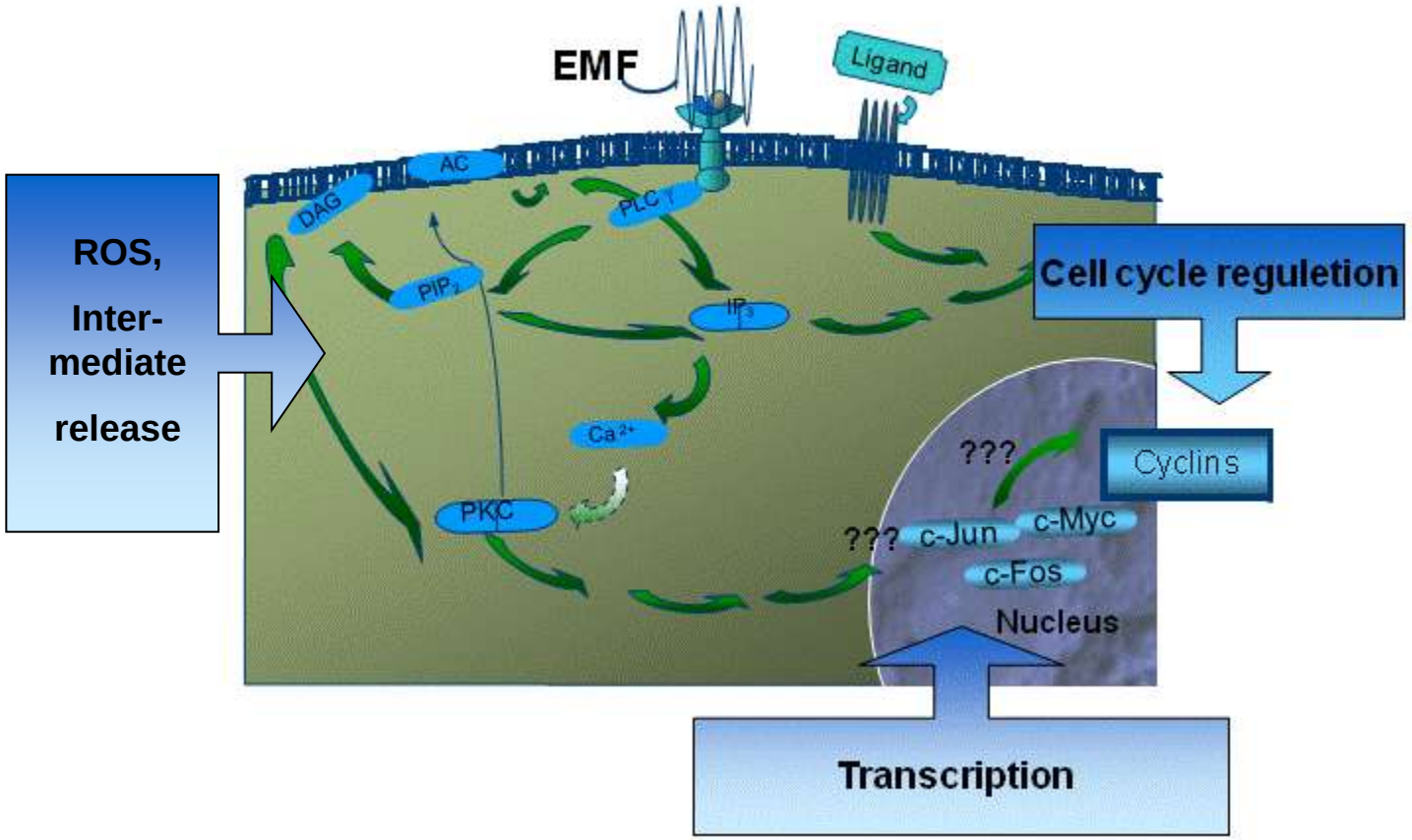
ELF- magnetic field and immune response modulation

Prof. Myrtill Simkó

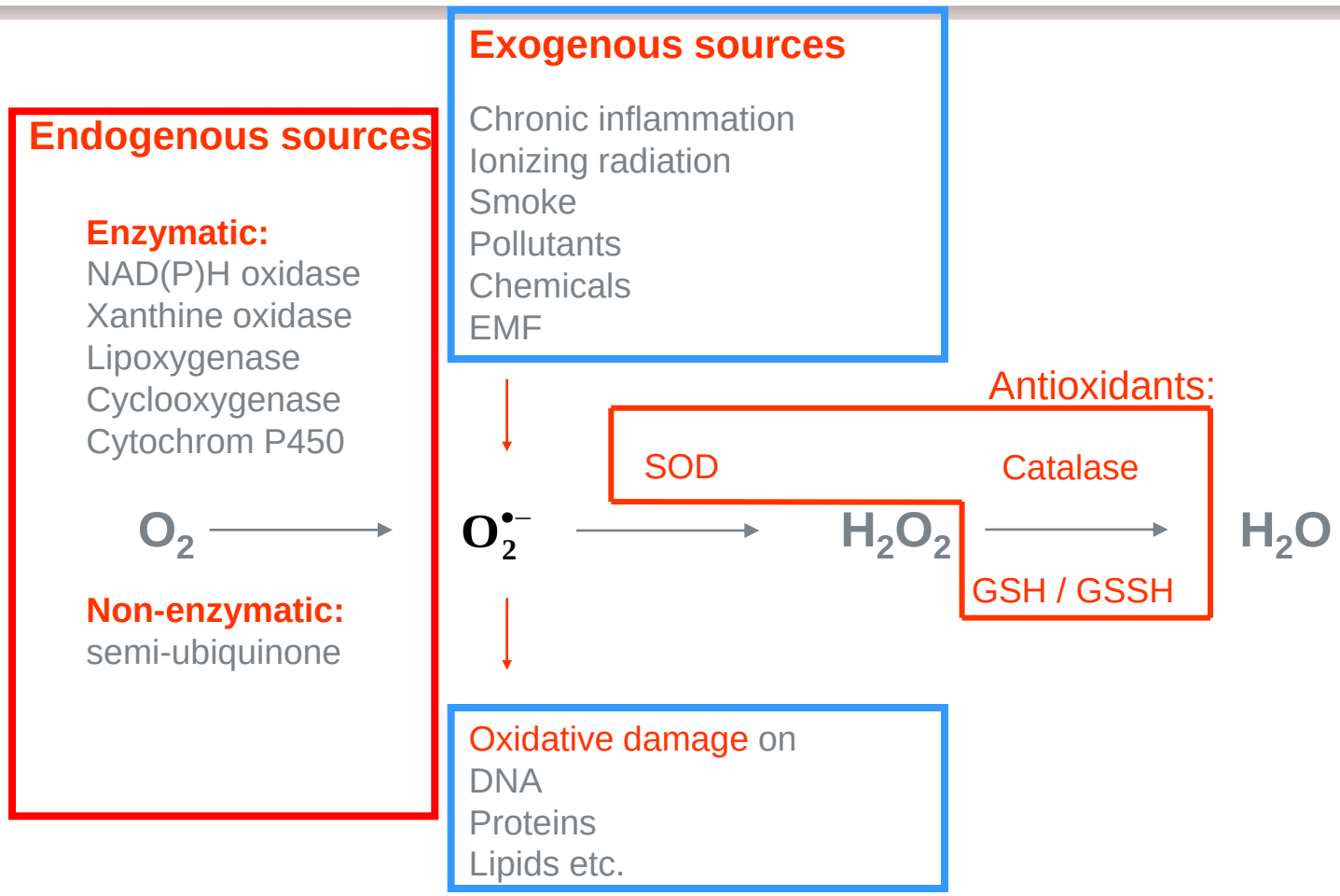
Health & Environment Department
AIT Austrian Institute of Technology GmbH
Konrad-Lorenz-Straße 24
3430 Tulln
Austria

