Reactive Oxygen Species (ROS), Magnetic Fields, Cancer

https://pubmed.ncbi.nlm.nih.gov/35919980/
Magnetic field effects in biology from the perspective of the radical pair mechanism 2022
Hundreds of studies have found that weak magnetic fields can significantly influence various biological systems. However, the underlying mechanisms behind these phenomena remain elusive. Remarkably, the magnetic energies implicated in these effects are much smaller than thermal energies. Here, we review these observations, and we suggest an explanation based on the radical pair mechanism, which involves the quantum dynamics of the electron and nuclear spins of transient radical molecules.
ROS are the collection of derivatives of molecular oxygen that occur in biology, which can be categorized into two types, free radicals and non-radical species. The non-radical species are hydrogen peroxide (H 2O 2), organic hydroperoxides (ROOH), singlet molecular oxygen (1 O 2), electronically excited carbonyl, ozone (O3), hypochlorous acid (HOCl, and hypobromous acid HOBr). Free radical species are super-oxide anion radical (O 2•−), hydroxyl radical (•OH), peroxyl radical (ROO•) and alkoxyl radical (RO•) [130]. Any imbalance of ROS can lead to adverse effects. H2 O 2 and O 2 •− are the main redox signalling agents. The cellular concentration of H2 O 2 is about 10−8 M, which is almost a thousand times more than that of O2 •−.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5666856/
Magnetic Fields and Reactive Oxygen Species 2017
In this review, we summarize reported studies about the influences of magnetic fields (MFs) on ROS levels. Although in most cases, MFs increased ROS levels in human, mouse, rat cells, and tissues, there are also studies showing that ROS levels were decreased or not affected by MFs. Multiple factors could cause these discrepancies, including but not limited to MF type/intensity/frequency, exposure time and assay time-point, as well as different biological samples examined.

https://pubmed.ncbi.nlm.nih.gov/22253132/
Effect of stationary magnetic field strengths of 150 and 200 mT on reactive oxygen species production in soybean 2012
In this study, soybean seeds treated with static magnetic fields of 150 and 200 mT for 1 h were evaluated for reactive oxygen species (ROS) and activity of antioxidant enzymes.
Magnetic field treatment resulted in enhanced production of ROS mediated by cell wall peroxidase while ascorbic acid content, superoxide dismutase and ascorbate peroxidase activity decreased in the hypocotyl of germinating seeds.

https://pubmed.ncbi.nlm.nih.gov/20519170/
Effect of ELF-EMF on number of apoptotic cells; correlation with reactive oxygen species and HSP 2010
It is by now accepted that extremely low frequency electromagnetic fields ELF-EMF (0-300 Hz) affect biological systems although the mechanism has not been elucidated yet. In this study the effect of ELFEMF on the number of apoptotic cells of K562 human leukemia cell line induced or not with oxidative stress and the correlation with heat-shock protein 70 (hsp70) levels was investigated. One sample was treated with H 2 O 2 while the other was left untreated. ELF-EMF (1 mT, 50 Hz) was applied for 3 hours. ELF-EMF alone caused a decrease in the number of apoptotic cells and a slight increase in viability. However, it increased the number of apoptotic cells. In cells treated with H 2 O 2 . hsp70 and reactive oxygen species (ROS) levels were increased by ELF-EMF.

https://pubmed.ncbi.nlm.nih.gov/26850078/
Exposure to a 50-Hz magnetic field induced mitochondrial permeability transition through the ROS/GSK-3β signaling pathway 2016
Exposure to the MF at 0.4 mT for 60 min transiently induced mitochondrial permeability transition (MPT) and Cyt-c release, although there was no significant effect on mitochondrial membrane potential (ΔΨm).
In addition, cells exposed to the MF showed increased intracellular reactive oxidative species (ROS) levels and glycogen synthase kinase-3β (GSK-3β) dephosphorylation at 9 serine residue (Ser(9)).

https://pubmed.ncbi.nlm.nih.gov/29109418/
Extremely low frequency pulsed electromagnetic fields cause antioxidative defense mechanisms in human osteoblasts via induction of •O2- and H2O2 2017
Recently, we identified a specific extremely low-frequency pulsed electromagnetic field (ELF-PEMF) that supports human osteoblast (hOBs) function in an ERK1/2-dependent manner, suggesting reactive oxygen species (ROS) being key regulators in this process. Thus, this study aimed at investigating how ELF-PEMF exposure can modulate hOBs function via ROS. Our results show that single exposure to ELF-PEMF induced ROS production in hOBs, without reducing intracellular glutathione. Repetitive exposure (>3) to ELF-PEMF however reduced ROS-levels, suggesting alterations in the cells antioxidative stress response. The main ROS induced by ELF-PEMF were •O2- and H2O2, therefore expression/activity of antioxidative enzymes related to these ROS were further investigated. ELF-PEMF exposure induced expression of GPX3, SOD2, CAT and GSR on mRNA, protein and enzyme activity level. Scavenging •O2- and H2O2 diminished the ELF-PEMF effect on hOBs function (AP activity and mineralization). Challenging the hOBs with low amounts of H2O2 on the other hand improved hOBs function. In summary, our data show that ELF-PEMF treatment favors differentiation of hOBs by producing non-toxic amounts of ROS, which induces antioxidative defense mechanisms in these cells. Thus, ELF-PEMF treatment might represent an interesting adjunct to conventional therapy supporting bone formation under oxidative stress conditions, e.g. during fracture healing

https://pubmed.ncbi.nlm.nih.gov/26940444/
Pulsed electromagnetic field (PEMF) prevents pro-oxidant effects of H2O2 in SK-N-BE(2) human neuroblastoma cells 2016
Purpose The redox milieu, together with reactive oxygen species (ROS) accumulation, may play a role in mediating some biological effects of extremely-low-frequency electromagnetic fields (ELF-EMF). Some of us have recently reported that a pulsed EMF (PEMF) improves the antioxidant response of a drug-sensitive human neuroblastoma SH-SY5Y cell line to pro-oxidants. Since drug resistance may affect cell sensitivity to redox-based treatments, we wanted to verify whether drug-resistant human neuroblastoma SK-N-BE(2) cells respond to a PEMF in a similar fashion. Materials and methods SK-N-BE(2) cells were exposed to repeated **2 mT, 75 Hz** PEMF (15 min each, repeated 3 times over 5 days), and ROS production, Mn-dependent superoxide dismutase (MnSOD)-based antioxidant protection and viability were assessed after 10 min or 30 min 1 mM hydrogen peroxide. Sham controls were kept at the same time in identical cell culture incubators. Results The PEMF increased the MnSOD-based antioxidant protection and reduced the ROS production in response to a pro-oxidant challenge. Conclusions Our work might lay foundation for the development of non-invasive PEMF-based approaches aimed at elevating endogenous antioxidant properties in cellular or tissue models

https://pubmed.ncbi.nlm.nih.gov/25708841/
Pre-exposure of neuroblastoma cell line to pulsed electromagnetic field prevents H2 O2 -induced ROS production by increasing MnSOD activity 2015

