarez-Roca H, Zavala M, Montiel N. Association between HSV-2 infection and serum anti-rat brain antibodies in patients with autism. Invest Clin 2009;50(3):315–26. Spanish.
[241] Stubbs EG, Crawford ML. Depressed lymphocyte responsiveness in autistic children. J Autism Child Schizophr 1977;7(1):49–55.
[242] Stubbs EG. Autistic symptoms in a child with congenital cytomegalovirus infection. J Autism Child Schizophr 1978;8(1):37–43.
[243] Stubbs EG, Ash E, Williams CP. Autism and congenital cytomegalovirus. J Autism Dev Disord 1984;14(2):183–9.
[244] Yamashita Y, Fujimoto C, Nakajima E, Isagai T, Matsuishi T. Possible association between congenital cytomegalovirus infection and autistic disorder. J Autism Dev Disord 2003;33(4):455–9.
[245] Nicolson GL, Gan R, Nicolson NL, Haier J. Evidence for Mycoplasma ssp., Chlamydia pneunomiae, and human herpes virus-6 coinfections in the blood of patients with autistic spectrum disorders. J Neurosci Res 2007;85(5):1143–8.
[246] Kidd PM. Autism, an extreme challenge to integrative medicine. Part 2: medical management. Altern Med Rev 2002;7(6):472–99.
[247] Ekiel A, Aptekorz M, Kazek B, Wiechuła B, Wilk I, Martirosian G. Intestinal microflora of autistic children. Med Dosw Mikrobiol 2010;62(3):237–43 [Polish].
[248] Burrus CJ. A biochemical rationale for the interaction between gastrointestinal yeast and autism. Med Hypotheses 2012;79(6):784–5. http://dx.doi.org/10.1016/j.mehy.2012.08.029 [Epub 2012 Sep 26].
[249] Kilburn KH, Thrasher JD, Immers NB. Do terbutaline- and mold-associated impairments of the brain and lung relate to autism? Toxicol Ind Health 2009;25(9–10):703–10. http://dx.doi.org/10.1177/0748233709348391 [Epub 2009 Sep 30].
[250] Bransfield RC, Wulfman JS, Harvey WT, Usman AI. The association between tick-borne infections, Lyme borreliosis and autism spectrum disorders. Med Hypotheses 2008;70(5):967–74 [Epub 2007 Nov 5].
[251] Bekdas M, Tufan AE, Hakyemez IN, Tas T, Altunhan H, Demircioglu F. Subclinical immune reactions to viral infections may correlate with child and adolescent diagnosis of attention-deficit/hyperactivity disorder: a preliminary study from Turkey. Afr Health Sci 2014;14(2):439–45. http://dx.doi.org/10.4314/ahs.v14i2.21.
[252] Kidd PM. Attention deficit/hyperactivity disorder (ADHD) in children: rationale for its integrative management. Altern Med Rev 2000;5(5):402–28.
[253] Rucklidge JJ. Could yeast infections impair recovery from mental illness? A case study using micronutrients and olive leaf extract for the treatment of ADHD and depression. Adv Mind Body Med. 2013;27(3):14–8.
[254] Gaskin F, Kingsley BS, Fu SM. Autoantibodies to neurofibrillary tangles and brain tissue in Alzheimer's disease. Establishment of Epstein-Barr virus-transformed antibody-producing cell lines. J Exp Med 1987;165(1):245–50.
[255] Ounanian A, Guilbert B, Seigneurin JM. Characteristics of Epstein-Barr virus transformed B cell lines from patients with Alzheimer's disease and age-matched controls. Mech Ageing Dev 1992;63(1):105–16.
[256] Xu S, Gaskin F. Increased incidence of anti-beta-amyloid autoantibodies secreted by Epstein-Barr virus transformed B cell lines from patients with Alzheimer's disease. Mech Ageing Dev 1997;94(1–3):213–22.
[257] Carbone I, Lazzarotto T, Ianni M, et al. Herpes virus in Alzheimer's disease: relation to progression of the disease. Neurobiol Aging 2014;35(1):122–9. http://dx.doi.org/10.1016/j.neurobiolaging.2013.06.024 [Epub 2013 Aug 3].
[258] Lin WR, Wozniak MA, Wilcock GK, Itzhaki RF. Cytomegalovirus is present in a very high proportion of brains from vascular dementia patients. Neurobiol Dis 2002;9(1):82–7.
[259] Lin WR, Wozniak MA, Cooper RJ, Wilcock GK, Itzhaki RF. Herpes viruses in brain and Alzheimer's disease. J Pathol 2002;197(3):395–402.
[260] Strandberg TE, Pitkala KH, Linnavuori K, Tilvis RS. Cognitive impairment and infectious burden in the elderly. Arch Gerontol Geriatr Suppl 2004;9:419–23.
[261] Westman G, Berglund D, Widen J, et al. Increased inflammatory response in cytomegalovirus seropositive patients with Alzheimer's disease. PLoS One 2014;9(5):e96779. http://dx.doi.org/10.1371/journal.pone.0096779 [eCollection].
[262] Alonso R, Pisa D, Marina AI, Morato E, Rabano A, Carrasco L. Fungal infection in patients with Alzheimer's disease. J Alzheimers Dis 2014;41(1):301–11. http://dx.doi.org/10.3233/JAD-132681.
[263] Alonso R, Pisa D, Rabano A, Carrasco L. Alzheimer's disease and disseminated mycoses. Eur J Clin Microbiol Infect Dis 2014;33(7):1125–32. http://dx.doi.org/10.1007/s10096-013-2045-z [Epub 2014 Jan 23].