Situation:	**ELF-EMF interacts with biological systems!**
Fact:	**Mode of action is unknown!**
Hypothesis 1:	**ELF-EMF modulates oxidative response(s) dose (flux density and time) dependently**
Hypothesis 2:	**Different cell types react differently since they have different homeostatic capacity!**
Hypothesis 3:	**This modulation can be used positively.**

Hypothesis - Cell activation



Free radicals



Macrophages

(1 mT, 50 Hz, 45 min)

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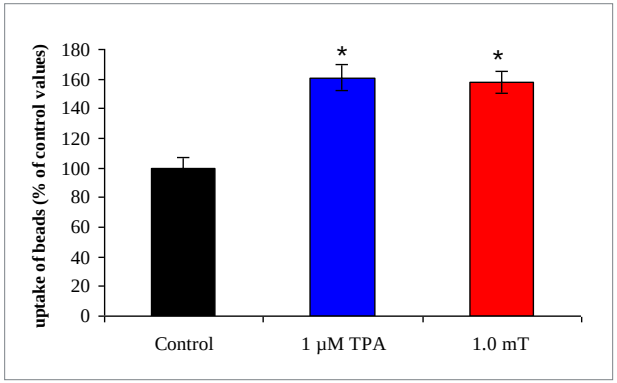
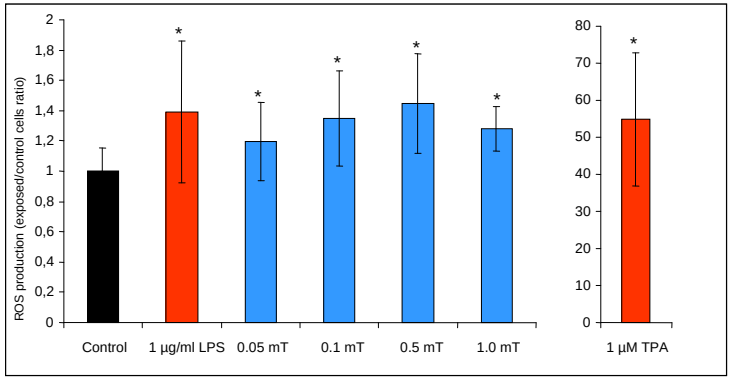
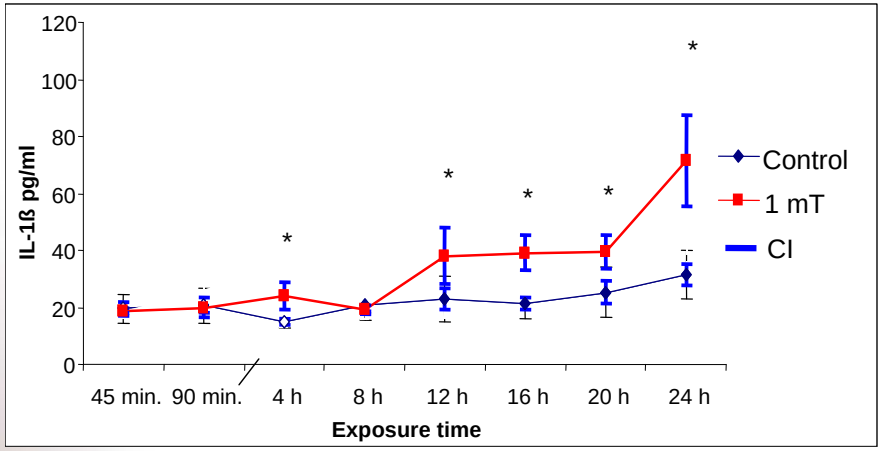
Phagocytic activity