Electromagnetic fields (EMFs) have been linked to increased risk of cancers and neurodegenerative diseases; however, EMFs can also elicit positive effects on biological systems, and redox status seems crucially involved in EMF biological effects. This study aimed to assess whether a short and repeated pulsed EMF (PEMF) could trigger adaptive responses against an oxidative insult in a neuronal cellular model. We found that a 40 min overall (four times a week, 10 min each) pre-exposure to PEMF did not affect major physiological parameters and led to a significant increase of Mn-dependent superoxide dismutase activity in the human neuroblastoma SH-SY5Y cell line. In addition, we found PEMF-pre-exposed cells exhibited **decreased reactive oxygen species** production following a 30 min H2 O2 challenge, with respect to non pre-exposed cells. Our findings might provide new insights on the role played by short and repeated PEMF stimulations in the enhancement of cellular defenses against oxidative insults. Although studies in normal neuronal cells would be useful to further confirm our hypothesis, we suggest that specific PEMF treatments may have potential biological repercussions in diseases where oxidative stress is implicated

https://pubmed.ncbi.nlm.nih.gov/37834077/

NET Formation Was Reduced via Exposure to Extremely Low-Frequency Pulsed Electromagnetic Fields 2023

Fracture-healing is a highly complex and timely orchestrated process. Non-healing fractures are still a major clinical problem and treatment remains difficult. A 16 Hz extremely low-frequency pulsed electromagnetic field (ELF-PEMF) was identified as non-invasive adjunct therapy supporting bone-healing by inducing reactive oxygen species (ROS) and Ca2+-influx. However, ROS and Ca2+-influx may stimulate neutrophils, the first cells arriving at the wounded site, to excessively form neutrophil extracellular traps (NETs), which negatively affects the healing process. Thus, this study aimed to evaluate the effect of this 16 Hz ELF-PEMF on NET formation. Neutrophils were isolated from healthy volunteers and exposed to different NET-stimuli and the 16 Hz ELF-PEMF. NETs were quantified using Sytox Green Assay and immunofluorescence, Ca2+-influx and ROS with fluorescence probes. In contrast to mesenchymal cells, ELF-PEMF exposure did not induce ROS and Ca2+-influx in neutrophils. ELF-PEMF exposure did not result in basal or enhanced PMA-induced NET formation but did reduce the amount of DNA released. Similarly, NET formation induced by LPS and H2O2 was reduced through exposure to ELF-PEMF. As ELF-PEMF exposure did not induce NET release or negatively affect neutrophils, the ELF-PEMF exposure can be started immediately after fracture treatment.

https://pubmed.ncbi.nlm.nih.gov/27959944/

BEMER Electromagnetic Field Therapy Reduces Cancer Cell Radioresistance by Enhanced ROS Formation and Induced DNA Damage 2016

One investigated approach is the application of low-dose electromagnetic fields (EMF) to modulate cellular processes. A particular system is the BEMER therapy as a Physical Vascular Therapy for which a normalization of the microcirculation has been demonstrated by a low-frequency, pulsed EMF pattern. Open remains whether this EMF pattern impacts on cancer cell survival upon treatment with radiotherapy, chemotherapy and the molecular-targeted agent Cetuximab inhibiting the epidermal growth factor receptor. Using more physiological, three-dimensional, matrix-based cell culture models and cancer cell lines originating from lung, head and neck, colorectal and pancreas, we show significant changes in distinct intermediates of the glycolysis and tricarboxylic acid cycle pathways and enhanced cancer cell radiosensitization associated with increased DNA double strand break numbers and higher levels of reactive oxygen species upon BEMER treatment relative to controls. Intriguingly, exposure of cells to the BEMER EMF pattern failed to result in sensitization to chemotherapy and Cetuximab. Further studies are necessary to better understand the mechanisms underlying the cellular alterations induced by the BEMER EMF pattern and to clarify the application areas for human disease.

https://pubmed.ncbi.nlm.nih.gov/15777847/

50-Hz extremely low frequency electromagnetic fields enhance cell proliferation and DNA damage: possible involvement of a redox mechanism 2005

HL-60 leukemia cells, Rat-1 fibroblasts and WI-38 diploid fibroblasts were exposed for 24-72 h to 0.5-1.0-mT 50-Hz extremely low frequency electromagnetic field (ELF-EMF). This treatment induced a dose-dependent increase in the proliferation rate of all cell types, namely about 30% increase of cell proliferation after 72-h exposure to 1.0 mT. This was accompanied by increased percentage of cells in the S-phase after 12- and 48-h exposure. The ability of ELF-EMF to induce DNA damage was also investigated by measuring DNA strand breaks. A dose-dependent increase in DNA damage was observed in all cell lines, with two peaks occurring at 24 and 72 h. A similar pattern of DNA damage was observed by measuring formation of 8-OHdG adducts. The effects of ELF-EMF on cell proliferation and DNA damage were prevented by pretreatment of cells with an antioxidant like alpha-tocopherol, suggesting that redox reactions were involved. Accordingly, Rat-1 fibroblasts that had been exposed to ELF-EMF for 3 or 24 h exhibited a significant increase in dichlorofluorescein-detectable reactive oxygen species, which was blunted by alpha-tocopherol pretreatment. Cells exposed to ELF-EMF and examined as early as 6 h after treatment initiation also exhibited modifications of NF kappa B-related proteins (p65-p50 and I kappa B alpha), which were suggestive of increased formation of p65-p50 or p65-p65 active forms, a process usually attributed to redox reactions. These results suggest that ELF-EMF influence proliferation and DNA damage in both normal and tumor cells through the action of free radical species. This information may be of value for appraising the pathophysiologic consequences of an exposure to ELF-EMF

https://pubmed.ncbi.nlm.nih.gov/15788236/

Oxidative DNA damage in rats exposed to extremely low frequency electro magnetic fields 2005

Extremely low frequency (ELF) electromagnetic field (EMF) is thought to prolong the life of free radicals and can act as a promoter or co-promoter of cancer. 8-hydroxy-2'-deoxyguanosine (8OHdG) is one of the predominant forms of radical-induced lesions to DNA and is a potential tool to asses the cancer risk. We examined the effects of extremely low frequency electro magnetic field (ELF-EMF) (50 Hz, 0.97 mT) on 8OHdG levels in DNA and thiobarbituric acid reactive substances (TBARS) in plasma. To examine the possible time-dependent changes resulting from magnetic field, 8OHdG and TBARS were quantitated at 50 and 100 days. Our results showed that the exposure to ELF-EMF induced oxidative DNA damage and lipid peroxidation (LPO). The 8OHdG levels of exposed group (4.39+/-0.88 and 5.29+/-1.16 8OHdG/dG.10(5), respectively) were significantly higher than sham group at 50 and 100 days (3.02+/-0.63 and 3.46+/-0.38 8OHdG/dG.10(5)) ($p<0.001$, $p<0.001$). The higher TBARS levels were also detected in the exposure group both on 50 and 100 days ($p<0.001$, $p<0.001$). In addition, the extent of DNA damage and LPO would depend on the exposure time ($p<0.05$ and $p<0.05$). Our data may have important implications for the long-term exposure to ELF-EMF which may cause oxidative DNA damage.

https://pubmed.ncbi.nlm.nih.gov/35746959/

Bidirectional Effect of Repeated Exposure to Extremely Low-Frequency Electromagnetic Field (50 Hz) of 1 and 7 mT on Oxidative/Antioxidative Status in Rat's Brain: The Prediction for the Vulnerability to Diseases 2022

