

ELF AND HEALTH EFFECTS – SOMETHING NEW FROM EXPERIMENTAL STUDIES?

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METHOD



2010, 2011, and 2012 peer-reviewed papers

Key words: ELF & cell; ELF & animal, 50/60 Hz, sinusoidal, magnetic fields

OUTCOME

65 papers, *in vitro* & *in vivo*

34 journals, 19 countries

Topics: DNA, genotoxicity, cancer, reactive oxygen species production, protein/gene expression, transcriptomics, proliferation, metabolism, brain, reproductive system, development, behaviour, apoptosis, Ca²⁺, immune system/cells, mast cells degranulation, etc.



Outline

DNA and Cancer

- Reactive Oxygen Species
- Gene/Protein expression
- Reproductive system
- Behaviour
- Co-exposures



DNA *in vitro*



- **No effects**

- **Ruiz-Gomez (2010)**: 2.45 mT, DNA ladder, yeasts deficient in DNA repair
- **Verschaeve (2011)**: 0.2-0.5 mT, mutation, bacteria
- **Luukkonen (2011)**: 0.1 mT, micronuclei, human neuroblastoma cells
- **Jin (2011); Jin (2012)**: 1 mT, micronuclei, human and mouse fibroblasts
- **Kim (2010)**: 6 mT, 30 min, DNA damage response, human primary fibroblasts & cancer cells
- **Lee (2012)**: 1 mT, 4 hr, NIH3T3 fibroblasts cell transformation assay

- **Effects**

- **Giorgi (2011)**: 1 mT, sinusoidal, transposition in E. Coli (decrease)
- **Kim (2010), Kim (2011)**: human primary fibroblasts & cancer cells
 - 7 mT, \leq 60 min, DNA damage response, no altered viability
 - 6 mT, 30 min/day, 3 days, DNA damage response, altered viability



DNA: a case study

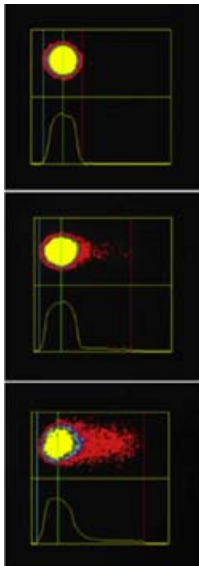
Mutation Research 683 (2010) 74–83



Contents lists available at ScienceDirect

Mutation Research/Fundamental and Molecular Mechanisms of Mutagenesis

journal homepage: www.elsevier.com/locate/molmut
Community address: www.elsevier.com/locate/mutres



DNA fragmentation in human fibroblasts under extremely low frequency electromagnetic field exposure

Frauke Focke^a, David Schuermann^a, Niels Kuster^b, Primo Schär^{a,*}

1 mT, Intermittent, 15 hr

Human primary fibroblasts

DNA fragmentation: comet assay

Only in proliferating cells

No effect on viability, no DNA oxidation

Possible effect on DNA replication and apoptosis (small cell fraction)

Could the “comet effect” be linked to other events such as epigenetics (e.g. active demethylation)?



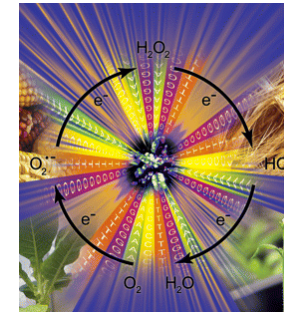
DNA *in vivo* & Cancer



- **Reversible DNA damage**
 - **Mariucci (2010)**: 1 mT, 1 or 7 days (15 hr/day)
CD1 mice (6 to 21/group)
DNA fragmentation (comet assay)
- **No co-promotion effect**
 - **Chung (2010)**: 0.005, 0.0833, and 0.5 mT, 40-42 weeks (21 h/day)
Lymphoma-prone AKR mice (40/group)
Parameters included: mean survival time, haematology, micronuclei, histopathology