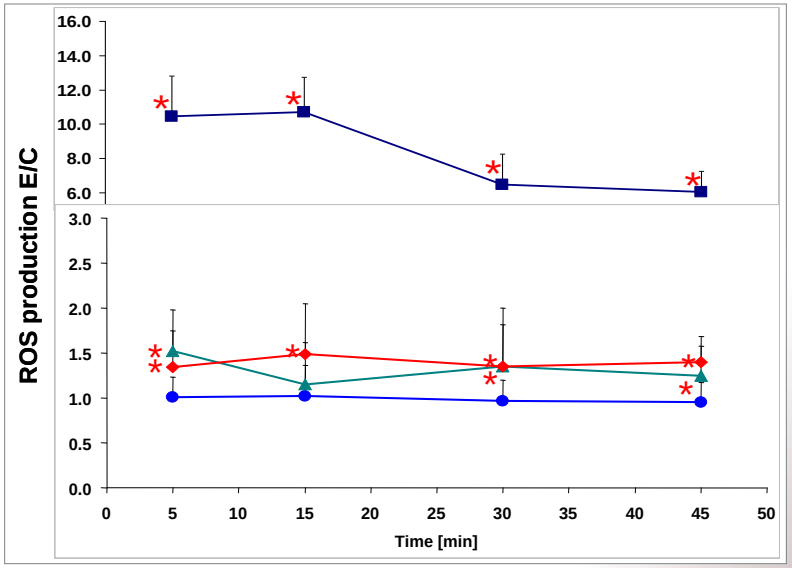
ROS production



Interleukin-1ß release

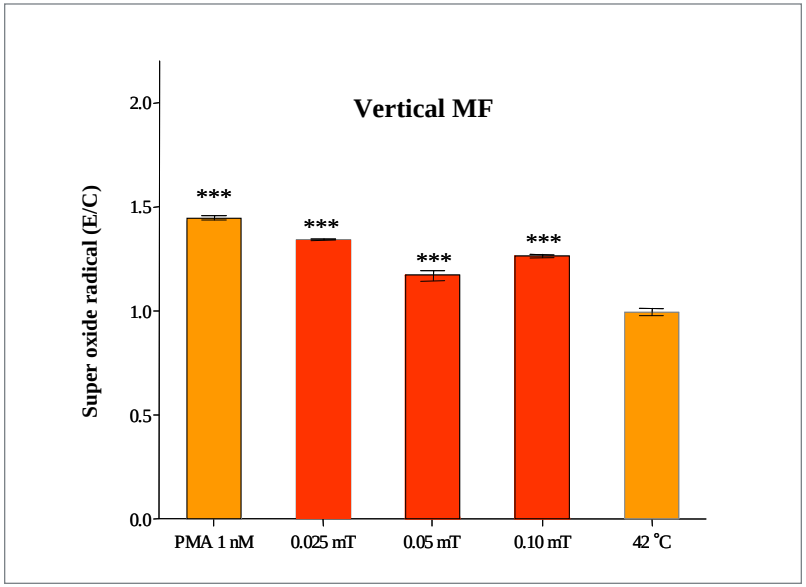


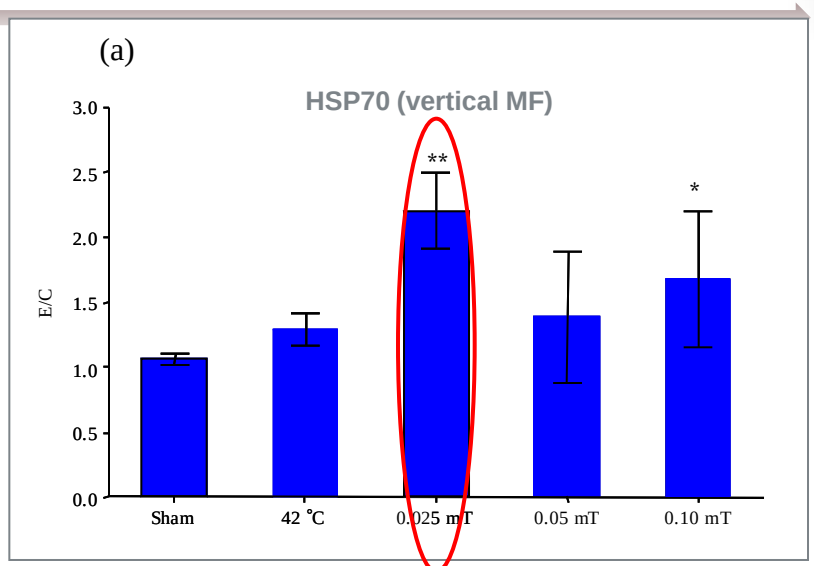
Time independent ROS production

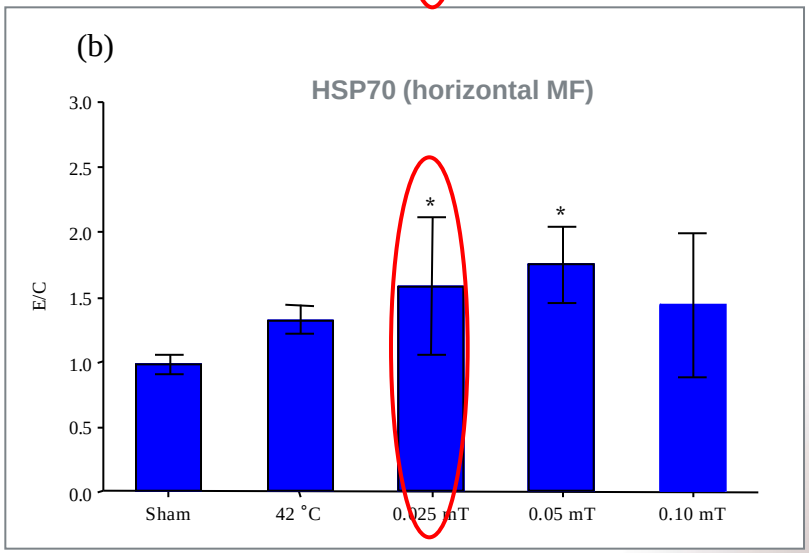


HSP70 protein in K562 cells

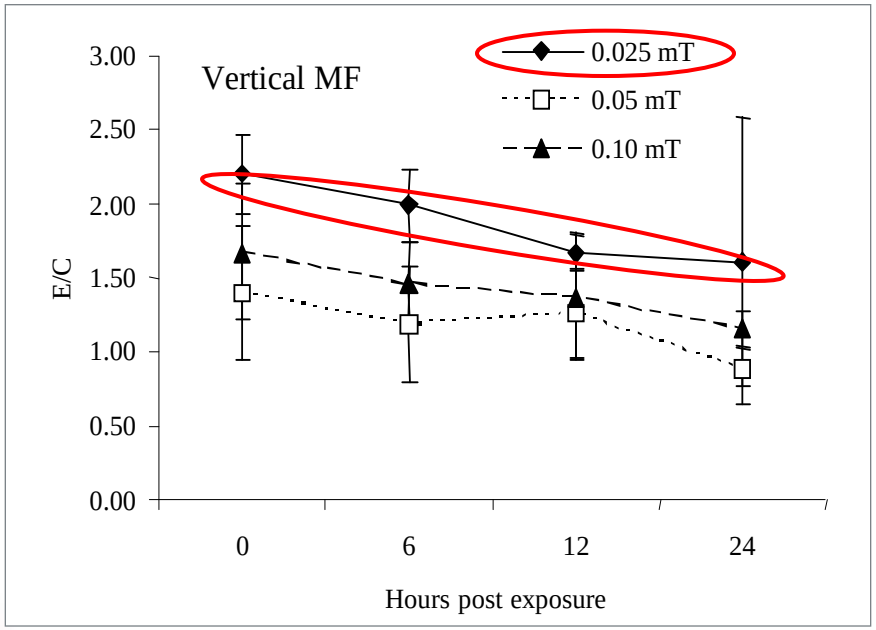
(1 h, 50 Hz MF)