Studies reported evidence for opposite effects of extremely low-frequency electromagnetic field (EMF): harmful, including the oxidative stress induction, and beneficial, such as the activation of antioxidant defense. People's exposure to EMF is often repeated or prolonged, and it is important to consider the cumulative effect of such kind of exposure on the organism. If changes evoked by repeated exposure to EMF are permanent, responsiveness to other stress factors can be modified. The aims of our study were (1) to evaluate changes in the levels of oxidative stress and antioxidant defense markers in the prefrontal cortex of adult rats after repeated exposure to 1 and 7 mT EMF and (2) to assess whether repeated EMF exposure can modify oxidative/antioxidative status in response to other stress factors. Rats were exposed to EMF 1 h/day for 7 days, one, twice, or three times. After each exposure, 8-isoprostanes, protein carbonyl groups, and the total antioxidant capacity were assessed. Part of the animals, after EMF treatment, was exposed to another stress factor-open field. Results showed that repeated exposure changed the oxidative/antioxidative status depending on the intensity of the EMF and the number of exposures. 1 mT EMF created weak changes in the

oxidative status in the brain; however, 7 mT EMF moved the balance to a clearly higher level. The changes in the oxidative status after 1 mT EMF were enough to reduce, and after 7 mT EMF to intensify oxidative processes in response to the next stress. We concluded that the organism might adapt to "weak" EMF, while "strong" EMF exceeds the adaptive capacity of the organism and sensitizes it to subsequent stress, and thus may modulate vulnerability to diseases. Our results also provide new insights into the possible therapeutic properties of the magnetic field, as 1 mT EMF appears to have a potentially protective impact on the brain

https://pubmed.ncbi.nlm.nih.gov/20005945/

Modulation of redox status and calcium handling by extremely low frequency electromagnetic fields in C2C12 muscle cells: A real-time, single-cell approach 2009

The biological effects of electric and magnetic fields, which are ubiquitous in modern society, remain poorly understood. Here, we applied a single-cell approach to study the effects of short-term exposure to extremely low frequency electromagnetic fields (ELF-EMFs) on muscle cell differentiation and function using C2C12 cells as an in vitro model of the skeletal muscle phenotype. Our focus was on markers of oxidative stress and calcium (Ca(2+)) handling, two interrelated cellular processes previously shown to be affected by such radiation in other cell models. Collectively, our data reveal that ELF-EMFs (1) **induced reactive oxygen species** production in myoblasts and myotubes with a concomitant decrease in mitochondrial membrane potential; (2) activated the cellular detoxification system, increasing catalase and glutathione peroxidase activities; and (3) altered intracellular Ca(2+)homeostasis, increasing the spontaneous activity of myotubes and enhancing cellular reactivity to a depolarizing agent (KCl) or an agonist (caffeine) of intracellular store Ca(2+)channels. In conclusion, our data support a possible link between exposure to ELF-EMFs and modification of the cellular redox state, which could, in turn, increase the level of intracellular Ca(2+)and thus modulate the metabolic activity of C2C12 cells.

https://pubmed.ncbi.nlm.nih.gov/33857627/

Necroptosis triggered by ROS accumulation and Ca2+ overload, partly explains the inflammatory responses and anti-cancer effects associated with 1Hz, 100 mT ELF-MF in vivo 2021

Whereas the anti-neoplastic activity of extremely low frequency magnetic fields (ELF-EMF) is well-documented in literature, little is known about its underlying anti-cancer mechanisms and induced types of cell death. Here, for the first time, we reported induction of necroptosis, a specific type of programed necrotic cell death, in MC4-L2 breast cancer cell lines following a 2 h/day exposure to a 100 Hz, 1 mT ELF-EMF for five days. For in vivo assessment, inbred BALB/c mice bearing established MC-4L2 tumors were exposed to 100 mT, 1 Hz ELF-EMF 2 h daily for a period of 28-day, following which tumors were dissected and fixed for evaluation of tumor biomarkers expression and types of cell death induced using TUNEL assay, Immunohistochemistry and H&E staining. Peripheral blood samples were also collected for assessing pro-inflammatory cytokine profile following exposure. An exaggerated proinflammatory response evident form enhancement of IFN-γ (4.8 ± 0.24 folds) and TNF-α (3.1 ± 0.19 folds) and number of tumors infiltrating lymphocytes (TILs), specially CD8+ Th cells (~20 folds), proposed occurrence of necroptosis in vivo. Meanwhile, exposure could effectively suppress tumor growth and expression of Ki-67, CD31, VEGFR2 and MMP-9. In vitro studies on ELF-EMF exposed MC-4L2 cells demonstrated a meaningful increase in phosphorylation of RIPK1/RIPK3/MLKL proteins and cleavage of caspase-9/caspase-3, confirming occurrence of both necroptosis and apoptosis. Complementary in vitro studies by treating ELF-EMF exposed MC-4L2 cells with verapamil (a calcium channel inhibitor), N-acetyl cysteine (a ROS scavenger) or calcium chloride confirmed the role of elevated intracellular calcium and ROS levels in ELF-EMF induced necroptosis.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9939155/

Is extremely low frequency pulsed electromagnetic fields applicable to gliomas? A literature review of the underlying mechanisms and application of extremely low frequency pulsed electromagnetic fields 2023

REACTIVE OXYGEN SPECIES

Reactive oxygen species (ROS), including oxygen anions; superoxide; hydroxyl radicals; and peroxides such as hydrogen peroxide (H2O2), have been regarded to be crucial in cancers, including gliomas. 70 ROS are thought to contribute to the occurrence and development of cancer by inflicting DNA damage. 71 Given that cancer cells tend to be highly sensitive to elevated ROS, 72 the accumulation of ROS to a certain extent can be cytotoxic to cancer cells without affecting normal cells, thus enabling the use of ROS in selective anti-cancer therapy. 73 , 74

Akbarnejad 63 carried out an experiment to explore the effect of ELF-PEMF (100 Hz, 10 mT) exposure with 100 μM TMZ on U87 and T98G cells. In the experiment, the heme oxygenase-1 gene (HO-1), which generates oxidative cellular stress via ROS production, was found to be overexpressed, 75 and cell viability decreased as ROS production increased.

A study 21 observed that actin affected by ELF-PEMF led to morphological changes in T47D human breast cancer cells while apoptosis was not observed. These effects might be explained by the parameters of ELF-PEMF including frequency and duration. The study showed that the effects of ELF-PEMF on cellular growth and ROS generation depended on time and frequency.

A system with ELF-PEMF(max. 35 μT) was employed in multiple sclerosis with fatigue 76 and was found to improve organ blood flow. 77 In another research, 78 the system was applied to cells from different solid tumors (Table 1). The results illustrated that ELF-PEMF exerted some effects on glycolysis and TCA cycle pathways and increased ROS levels. The researchers performed a single ELF-PEMF treatment followed by RT at short intervals and observed the potential of ELF-PEMF to mediate radiosensitization by increasing the levels of ROS and the subsequent generation of DNA damage to explore the therapeutic implications of these changes.