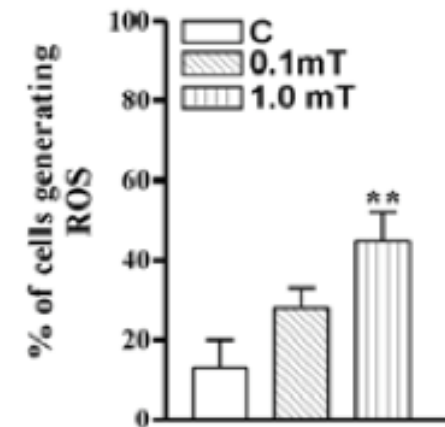


ROS production



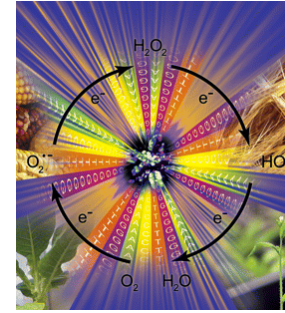
- **Increased**

- **Farina (2010)**: 0.1, 1 mT, PC12, glioblastoma & skeletal muscle cells
- **Morabito (2010)**: 1 mT, undifferentiated PC12 cells
- **Ayse (2010)**: 5 mT, human leukaemia cells
- **Frahm (2010)**: 1 mT, mouse macrophages (bone marrow)
- **Mannerling (2010)**: 0.025, 0.05 & 0.1 mT, human leukaemia cells
- **Akdag (2010)**: 0.1 & 0.5 mT, 2 h/d, 10 months, rat brains
- **Cho (2012)**: 2 mT, 5 d, rat brains





ROS production

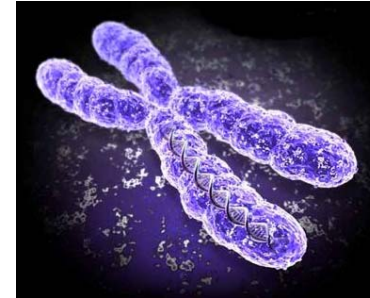


- **No change**

- **Kim (2011)**: 7 mT, 10-60 min, human primary fibroblasts & cancer cells
- **Hong (2012)**: 1 mT, 4 hr, human breast epithelial cells



Gene expression



- **No differential expression**

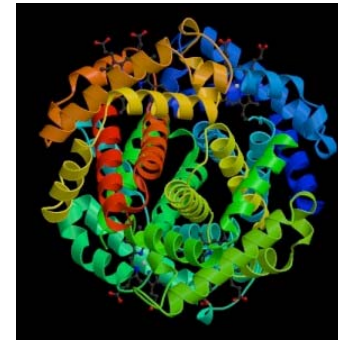
- **Heredia-Rojas (2010)**: 0.008 & 0.08 mT, hps70 promoter, mouse lymphoma cells
- **Sun (2010)**: 0.4 mT, human trophoblasts, apoptosis-related genes
- **Chen (2012)**: 0.4 mT, Yeast cells, Microarrays (6 000 genes) + confirmation
- **Huwiler (2012)**: 1 mT, Escherichia Coli, Microarrays (4 358 genes)

- **Differential expression**

- **Heredia-Rojas (2010)**: 0.008 & 0.08 mT, hps70 promoter, human lung cancer cells



Protein expression



- **Proteins: differential expression**

- **Mannerling (2010): Hsp70**

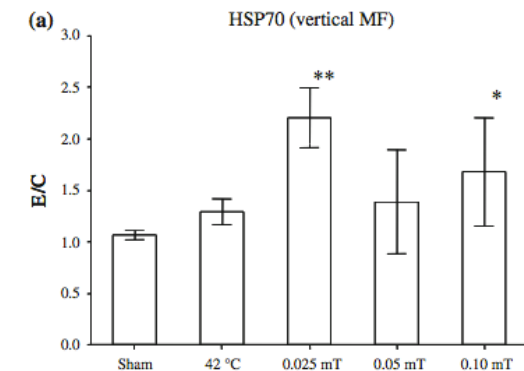
- 0.025, 0.1 mT, human leukaemia cells

- **Basile (2011): BAG-3**

- 30 A/m, human melanoma cells

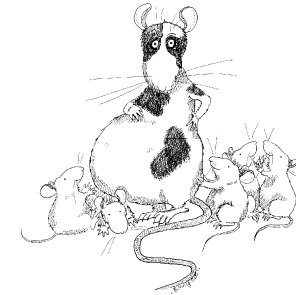
- **Frahm (2010): Redox-related proteins (Clathrin, hsp110, etc.)**