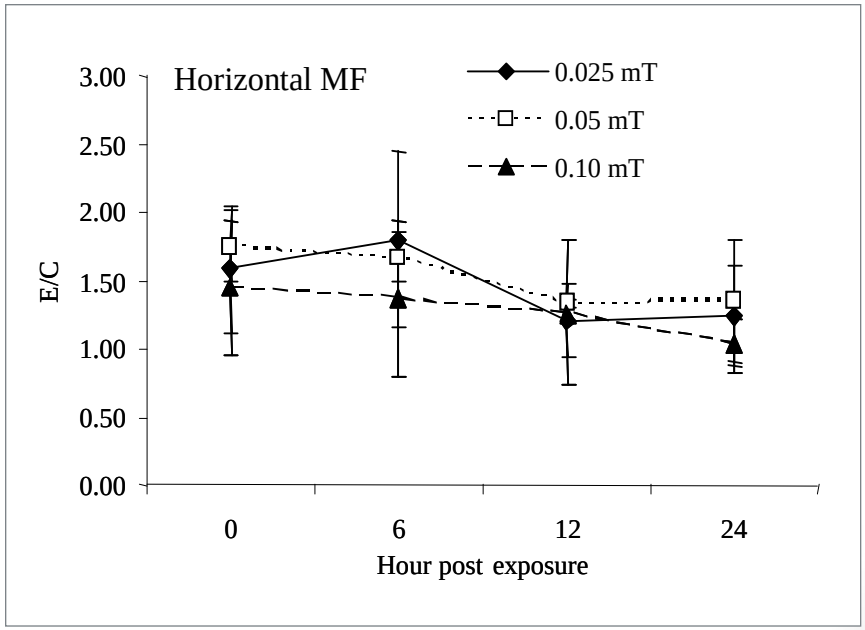






HSP70 protein in K562 cells post exposure





Free radical and HSP70 in the presence of antioxidants

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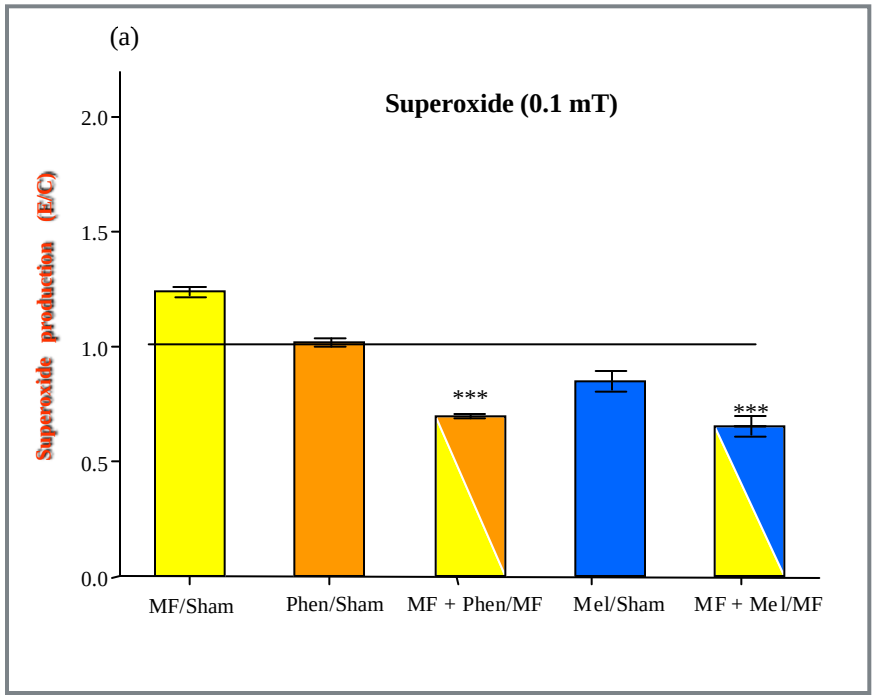
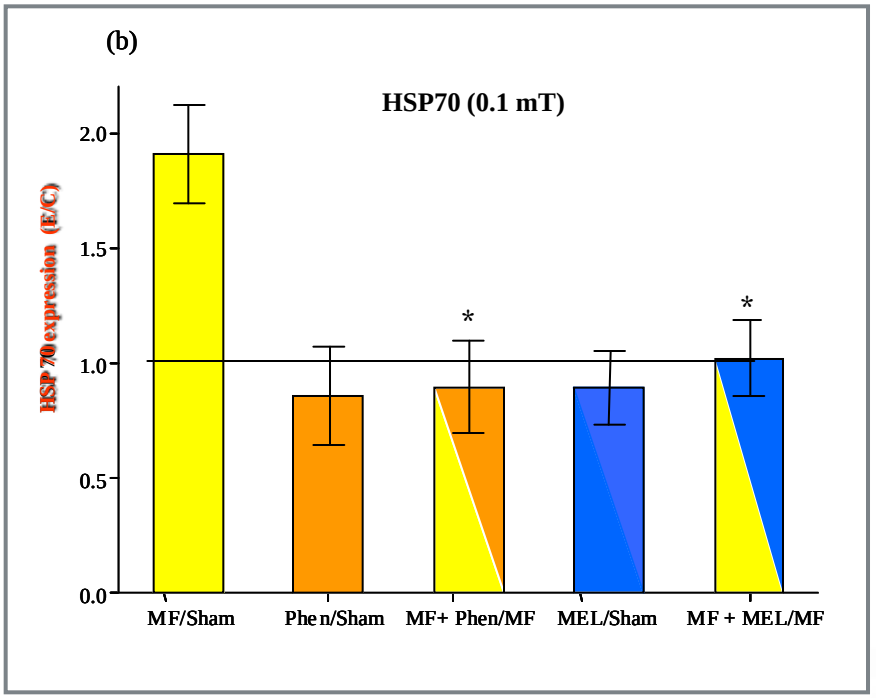
in K562 cells





1,10-phenantroline (Phen; 1 mM) and melatonin (Mel; 1.5 µM) were added 1 h prior exposure

Phen: iron chelator, scavenging the formation of OH radicals from H_2O_2

Mel: peroxyl radical scavenger

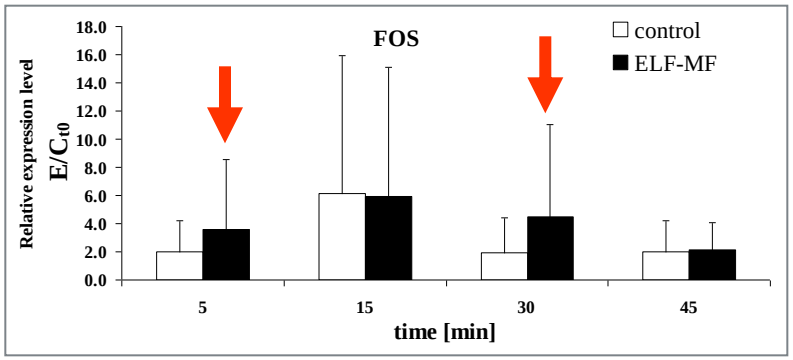
Changes on expression

Protein (ca. 1000 anti bodies)	
ca. 150 regulated proteins	
40 up regulation	110 down regulation

RNA (75.000 clones and 5356 fully annotated genes)	
ca. 1000 regulated genes	
66 up regulation	340 down regulation