Two experiments 79 , 80 studied the effects of ELF-PEMF (75 Hz, 2 mT) exposure on the stress and oxidative pathways of human neuroblastoma SH-SY5Y cells, neuronal-like cells, 53 which are often used to determine cellular responses on redox basis. 81 They observed that ELF-PEMF could exert a cytoprotective effect by altering redox status, such as by increasing the free radical scavenger superoxide dismutase-1 enzyme (SOD-1) and decreasing mitochondrial activity. Furthermore, a growing body of evidence shows that increasing SOD may act as a tumor suppressor. 82 A further study indicated that ELF-PEMF treatment could increase the activity of Mn-dependent superoxide dismutase (MnSOD) which is an essential antioxidant enzyme that is believed to reduce ROS levels. 83 They summarized that exposure to ELF-PEMF could act as a catalyst for the major antioxidant enzymatic defense.

All in all, ELF-PEMF is likely to act on the redox status of cells. Some experiments showed the possibility of its protective effect on normal neurons. Despite different modes, ELF-PEMF has promising prospects in terms of clinical use.

https://www.nature.com/articles/s41420-023-01490-2

Recent progress in the effect of magnetic iron oxide nanoparticles on cells and extracellular vesicles 2023

When the exposure concentration of nano-magnetite particles is greater than 50 μg/ml, it will produce greater cytotoxicity in the form of reduced activity, and **increase ROS**, reduce cell membrane potential and reduce the rate of cell apoptosis [30]. Therefore, as long as the specific parameters of IONPs are controlled, they will not have adverse effects on cell viability, metabolic activity, oxidative stress, proliferation and differentiation [9, 35, 36].

However, iron overload can trigger the generation of reactive oxygen species (ROS) [32, 37]. The main reason for the cytotoxicity of IONPs is the excessive production of ROS. ROS can cause oxidative stress in cells by activating pro-inflammatory mediators, and eventually lead to cell necrosis or apoptosis [38]. Therefore, autophagy induced by IONPs can affect cell metabolism, cytotoxicity, therapeutic effect [39], and even host immune system [40,41,42].

However, it is usually difficult to produce enough •OH, which is limited by intracellular H2O2 concentration to induce iron death of cancer cells [71]. In order to achieve sufficient anti-tumor effect. It is reported that the intracellular cascade reaction can increase the concentration of H2O2 in cells, thus improving the high-level production of •OH through the joint transport of **metal catalysts** and H2O2 producers [72, 73]. Cisplatin can indirectly produce H2O2 to further accelerate Fenton reaction. It can induce intracellular cascade reaction to produce enough •OH for iron death treatment [74]. In addition, the liposome is embedded with PEG-coated The liposome bilayer of γ-Fe2O3 nanoparticles improves the permeability of H2O2 and •OH [75], resulting in the effective activation of lipid peroxidation [76]. Moreover, 808 nm laser irradiation heat-induced Fe3O4 in situ burst release produces effective reactive oxygen species through Fenton reaction in tumor microenvironment [77].

https://pubmed.ncbi.nlm.nih.gov/32331350/

Low-Frequency Magnetic Fields (LF-MFs) Inhibit Proliferation by Triggering Apoptosis and Altering Cell Cycle Distribution in Breast Cancer Cells 2020

In this study, we found that in exposure to low-frequency magnetic fields (LF-MFs) with an intensity of 1 mT and frequencies of 50, 125, 200, and 275 Hz, separately, the proliferation of breast cancer cells was inhibited and LF-MF with 200 Hz reached the optimum inhibition effect, on exposure time-dependently. Notably, we found that exposure to LF-MF led to MCF-7 and ZR-75-1 cell apoptosis and cell cycle arrest. Moreover, we also discovered that LF-MF effectively increased the level of reactive oxygen species (ROS), suppressed the PI3K/AKT signaling pathway, and activated glycogen synthase kinase-3β (GSK-3β). We demonstrated that the GSK3β activity contributed to LF-MF-induced cell proliferation inhibition and apoptosis, while the underlying mechanism was associated with the inhibition of PI3K/AKT through increasing the intracellular ROS accumulation. These results indicate that LF-MF with a specific frequency may be an attractive therapy to treat breast cancers.

https://pubmed.ncbi.nlm.nih.gov/35929424/

Is extremely low frequency pulsed electromagnetic fields applicable to gliomas? A literature review of the underlying mechanisms and application of extremely low frequency pulsed electromagnetic fields 2023

Gliomas refer to a group of complicated human brain tumors with a low 5-year survival rate and limited therapeutic options. Extremely low-frequency pulsed electromagnetic field (ELF-PEMF) is a specific magnetic field featuring almost no side effects. However, the application of ELF-PEMF in the treatment of gliomas is rare. This review summarizes five significant underlying mechanisms including calcium ions, autophagy, apoptosis, angiogenesis, and **reactive oxygen species**, and applications of ELF-PEMF in glioma treatment from a clinical practice perspective. In addition, the prospects of ELF-PEMF in combination with conventional therapy for the treatment of gliomas are reviewed. This review benefits any specialists, especially oncologists, interested in this new therapy because it can help treat patients with gliomas properly.

https://pubmed.ncbi.nlm.nih.gov/37935811/

Spinning magnetic field patterns that cause oncolysis by oxidative stress in glioma cells 2023 Bassett

Raising reactive oxygen species (ROS) levels in cancer cells to cause macromolecular damage and cell death is a promising anticancer treatment strategy. Observations that electromagnetic fields (EMF) elevate intracellular ROS and cause cancer cell death, have led us to develop a new portable wearable EMF device that generates spinning oscillating magnetic fields (sOMF) to selectively kill cancer cells while sparing normal cells in vitro and to shrink GBM tumors in vivo through a novel mechanism. Here, we characterized the precise configurations and timings of sOMF stimulation that produce cytotoxicity due to a critical rise in superoxide in two types of human glioma cells. We also found that the antioxidant Trolox reverses the cytotoxic effect of sOMF on glioma cells indicating that ROS play a causal role in producing the effect. Our findings clarify the link between the physics of magnetic stimulation and its mechanism of anticancer action, facilitating the development of a potential new safe noninvasive device-based treatment for GBM and other gliomas.

https://pubmed.ncbi.nlm.nih.gov/19115234/

Fifty hertz extremely low-frequency magnetic field exposure elicits redox and trophic response in rat-cortical neurons 2009

Large research activity has raised around the mechanisms of interaction between extremely low-frequency magnetic fields (ELF-MFs) and biological systems. ELF-MFs may interfere with chemical reactions involving reactive oxygen species (ROS), thus facilitating oxidative damages in living cells. Cortical neurons are particularly susceptible to oxidative stressors and are also highly dependent on the specific factors and proteins governing neuronal development, activity and survival. The aim of the present work was to investigate the effects of exposures to two different 50 Hz sinusoidal ELF-MFs intensities (0.1 and 1 mT) in maturing rat cortical neurons' major anti-oxidative enzymatic and non-enzymatic cellular protection systems, membrane peroxidative damage, as well as growth factor, and cytokine expression pattern. Briefly, our results showed that ELF-MFs affected positively the cell viability and concomitantly reduced the levels of apoptotic death in rat neuronal primary cultures, with no significant effects on the main anti-oxidative defences. Interestingly, linear regression analysis suggested a positive correlation between reduced glutathione (GSH) and ROS levels in 1 mT MF-exposed cells. On this basis, our hypothesis is that GSH could play an important role in the antioxidant defence towards the ELF-MF-induced redox challenge. Moreover, the GSH-based cellular response was achieved together with a brain-derived neurotrophic factor over-expression as well as with the interleukin 1beta-dependent regulation of pro-survival signaling pathways after ELF-MF exposure.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8049370/