[264] Pisa D, Alonso R, Juarranz A, Rabano A, Carrasco L. Direct visualization of fungal infection in brains from patients with Alzheimer's disease. J Alzheimers Dis 2015;43(2):613–24. http://dx.doi.org/10.3233/JAD-141386.
[265] Santini R, Seigne M, Bonhomme-Faivre L. Danger of cellular telephones and their relay stations. Pathol Biol 2000;48(6):525–8 [Paris].
[266] Santini R, Santini P, Danze JM, Le Ruz P, Seigne M. Investigation on the health of people living near mobile telephone relay stations: Incidence according to distance and sex. Pathol Biol (Paris) 2002;50(6):369–73 [French].
[267] Santini R, Santini P, Danze JM, Le Ruz P, Seigne M. Symptoms experienced by people in vicinity of base stations: II/ Incidences of age, duration of exposure, location of subjects in relation to the antennas and other electromagnetic factors. Pathol Biol (Paris). 2003;51(7):412–5. French.

[268] Roosli M, Moser M, Baldinini Y, Meier M, Braun-Fahrlander C. Symptoms of ill health ascribed to electromagnetic field exposure–a questionnaire survey. Int J Hyg Environ Health 2004;207(2):141–50.
[269] Bortkiewicz A, Zmyslony M, Szyjkowska A, Gadzicka E. Subjective symptoms reported by people living in the vicinity of cellular phone base stations: review. Med Pr 2004;55(4):345–51 [Polish].
[270] Hutter HP, Moshammer H, Wallner P, Kundi M. Subjective symptoms, sleeping problems, and cognitive performance in subjects living near mobile phone base stations. Occup Environ Med 2006;63(5):307–13.
[271] Abdel-Rassoul G, El-Fateh OA, Salem MA, et al. Neurobehavioral effects among inhabitants around mobile phone base stations. Neurotoxicology 2007;28(2):434–40 [Epub 2006 Aug 1].
[272] Huss A, Roosli M. Consultations in primary care for symptoms attributed to electromagnetic fields–a survey among general practitioners. BMC Public Health 2006;30(6):267.
[273] Khurana VG, Hardell L, Everaert J, Bortkiewicz A, Carlberg M, Ahonen M. Epidemiological evidence for a health risk from mobile phone base stations. Int J Occup Environ Health 2010;16(3):263–7.
[274] Roosli M, Frei P, Mohler E, Hug K. Systematic review on the health effects of exposure to radiofrequency electromagnetic fields from mobile phone base stations. Bull World Health Organ 2010;88(12):887–896F. http://dx.doi.org/10.2471/BLT.09.071852 [Epub 2010 Oct 5].
[275] Bortkiewicz A, Gadzicka E, Szyjkowska A, et al. Subjective complaints of people living near mobile phone base stations in Poland. Int J Occup Med Environ Health 2012;25(1):31–40. http://dx.doi.org/10.2478/s13382-012-0007-9 [Epub 2012 Jan 5].
[276] Center for Disease Control (CDC) [Internet]. Atlanta (GA): Centers for Disease Control and Prevention; [date unknown] [cited 2015 Feb 19]. Chronic Fatigue Syndrome: Symptoms. Available from: http://www.cdc.gov/cfs/symptoms/.
[277] Boscolo P, Bergamaschi A, Di Sciascio MB, et al. Effects of low frequency electromagnetic fields on expression of lymphocyte subsets and production of cytokines of men and women employed in a museum. Sci Total Environ 2001;270(1–3):13–20.
[278] Ichinose TY, Burch JB, Noonan CW, et al. Immune markers and ornithine decarboxylase activity among electric utility workers. J Occup Environ Med 2004;46(2):104–12.
[279] Bonhomme-Faivre L, Marion S, Forestier F, Santini R, Auclair H. Effects of electromagnetic fields on the immune systems of occupationally exposed humans and mice. Arch Environ Health 2003;58(11):712–7.
[280] Di Giampaolo L, Di Donato A, Antonucci A, et al. Follow up study on the immune response to low frequency electromagnetic fields in men and women working in a museum. Int J Immunopathol Pharmacol 2006;19 (Suppl. 4):37–42.
[281] Gobba F, Bargellini A, Bravo G, Scaringi M, Cauteruccio L, Borella P. Natural killer cell activity decreases in workers occupationally exposed to extremely low frequency magnetic fields exceeding 1 microT. Int J Immunopathol Pharmacol 2009;22(4):1059–66.
[282] Johansson O. Disturbance of the immune system by electromagnetic fields — a potentially underlying cause for cellular damage and tissue repair reduction which could lead to disease and impairment. Pathophysiology 2009;16:157–77.
[283] Hallberg O, Johansson O. Melanoma incidence and frequency modulation (FM) broadcasting. Arch Environ Health 2002;57(1):32–40.
[284] Hallberg O, Johansson O. Malignant melanoma of the skin - not a sunshine story! Med Sci Monit 2004;10(7):CR336–40 [Epub 2004 Jun 29].
[285] Hallberg O, Johansson O. Increasing rates of head melanoma in Nordic countries. Pathophysiology 2011;18(4):313–5. http://dx.doi.org/10.1016/j.pathophys.2011.05.002 [Epub 2011 Jun 16].
[286] Hallberg O, Johansson O. Increasing melanoma-too many skin cell damages or too few repairs? Cancers (Basel) 2013;5(1):184–204. http://dx.doi.org/10.3390/cancers5010184.