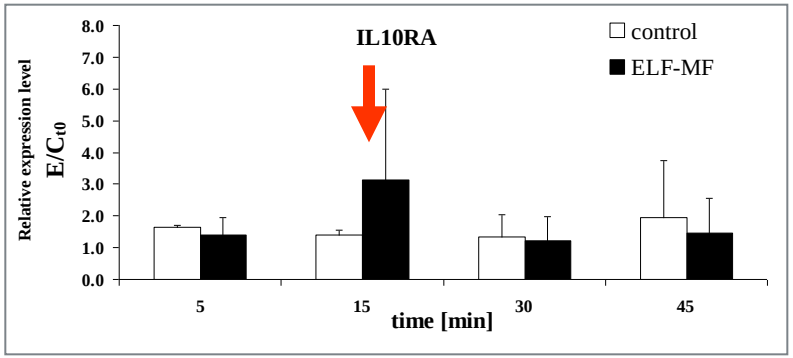
Gene expression – primary monocytes

1



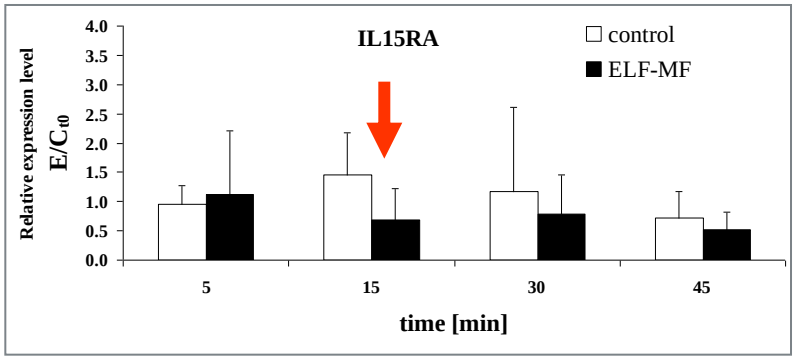
Transcription factor

2a



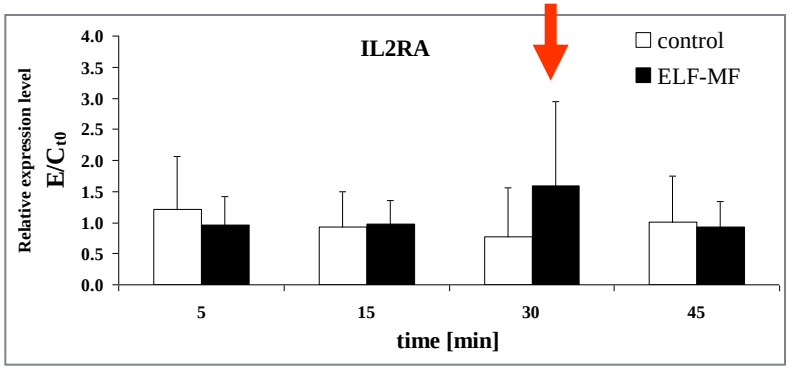
Anti inflammatory factor

2b



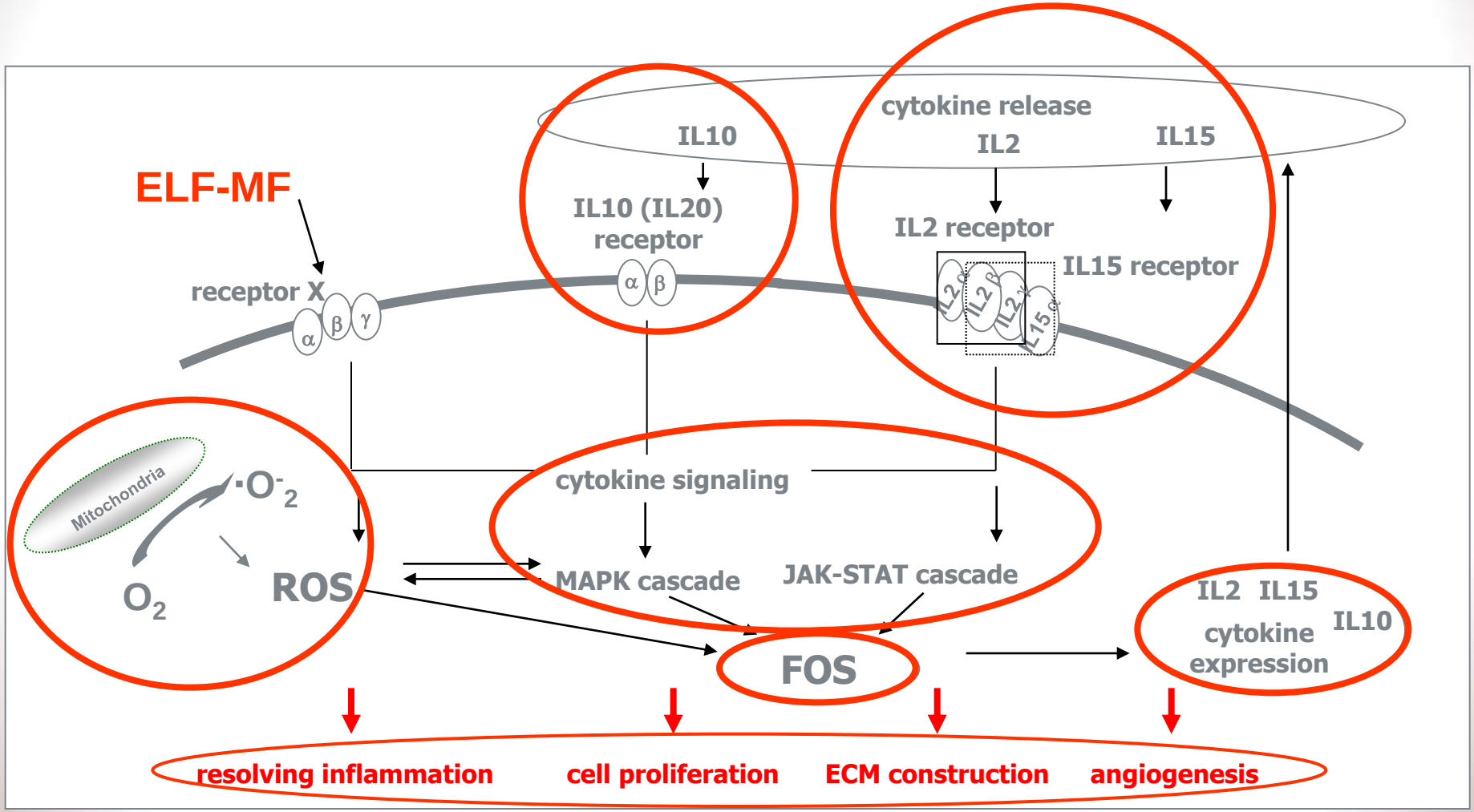
Positive regulation of inflammation

3



Associated with adaptive immunity

Alternative activation pathway



Monocyte / Macrophage activation

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Antigen-presenting phagocytes, secrete pro-inflammatory and antimicrobial mediators