Advances in Imaging Reactive Oxygen Species 2021

Reactive oxygen species (ROS) play a pivotal role in many cellular processes and can be either beneficial or harmful. The design of ROS-sensitive fluorophores has allowed for imaging of specific activity and has helped elucidate mechanisms of action for ROS. Understanding the oxidative role of ROS in the many roles it plays allows us to understand the human body. This review provides a concise overview of modern advances in the field of ROS imaging.

https://pubmed.ncbi.nlm.nih.gov/22131325/

Extremely low frequency magnetic field induces oxidative stress in mouse cerebellum 2011

We have investigated whether extremely low frequency magnetic field (ELF-MF) induces lipid peroxidation and reactive oxygen species in mouse cerebellum. After exposure to 60 Hz ELF-MF at 2.3 mT intensity for 3 hours, there was a significant increase in malondialdehyde level and hydroxyl radical. While glutathione contents were not altered, ascorbic acid levels were significantly decreased by ELF-MF exposure. These results indicate that ELF-MF may induce oxidative stress in mouse cerebellum.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3839120/pdf/OXIMED2013-529173.pdf

Protective Effects of Low-Frequency Magnetic Fields on Cardiomyocytes from Ischemia Reperfusion Injury via ROS and NO/ONOO− 2013

We generated magnetic fields with different amplitudes in a range of 1.5 mT to 6.0 mT and varying sinusoidal currents of 15 Hz or 20 Hz. Eight different parameters of magnetic fields were applied in this experiment: 1.5 mT/15 Hz, 1.5 mT/20 Hz, 3.0 mT/15 Hz, 3.0 mT/20 Hz, 4.5 mT/15 Hz, 4.5 mT/20 Hz, 6.0 mT/15

Hz, and 6.0 mT/20 Hz, respectively. Timing and duration of LFMFs treatment were 1 h, 3 h, and 5 h before or after H/R treatment, respectively.
Compared with cells treated with H/R, the LFMFs-treated groups showed a significant decline in apoptotic cells, especially under the condition of 4.5 mT/15 Hz and 3 h before or after H/R treatment (Figures 1(e) and 1(f)).
4.5 mT/15 Hz, 3 h before or after H/R treatment, significantly suppressed O_2^-
It is recognized that ROS production is elevated by I/R injury and ROS exert crucial effects on I/R injury [7, 8]. ROS, including superoxide radical (O_2^-), hydroxyl radical (OH^-), hydrogen peroxide (H_2O_2), and peroxynitrite ($ONOO^-$), are able to result in cardiomyocytes' oxidative stress. Oxidative stress could mediate I/R injury by bringing about cardiomyocytes' dysfunction and apoptosis [8]. Lines of evidences have shown that oxidative stress is involved in myocardial damage [9] and antioxidative agents are capable of reducing myocardial injury [10]. Our study revealed similar results. In comparison with control group, the generation of ROS in H/R group was significantly increased which was compromised in the LFMFs-treated groups.

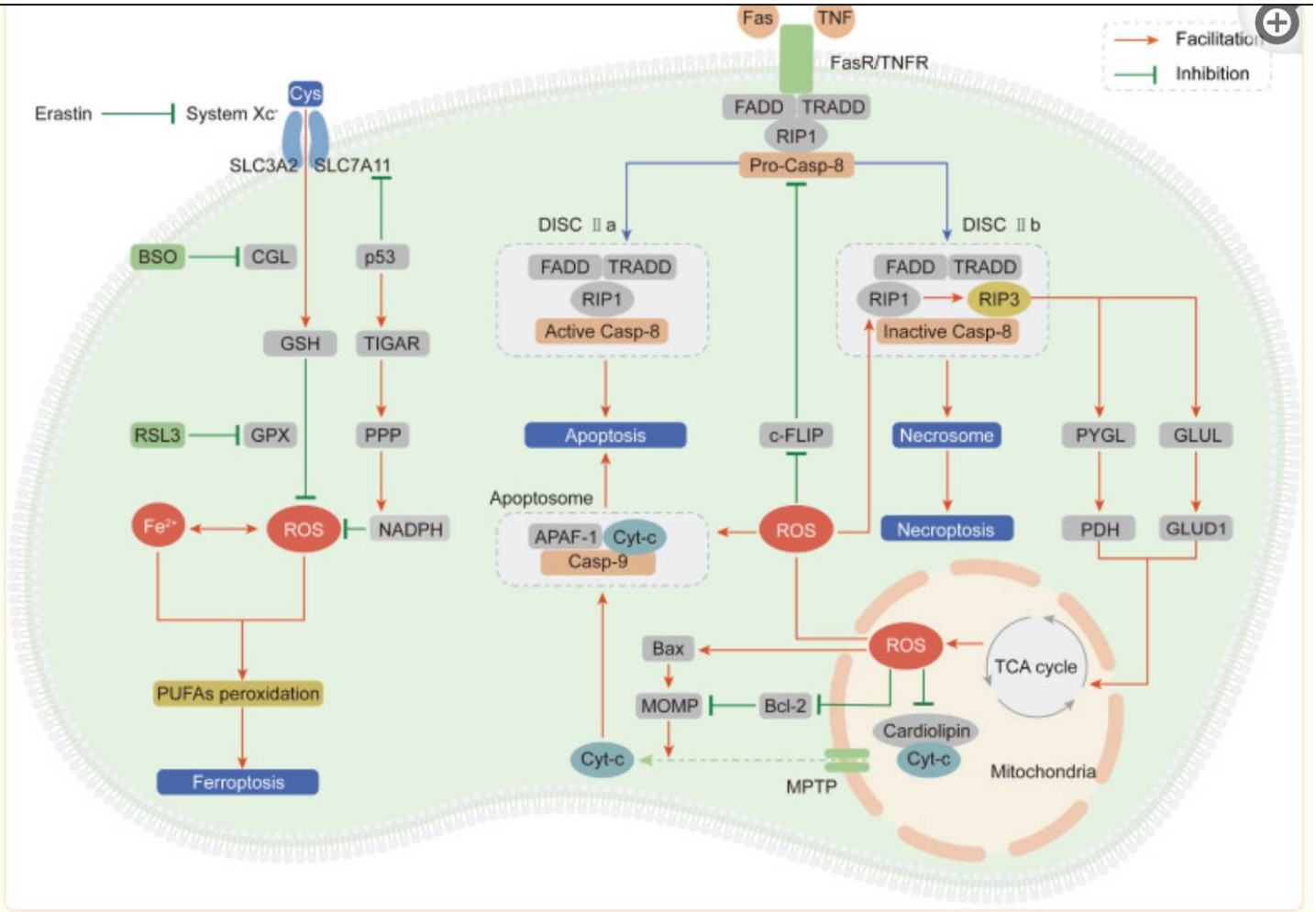


Figure 3

ROS induce cell death, mainly including apoptosis, necroptosis and ferroptosis. (I) Exceeding ROS promote both the extrinsic and intrinsic apoptosis pathway: ROS activate extrinsic apoptosis pathway by accelerating the ubiquitin degradation of c-FLIP, then enhancing the binding between the adaptor protein and pro-caspase-8; ROS induce intrinsic apoptosis by facilitating the release of Cyt-c from mitochondria to cytoplasm to form apoptosome with casp-9 and APAF-1. (II) ROS and necroptosis form a positive feedback loop: ROS stabilize RIP3 protein to lead to the formation of DISC IIb (necrosome); in turn, RIP3 can facilitate the TCA cycle and aerobic respiration in mitochondria to induce ROS generation. (III) Ferroptosis is a ROS-dependent form of RCD: the basic of ferroptosis is GSH anabolism disorder leads to the lethal accumulation of PUFAs peroxidation; p53 plays opposite roles on ROS and ferroptosis by inhibiting SLC7A11 expression or increasing NADPH production.

