Identification and grouping of relevant experimental parameters to evaluate the effects of radiofrequency magnetic fields in *in vitro* studies (GROUPER)

Introduction: The scientific literature contains numerous experimental studies about biological effects after exposure to radiofrequency electromagnetic fields (RF-EMF), reporting various biological effects (see e.g. Progress report from WHO International EMF project or the comprehensive overviews in the opinions of SCENIHR 2007, 2009). The outcome of the studies is very diverse and the relevance of the results is unclear. Based on the literature, a correlation to any kind of disease development is relatively vague. Usually review studies are not able to compare the available data, due to the large complexity of the applied exposure conditions and biological systems. Therefore we aim to perform the project "Identification and Grouping of relevant experimental parameters to evaluate the effects of radiofrequency magnetic fields in *in vitro* studies" (GROUPER) which can contribute to a better understanding of RF-EMF exposure and cellular response(s).

Objectives: The project GROUPER will focus on the identification of relevant parameters used in RF-EMF related *in vitro* studies to identify so called "groups" for data evaluation. The main objectives of project are therefore 1) the identification of a relevant group of biological endpoints representing a cell physiological response such as "cell living" including cell proliferation and apoptosis, and 2) the use of the "grouping approach" to exposure and experimental parameters (see: Mattsson and Simkó, 2014). The main focus however will be on the data evaluation, to detect, if any causative association exists between RF-EMF and cellular responses. Using a systems-biology-network-analysis-method we think that these data will enable a more complex correlation-analysis between cellular response(s) and experimental parameters used. Furthermore this data evaluation allows an independent and unbiased execution of the study. We believe that the proposed GROUPER project represents a unique and timely opportunity for the application of an up-to-date approach to identify relevant correlation(s) between RF-EMF exposure and cell responses.

Methods: Here, we propose that RF-EMF exposure in vitro causes changes in "cell living" related biological endpoints. Therefore we want to test this hypothesis by scrutinizing the literature and applying clearly defined quality criteria (see Zeni and Scarfi 2012), and applying a grouping approach for analyzing relevant biological properties and exposure conditions. The first group therefore will be the collection of "cell living" related effects such as cell proliferation, cell vitality, cell cycle control, cell death, apoptosis, and related endpoints on protein or DNA/RNA level. A further analysis will be to identify the applied cell types, exposure conditions (SAR, frequency, exposure time, co-exposure, etc.) and identify the quality of the studies (sham, p-value, etc.). The grouping approach and data analysis is planned to be performed by using a systems-biology-network-analysis-method in cooperation with Dr. D. Remondini, Physics and Astronomy Department, Bologna University, Bologna, and Dr. MR. Scarfi and CNR-IREA, Naples, Italy. It is planned to assign two M.Sc. students for the project.

Expected results: To our knowledge, the use of the grouping approach combined with a complex analysis method of the data has not been performed so far. Therefore we expect that the project will lead to a better understanding and estimation of RF-EMF exposure and cellular response(s). This in turn is a prerequisite for a science-based discussion of possible health effects of RF-EMF.

References:

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3.2 List of own recent and relevant publications

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7. Frahm, J., M.O. Mattsson, and M. Simkó, Exposure to ELF magnetic fields modulate redox related protein expression in mouse macrophages. Toxicology Letters, 2010. 192(3): p. 330-336.
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9. Ahlbom, A., et al., Possible effects of electromagnetic fields (EMF) on human health--opinion of the scientific committee on emerging and newly identified health risks (SCENIHR). Toxicology, 2008. 246(2-3): p. 248-250.
10. Simkó, M., Cell type specific redox status is responsible for diverse electromagnetic field effects. Current Medicinal Chemistry, 2007. 14(10): p. 1141-1152.