Classically activated macrophages:

PROMOTES:

inflammation
extracellular matrix (ECM) destruction
apoptosis

phagocytosis → oxidative burst
tends to elicit chronic inflammation and tissue injury

Lectine dependent activation

Alternatively activated macrophages:

PROMOTES:

cell proliferation
ECM construction
angiogenesis

pinocytosis → free radical release
tends to resolve inflammation and facilitate wound healing

Summary of own results

- EMF induce immune cell activation: ROS, IL-1ß, phagocytosis, HSP70
- Seems to be cell type specific responses (different redox status, specific physiologic function), not in a general way
- ROS and HSP70 production: dose independency (flux density, time)
- Radical scavengers inhibit ROS and HSP70
- Modulation of the redox homeostasis leads to the activation of the **alternative pathway** in immune relevant cells

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PUBLIC HEALTH

HYPOTHESIS AND THEORY ARTICLE
published: 02 September 2014
doi: 10.3389/fpubh.2014.00132

Grouping of experimental conditions as an approach to evaluate effects of extremely low-frequency magnetic fields on oxidative response in *in vitro* studies

Mats-Olof Mattsson* and Myrtill Simkó

Environmental Resources and Technologies, Department Health and Environment, AIT Austrian Institute of Technology, Tulln, Austria

Edited by:
Dariusz Leszczynski, University of Helsinki, Finland

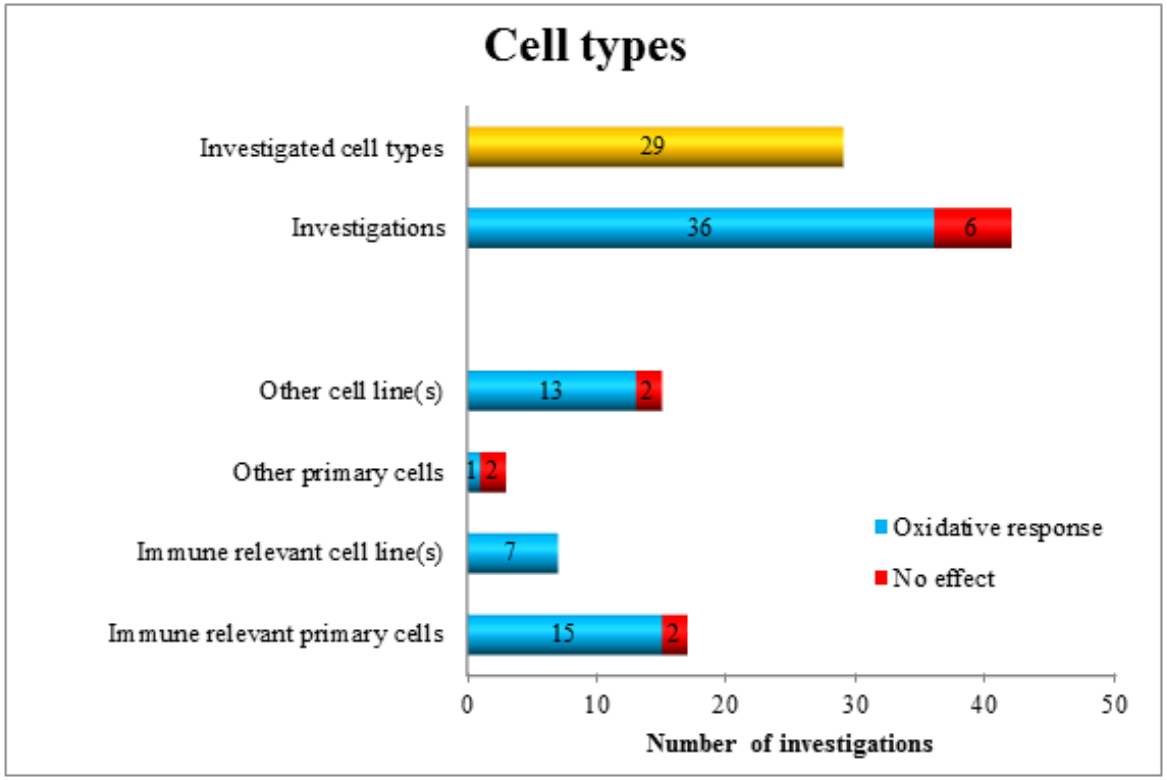
Reviewed by:
Rony Seger, Weizmann Institute of Science, Israel
Marko Markov, Research International, USA

****Correspondence:***
Mats-Olof Mattsson, Environmental Resources and Technologies, Department Health and Environment, AIT Austrian Institute of Technology, Konrad-Lorenz-Strasse 24, Tulln A-3430, Austria
e-mail: mats-olof.mattsson@ait.ac

A large body of literature deals with biological effects of extremely low-frequency magnetic fields (ELF MFs) studied *in vitro*. Despite the multitude of studies, no coherent picture has evolved regarding the plausibility of effects at low-flux densities or regarding the interaction mechanisms. Here, we propose that ELF MF exposure *in vitro* causes changes in oxidative status as an early response. We tested this hypothesis by scrutinizing the literature and applying a grouping approach for analyzing relevant biological properties and exposure conditions. A total of 41 scientific original publications were analyzed for this purpose. The conclusion from the work is that ELF MF (modulated or unmodulated) consistently can influence the oxidative status, at or above 1 mT, in a broad range of cell types and independent of exposure duration. A response at lower flux densities is seen in certain studies, although not consistently. Further studies with stringent protocols for sham exposure, blinding, and statistical analysis as well as appropriate positive controls are needed to establish if true dose-relationships for effects on oxidative status exist.