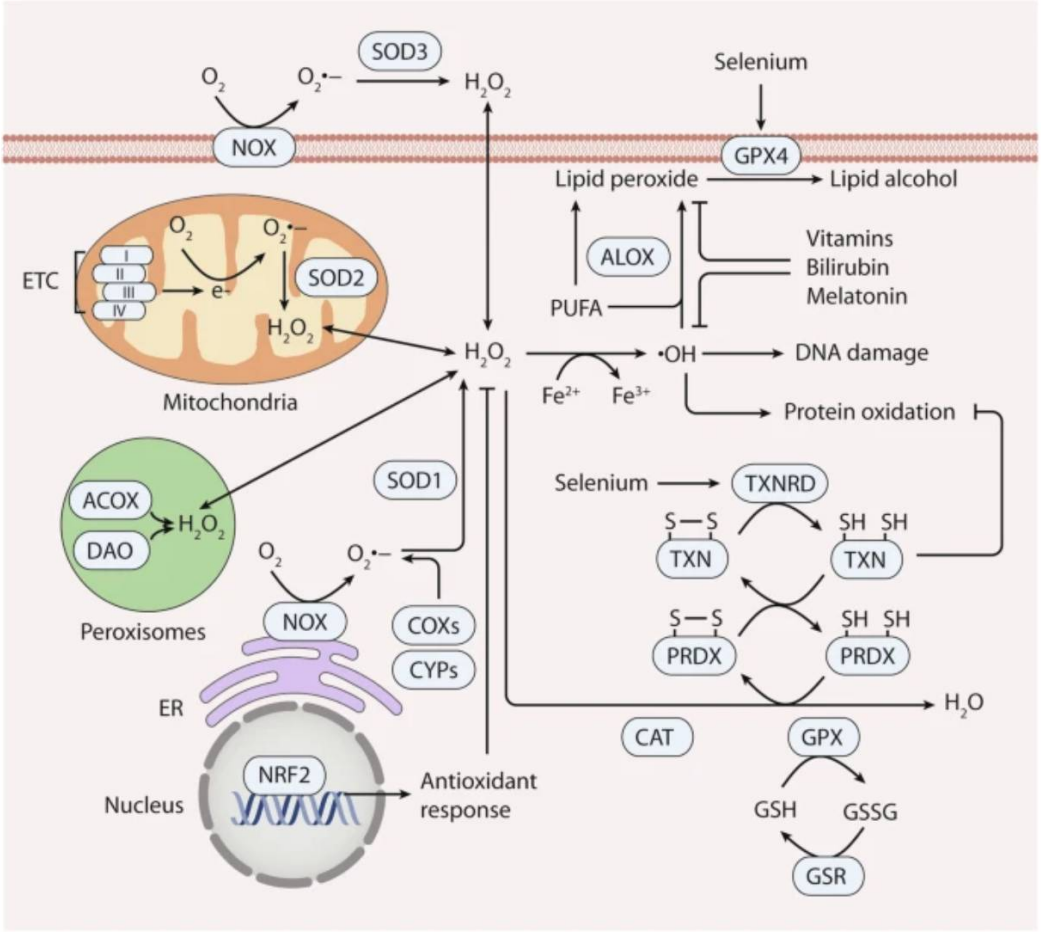
https://pubmed.ncbi.nlm.nih.gov/29124687/
Ultraviolet Light Induced Generation of Reactive Oxygen Species 2017
More specifically UV light can induce ROS by affecting the enzyme catalase and up-regulating nitric oxide synthase (NOS) synthesis. It may also cause a decrease in protein kinase C (PKC) expression leading to increased ROS production. UVR is capable of modifying DNA and other chromophores resulting in elevated ROS levels. The effects of raised ROS levels can vary based on the intracellular oxidant status of the cell.

https://www.nature.com/articles/s41419-024-06939-5
Oxidative cell death in cancer: mechanisms and therapeutic opportunities 2024

Reactive oxygen species (ROS) are highly reactive oxygen-containing molecules generated as natural byproducts during cellular processes, including metabolism. Under normal conditions, ROS play crucial roles in diverse cellular functions, including cell signaling and immune responses. However, a disturbance in the balance between ROS production and cellular antioxidant defenses can lead to an excessive ROS buildup, causing oxidative stress. This stress damages essential cellular components, including lipids, proteins, and DNA, potentially culminating in oxidative cell death. This form of cell death can take various forms, such as ferroptosis, apoptosis, necroptosis, pyroptosis, paraptosis, parthanatos, and oxeiptosis, each displaying distinct genetic, biochemical, and signaling characteristics. The investigation of oxidative cell death holds promise for the development of pharmacological agents that are used to prevent tumorigenesis or treat established cancer. Specifically, targeting key antioxidant proteins, such as SLC7A11, GCLC, GPX4, TXN, and TXNRD, represents an emerging approach for inducing oxidative cell death in cancer cells. This review provides a comprehensive summary of recent progress, opportunities, and challenges in targeting oxidative cell death for cancer therapy.

While moderate ROS levels are involved in a spectrum of signaling pathways that are vital for cell growth, differentiation, and progression, elevated ROS levels are potent triggers of cell death [7]. In cancer cells, heightened oxidative stress results from increased ROS production and/or compromised ROS-scavenging capacity [8]. Even a slight elevation in ROS levels within cancer cells relative to that in normal cells can surpass a critical threshold, inducing cancer cell death and suppressing tumor development [9]. Thus, agents that induce ROS generation hold the potential to be used in targeted strategies for eradicating malignancies.

Fig. 1: Overview of ROS generation and elimination.



