

RF and ELF-EMF: Gene-Pathway-Disease Analysis

Summary

Background: In the last 20 years, there has been an explosion in the technology that allows us to evaluate the molecular biology of mammalian cells, both in-vitro and in-vivo. Through genomics, proteomics, metabolomics and similar technologies, we have been able to develop interactomes that describe the interplay between the various components of the cell and their functional outcome. These interactomes generally describe all or parts of the metabolic and signal transduction pathways defined in cells. It is through these pathways that the everyday work of the cell is performed. Distortions in the functioning of these pathways will provide predictable changes in the cell that can eventually lead to disease and death.

Objectives: The objective of this project is to identify the cellular components that are modified by exposure to low and radiofrequency electric and magnetic fields (ELF and RF-EMF), link these components to their pathways and then use existing linkage between these pathways and disease to develop hypotheses regarding the potential for human disease under chronic exposure.

Methods: (1) A literature search will be used to identify studies that have already explored the ability of RF-EMF to alter gene expression, protein levels, etc. in mammalian cells. The genes and proteins involved will be cross-referenced to the human orthologs. Using pathway enrichment analyses (Subramanian et al. 2005; Thomas et al. 2009), the most commonly affected pathways will be identified. Using gene ontology databases (Barrell et al. 2009) and pathway-disease models (Goh et al. 2007; Gohlke et al. 2009) from the literature, these enriched pathways will be used to identify the most likely physiological impacts due to RF-EMF. (2) Based on the findings from (1), an appropriate human cell line will be cultured and exposed to multiple levels of RF-EMF at levels and durations suggested by the literature. RNA will be isolated from the cells, hybridized onto microarray chips and full genome scans performed using microarrays. (3) The microarray data will be appropriately normalized, then analyzed using the same pathway enrichment methods to verify that the literature-based pathways are being modified in the human cells.

Expected Results: This proposal is intended to guide further studies in laboratory models. It is hoped that by using these linked databases and a carefully designed microarray study, it will be possible to identify reasonably anticipated physiological changes in mammalian systems that could be linked to disease. If the work can show significant changes in critical cellular pathways, this would lead to hypotheses that can be further explored in murine models targeted to the anticipated pathway/physiological change to further study the impact in the whole animal.

References:

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