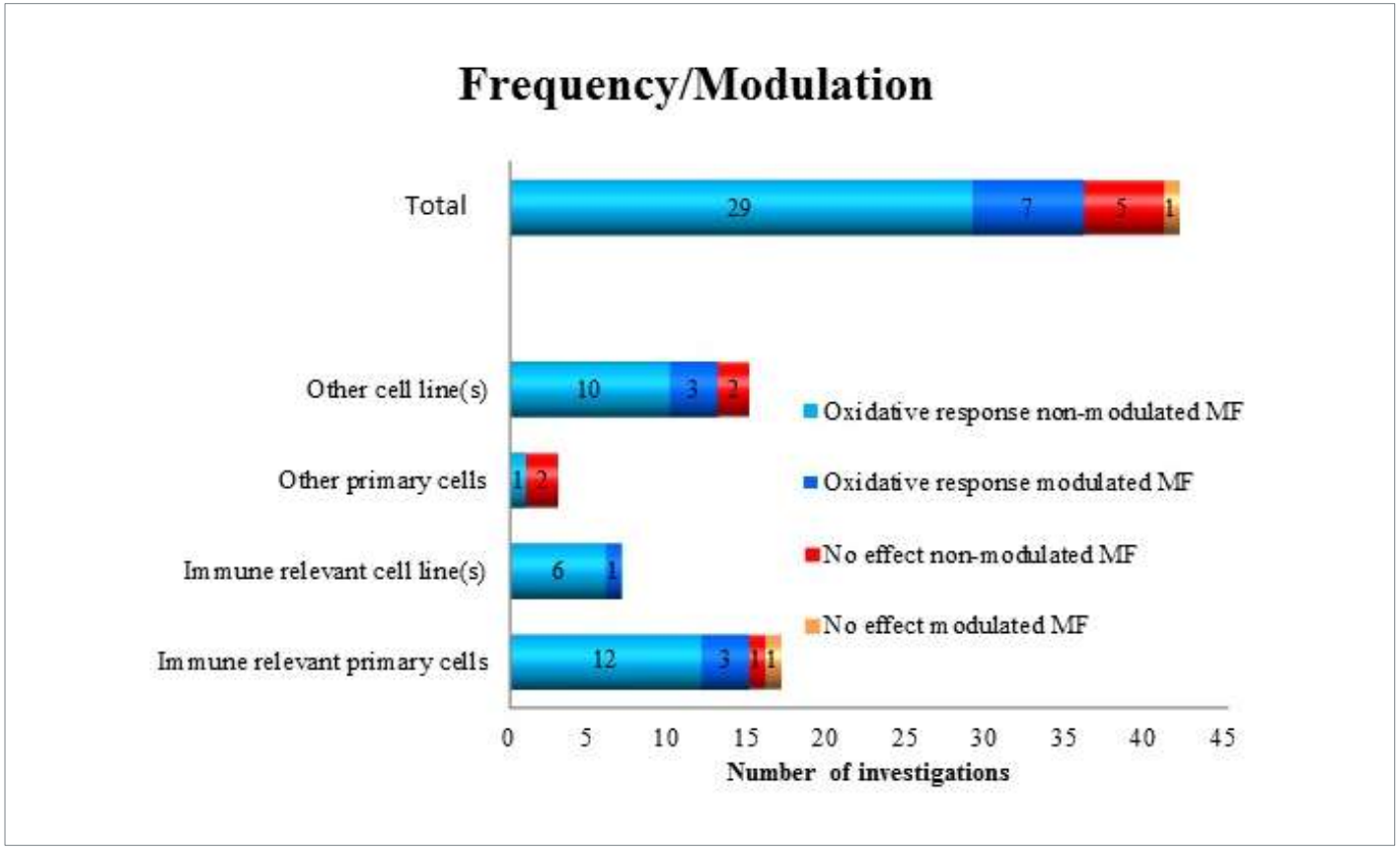
Keywords: mammalian cells, immune-relevant cells, flux density, exposure duration, ROS