Reactive oxygen species (ROS) are labile oxygen-containing molecules primarily generated by the mitochondrial electron transport chain (ETC), peroxisomes, NADPH oxidase (NOX), lipoxygenase (ALOX), cyclooxygenases (COXs), and cytochrome P450s (CYPs). ROS elimination is facilitated by antioxidant systems, encompassing enzymatic antioxidants (e.g., SOD, CAT, GPX, and the thioredoxin [TXN]-thioredoxin reductase [TXNRD] system) and non-enzymatic antioxidants (e.g., glutathione [GSH], vitamins or analogs, selenium, and metabolites such as bilirubin and melatonin). Superoxide dismutase (SOD) transforms $O_2^{\bullet-}$ into H_2O_2, subsequently reduced to H_2O by catalase (CAT), glutathione peroxidase (GPX), or peroxiredoxins (PRDX). Among these, ALOX significantly contributes to lipid peroxidation, while GPX4, a selenocysteine-containing enzyme, quenches lipid peroxides. Central to the antioxidant network, TXNRD—a pivotal selenoprotein antioxidant—donates electrons to the TXN–PRDX axis. Moreover, the transcription factor NRF2 prominently regulates the antioxidant system, orchestrating the expression of genes crucial to antioxidant defense mechanisms.

https://www.sciencedirect.com/science/article/pii/S0160412024001211

Current insights and future perspectives of ultraviolet radiation (UV) exposure: Friends and foes to the skin and beyond the skin 2024

6. UV light as a treatment

UV light is a double-edged sword for health. Although UV light can damage the body's health, it can also be involved in the synthesis of some beneficial substances and can be used as a means of treating some diseases (Table 1). UV involved in the synthesis of vitamin D in the human body, which is not deficient in the right amount of sunlight exposure (Knuschke, 2021). UVB radiation induces the synthesis of pro-vitamin D3 in the skin, and 7-dehydrocholesterol or vitamin D3 precursors undergo photochemical reactions in the epidermal layer of spiny cells and basal cell layer to form vitamin D3, which then goes to the liver and kidneys for a series of transformations to eventually form vitamin D (Mohania et al., 2017).

UV radiation may be associated with reduced cancer risks. Vitamin D synthesis is largely determined by UV exposure, from which 70 % of vitamin D is derived. In an animal study, Fabpl-Cre; Apc15flox/+ mice that developed intestinal tumors were used, and UVB irradiation were applied. The UV-irradiated group exhibited reduced progression to malignancy in comparison to the control group (Rebel et al., 2015).

Phototherapy is extensively employed in the treatment of bone cancer, which is clinically accepted, minimally invasive and highly targeted. When subjected to irradiation at specific wavelengths, the photosensitizer in PDT can **elevate intracellular ROS levels**, while the photothermal agent in PTT can induce photothermal conversion, effectively eliminating tumor cells (Sun et al., 2021).

https://pubmed.ncbi.nlm.nih.gov/32331350/
Low-Frequency Magnetic Fields (LF-MFs) Inhibit Proliferation by Triggering Apoptosis and Altering Cell Cycle Distribution in Breast Cancer Cells 2020
Magnetic fields, as a non-invasive therapy, have shown anti-tumor effects in vitro and in vivo; however, the detailed mechanisms involved are still not clear. In this study, we found that in exposure to low-frequency magnetic fields (LF-MFs) with an intensity of 1 mT and frequencies of 50, 125, 200, and 275 Hz, separately, the proliferation of breast cancer cells was inhibited and LF-MF with 200 Hz reached the optimum inhibition effect, on exposure time-dependently. Notably, we found that exposure to LF-MF led to MCF-7 and ZR-75-1 cell apoptosis and cell cycle arrest. Moreover, we also discovered that LF-MF effectively increased the level of reactive oxygen species (ROS), suppressed the PI3K/AKT signaling pathway, and activated glycogen synthase kinase-3β (GSK-3β). We demonstrated that the GSK3β activity contributed to LF-MF-induced cell proliferation inhibition and apoptosis, while the underlying mechanism was associated with the inhibition of PI3K/AKT through increasing the intracellular ROS accumulation. These results indicate that LF-MF with a specific frequency may be an attractive therapy to treat breast cancers.

https://pubmed.ncbi.nlm.nih.gov/20610864/
Effects of extremely low frequency magnetic field on the parameters of oxidative stress in heart 2010
Exposure to ELF-MF (40 Hz, 7 mT, 30 min/day for 2 weeks) did not significantly alter tissue TBARS, H(2)O(2), total free -SH groups, reduced glutathione (GSH) and total antioxidant capacity of plasma. By contrast, ELF-MF with the same frequency and induction but used for 60 min/day for 14 days caused significant increase in TBARS and H(2)O(2) concentration ($P<0.01$) and decrease in the concentration of GSH ($P<0.05$) and total free -SH groups in heart homogenates. Moreover, exposure of rats to ELF-MF (40 Hz, 7 mT, 60 min/day for 2 weeks) resulted in the decrease of plasma antioxidant capacity. Our results indicate that effects of ELF-MF on ROS generation in the heart tissue and antioxidant capacity of plasma depend on its working time.

https://pubmed.ncbi.nlm.nih.gov/22314568/
Effects of extremely low frequency magnetic field on oxidative balance in brain of rats 2011
The animals were divided into 3 groups: I - control (shame) group; II - exposed to the following parameters of the magnetic field: 7 mT, 40 Hz, 30 min/day, 10 days; III - exposed to the ELF-MF parameters of 7 mT, 40 Hz, 60 min/day, 10 days.
The study has shown that ELF-MF applied for 30 min/day for 10 days can affect free radical generation in the brain. Prolongation of the exposure to ELF-MF (60/min/day) caused adaptation to this field. The effect of ELF-MF irradiation on oxidative stress parameters depends on the time of animal exposure to magnetic field.

https://pubmed.ncbi.nlm.nih.gov/35746959/
Bidirectional Effect of Repeated Exposure to Extremely Low-Frequency Electromagnetic Field (50 Hz) of 1 and 7 mT on Oxidative/Antioxidative Status in Rat's Brain: The Prediction for the Vulnerability to Diseases 2022
Results showed that repeated exposure changed the oxidative/antioxidative status depending on the intensity of the EMF and the number of exposures. 1 mT EMF created weak changes in the oxidative status in the brain; however, 7 mT EMF moved the balance to a clearly higher level. The changes in the oxidative status after 1 mT EMF were enough to reduce, and after 7 mT EMF to intensify oxidative processes in response to the next stress.

https://pubmed.ncbi.nlm.nih.gov/24334533/
Extremely low frequency magnetic fields induce oxidative stress in rat brain 2013
The continuous exposure to ELF-MF caused OS (oxidative stress) in all the examined regions of brain more significantly at 100 μT than at 50 μT.

https://pubmed.ncbi.nlm.nih.gov/27399314/
Magnetic fields, radicals and cellular activity 2016
Some effects of low-intensity magnetic fields on the concentration of radicals and their influence on cellular functions are reviewed. These fields have been implicated as a potential modulator of radical recombination rates. Experimental evidence has revealed a tight coupling between cellular function and radical pair chemistry from signaling pathways to damaging oxidative processes. The effects of externally applied magnetic fields on biological systems have been extensively studied, and the observed effects lack sufficient mechanistic understanding. Radical pair chemistry offers a reasonable explanation for some of the molecular effects of low-intensity magnetic fields, and changes in radical concentrations have been observed to modulate specific cellular functions. Applied external magnetic fields have been shown to induce observable cellular changes such as both inhibiting and accelerating cell growth. These and other mechanisms, such as cell membrane potential modulation, are of great interest in cancer research due to the variations between healthy and deleterious cells. Radical concentrations demonstrate similar variations and are indicative of a possible causal relationship. Radicals, therefore, present a possible mechanism for the modulation of cellular functions such as growth or regression by means of applied external magnetic fields.