- 1 mT, mouse macrophages (bone marrow)





Reproductive system



• Detrimental effects

- **Rajaei (2010); Borhani (2010):** 0.5 mT, 4 hr/d, 6 d/w, 2 w, female mice
- **Bernabo (2010):** 0.5, 0.75 & 1 mT, male & female swines
- **De Bruyn (2010):** 0.005, 0.77 mT, 2 generations, male & female mice
- **Tenorio (2010; 2011):** 1 mT, 3x30 min/d, GD13-21 ± PN D1-21/90, male rats
- **Sun W. (2010):** 0.2 & 0.4 mT, human trophoblasts

Parameters altered:

- Blastocystes number & DNA fragmentation, uterus morphology
- Acrosome damage in spermatozoa, fertilization *in vitro* & *in vivo*, early embryo development
- Living sperms number & sperms movement quality, *fertility not affected*
- Alteration to degeneration in testes, *no hormonal effect, large inter-individual differences*
- Secretion of human Chorionic Gonadotropin (hCG) & progesterone



Behaviour



- **Effects**

- **He (2011):** 2 mT, 4h/d, 4 w, male rats
anxiogenic effects, potentiation of spatial learning and long-term retention of spatial memory
- **Szemerszky (2010):** 0.5 mT, 24 h/d, 4-6 w, male rats
depressive-like behavior, hormonal stress reaction (proopiomelanocortine)
- **Sun H. (2010):** 2 mT, 1 h/d, embryonic days 12-18, isolated chicks (stress)
disruption of memory formation

- **No effects**

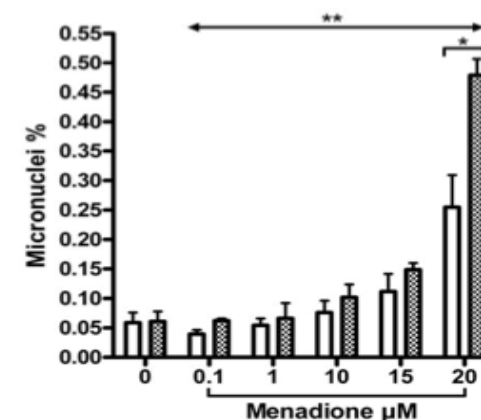
- **He (2011):** 2 mT, 1h/d, 4 w, male rats
- **Szemerszky (2010):** 0.5 mT, 8h/d, 5 d, male rats
- **Sun H. (2010):** 2 mT, 1 h/d, embryonic days 12-18, paired chicks (no stress)



Co-exposures

• Interaction

- **Marcantonio (2010)**: 1 mT ± all-trans retinoic acid, human neuroblastoma cells (decreased proliferation & increased differentiation, p21, cdk5, cyp19 gene expression)
- **Luukkonen (2011)**: 0.1 mT ± menadione, human neuroblastoma cells (increase in micronuclei)



• No interaction

- **Markkannen (2010)**: 0.1 & 0.3 mT ± UV, mouse fibroblasts (radical reactions)
- **Jin (2011); Lee (2012)**: 1 mT ± IR/H₂O₂/myc overexpression, human and mouse fibroblasts (micronuclei, cell transformation assay)
- **Rajkovic (2010)**, 0.1 & 0.3 mT ± Azatrazine, juvenile rats (thyroid gland)



Not new...

- **Suggested threshold for deleterious effects on DNA: 6 mT**
 - above ICNIRP critical level
- **No new clues to support the IARC 2B classification**
 - ARIMMORA FP7 project
- **Blind exposure and/or analysis rarely reported**



What's new?

- **Protein expression vs transcriptomics**
 - proteomics studies needed
 - post-transcriptional effect?
- **Increasing evidence for negative impact on reproductive functions & fertility**
 - better quality globally needed
 - rationale for epidemiological studies?
- **Behavioural effects of some exposures (≥ 0.5 mT, prolonged, stress)**
 - Relevant for occupational exposures?