Grouping approach



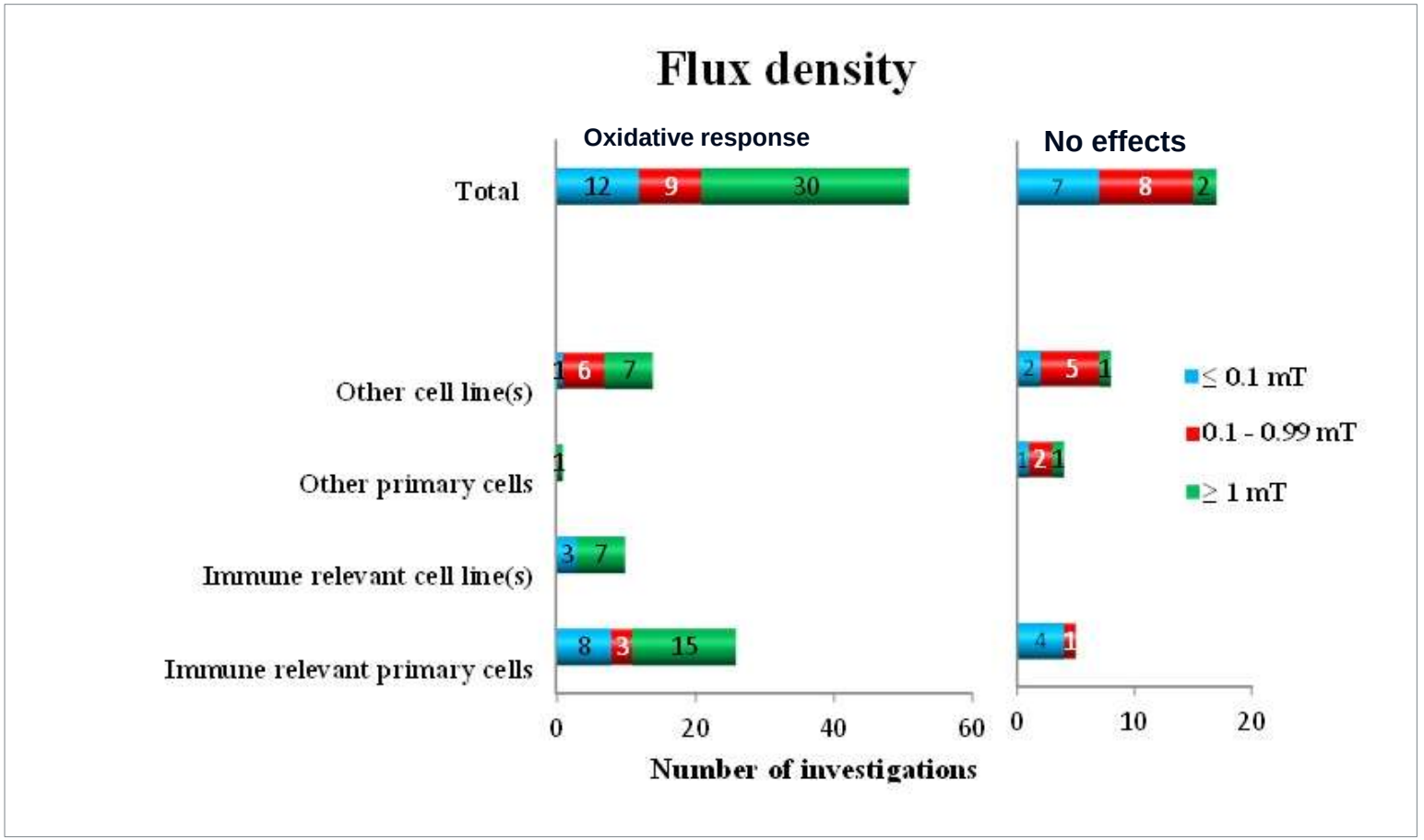
Seem not to be cell type dependent

Grouping approach



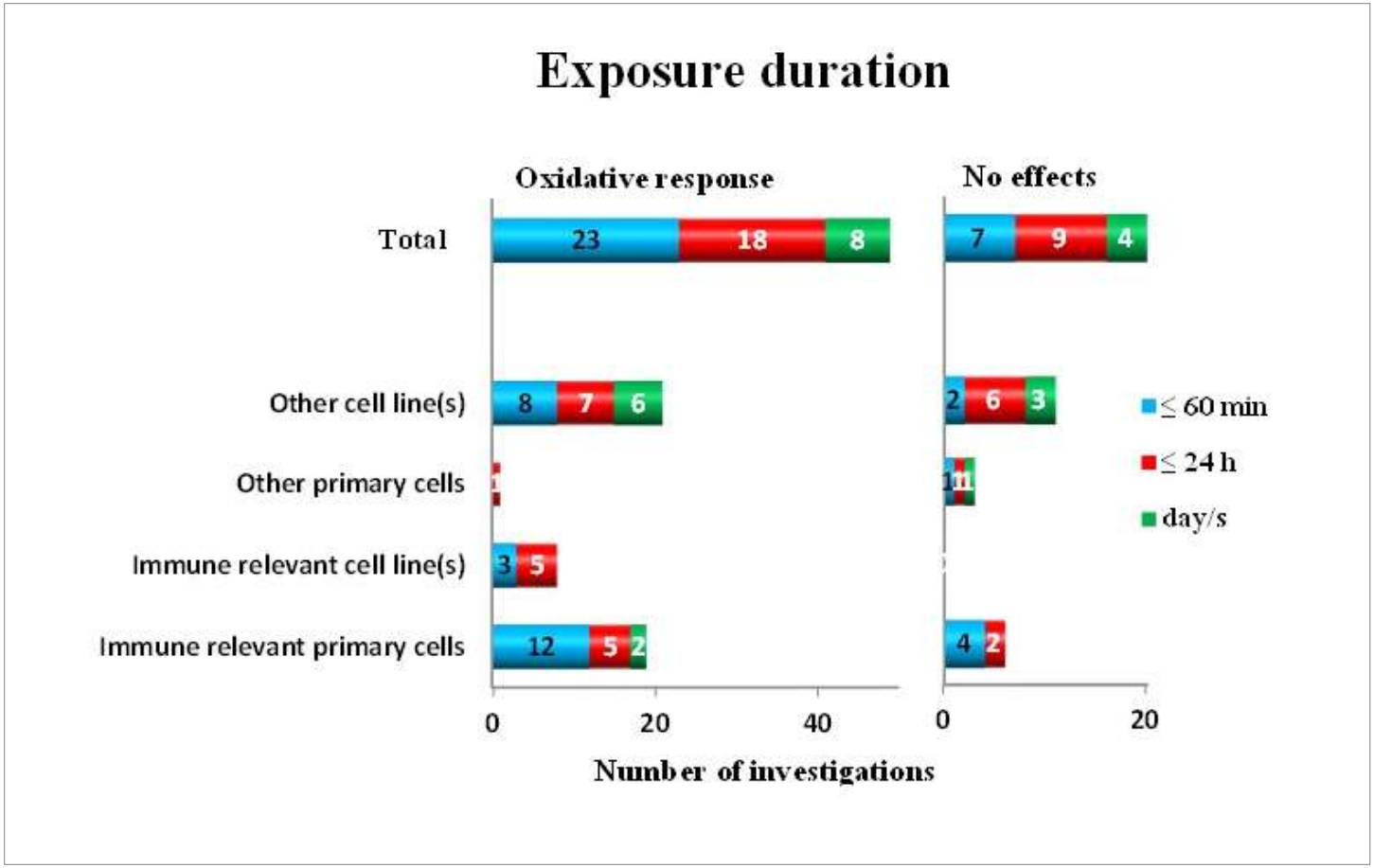
Seem not to be frequency/modulation dependent

Grouping approach



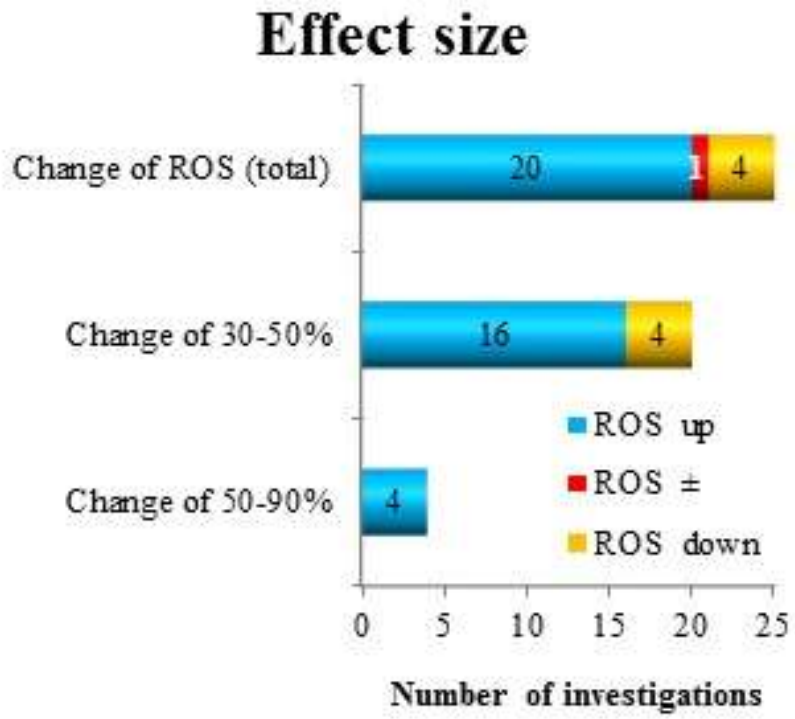
Seem to be flux density dependent

Grouping approach



Seem not to be exposure duration dependent

Grouping approach



Summary and objectives

- The interface between physics and biology is still unclear
- It might be on the membrane, on receptor(s) or at other cell organell(s), and/or in parallel
- MF seem to modulate cell specific oxidative responses which may depend on the cell´s metabolic state and redox potential state

- It is known that MF influence different medicinal related processes such as transcranial stimulation via MF, wound and bone healing, etc.
- There is a need to identify new areas of application (dental area: gingiva) and
- to specify targeted (optimization of exposure parameters) applications

The module goal

..is to focus on beneficial effects related to oxidative responses and modulation of immune system functions of EMF MF in order to

1) **provide a better understanding** of underlying physical and biological mode of action and

2) to contribute to the development of innovative EMF-based **medical treatment**.

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Thank you for your attention!