https://pubs.aip.org/aip/apl/article-abstract/125/10/103701/3311147/Radical-pair-mechanism-and-the-role-of-chirality?redirectedFrom=fulltext
Radical pair mechanism and the role of chirality-induced spin selectivity during planaria regeneration 2024
Planaria serve as an intriguing model system wherein the effects of electric and magnetic fields on various biochemical pathways during cell morphogenesis can be studied. Recent experimental observations have demonstrated the non-trivial modulation of reactive oxygen species (ROS) levels by a weak magnetic field (WMF) during planaria regeneration. However, the underlying biophysical mechanism behind this remains elusive. In this work, we investigate the role of the radical pair mechanism (RPM) and attempt to explain the experimental results of the effect of WMFs on ROS modulation during planaria regeneration.

https://royalsocietypublishing.org/doi/full/10.1098/rsif.2022.0325
Magnetic field effects in biology from the perspective of the radical pair mechanism 2022
Hundreds of studies have found that weak magnetic fields can significantly influence various biological systems. However, the underlying mechanisms behind these phenomena remain elusive. Remarkably, the magnetic energies implicated in these effects are much smaller than thermal energies. Here, we review these observations, and we suggest an explanation based on the radical pair mechanism, which involves the quantum dynamics of the electron and nuclear spins of transient radical molecules.
Sensitivity to weak magnetic fields is abundant throughout biology, as discussed in numerous review articles [1–24]. Effects of either static or oscillating weak magnetic fields have been reported on the circadian clock, electron transfer in cryptochrome, stem cells, calcium concentration, the brain's functions such as action potentials, reactive oxygen species (ROS), development, neuronal activities, DNA, memory, anxiety, analgaesia, genetics and many other functions (see §2). Despite the wealth of observations, thus far, there is no clear explanation for the mechanism behind these phenomena. This is mainly due to the fact that the

corresponding energies for such effects are far smaller than thermal energies.
However, there is a promising quantum physics (or spin chemistry) concept that can account for the effects of such weak fields, namely the radical pair mechanism [25,26].

https://onlinelibrary.wiley.com/doi/full/10.1002/qua.24943
Radical Pair Mechanism 2015
A radical is an atom, molecule or ion that has unpaired valence electrons. Radicals and radical pairs often play a very important role as intermediates in thermal, radiation, and photochemical reactions.1 The presence of unpaired electron spins in these systems allows one to influence and control these reactions using interactions between external magnetic fields and electron spins.2 However, until 1970, most scientists believed that ordinary magnetic fields had no significant effect on chemical or biochemical reactions, as the magnetic energy of typical molecules, under ordinary magnetic fields, is much smaller than the thermal energy at room temperature and is much smaller than the activation energies for those reactions.1, 2 This situation changed significantly in the 1970s after a series of experimental results were reported on magnetic field effects on chemical reactions.3-7 Because of these experimental studies, a number of researchers have made an effort to theoretically explain the magnetic field effects on the chemical reactions.8, 9 Thanks to these and the subsequent efforts, we are now able to explain systematically magnetic field effects in terms of the radical pair mechanism. The radical pair mechanism was then successfully applied to explain the chemically induced nuclear polarization and electron polarization, which were shown to be based on the spin dynamics of radical pairs.2

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6353618/
Weak magnetic fields alter stem cell–mediated growth 2019
Weak magnetic fields affect reactive oxygen species levels, stem cell proliferation/differentiation, and new tissue growth.
While strong magnetic fields are known to change chemical reaction rates and free radical concentrations, the debate remains about whether static weak magnetic fields (WMFs; <1 mT) also produce biological effects. Using the planarian regeneration model, we show that WMFs altered stem cell proliferation and subsequent differentiation via changes in reactive oxygen species (ROS) accumulation and downstream heat shock protein 70 (Hsp70) expression.
WMFs were also found to produce transient induction of the membrane permeability transition and increased cytosolic cytochrome c levels in human amniotic cells via an increase in reactive oxygen species (ROS) (*13*).

https://pubmed.ncbi.nlm.nih.gov/26807660/
Extremely low frequency magnetic fields regulate differentiation of regulatory T cells: Potential role for ROS-mediated inhibition on AKT 2016
Our previous studies showed that extremely low frequency magnetic fields (ELF-MFs) inhibited tumor growth and change proportion of splenic regulatory T cells (Treg cells). Here, we focus on the effect of ELF-MFs on lung metastatic melanoma mouse model and the regulatory mechanism of ELF-MFs on the differentiation of Treg cells. Tumor-bearing mice were exposed to sham ELF-MFs and ELF-MFs (0.4 T, 7.5 Hz) 2 h/day for 27 days. Metastatic tumor burden of lung was significantly decreased after ELF-MF treatment.
Taken together, our data show that ELF-MF exposure promoted the inhibitory effect of ROS on AKT pathway and decreased Foxp3 expression, which provides an explanation for why ELF-MF exposure can inhibit differentiation of Treg cells and enhance antitumor effect in metastatic melanoma mouse model.

https://www.mdpi.com/1422-0067/22/11/5785
Modulation of Cellular Response to Different Parameters of the Rotating Magnetic Field (RMF)—An In Vitro Wound Healing Study 2021
The presented study was conducted to determine whether a low-frequency RMF (rotating magnetic field) with different field parameters could evoke the cellular response in vitro and is possible to modulate the cellular response. The cellular metabolic activity, ROS and Ca^{2+} concentration levels, wound healing assay, and gene expression analyses were conducted to evaluate the effect of RMF. It was shown that different values of magnetic induction (B) and frequency (f) of RMF evoke a different response of cells, e.g., increase in the general metabolic activity may be associated with the increasing of ROS levels. The lower intracellular Ca^{2+} concentration (for 50 Hz) evoked the inability of cells to wound closure. It can be stated that the subtle balance in the ROS level is crucial in the wound for the effective healing process, and it is possible to modulate the cellular response to the RMF in the context of an in vitro wound healing.

https://pubmed.ncbi.nlm.nih.gov/28936716/
Induction of reactive oxygen species: an emerging approach for cancer therapy 2017
Reactive oxygen species (ROS), a group of ions and molecules, include hydroxyl radicals (·OH), alkoxyl radicals, superoxide anion (O_2·-), singlet oxygen ($^1O_2$) and hydrogen peroxide (H_2O_2). Hydroxyl radicals and alkoxyl radicals are extremely and highly reactive species respectively. Endogenous ROS are mainly formed in mitochondrial respiratory chain. Low levels of ROS play important roles in regulating biological functions in mammalian cells. However, excess production of ROS can induce cell death by oxidative damaging effects to intracellular biomacromolecules. Cancer cell death types induced by ROS include apoptotic, autophagic, ferroptotic and necrotic cell death. Since abnormal metabolism in cancer cells, they have higher ROS content compared to normal cells. The higher endogenous ROS levels in cancer cells endow them more susceptible to the ROS-induction treatment. Indeed, some anticancer drugs currently used in clinic, such as molecular targeted drugs and chemotherapeutic agents, effectively kill cancer cells by inducing ROS generation. In addition, photodynamic therapy (PDT) is mainly based on induction of ROS burst to kill cancer cells. The mechanism of cell death induced by radiotherapy using ionizing radiation also refers to ROS production. Moreover, ROS play an important role in tumor immune therapy. Altogether, combining above traditional treatments with ROS-induced agents will be considered as a promising strategy in cancer therapy. In this review, we focus on our current understanding of the anticancer effects of ROS.