Impact of mobile communication signals on the regulation of neural differentiation

Abstract

Our project aims at studying possible effects of radiofrequency electromagnetic fields (RF-EMF) on neuronal differentiation and related cellular pathways known to be involved in neurodegeneration and associated diseases. Focusing on pathways playing a role in neuronal differentiation and degeneration, we will investigate RF-EMF effects on distinct neuronal cell populations before and during differentiation and identify molecular pathways involved in a hypothesis-free genomic approach as well as in a hypothesis-driven approach. These goals will be achieved by applying cell culture-based experimentations including neuron-like and neuronal stem/progenitor cells. Progression of differentiation and phenotypic characterization will be assessed by fluorescence microscopy of stem cell and neuronal markers combined with high-content analysis and evaluation of morphology (i.e. neurite outgrowth). These analyses will be complemented by the assessment of key players of cellular pathways (e.g. the ERK/MAP-K, PI3-K/Akt, Wnt/β-catenin) underlying the morphological changes such as neurite outgrowth in a quantitative manner (e.g. by Western blotting and FRET-biosensor). Mitochondrial dysfunction during neurodegeneration was shown to increase the production of reactive oxygen species (ROS). Oxidative stress is a frequent early condition in the pathogenesis of neurodegenerative diseases, is often observed in cells upon EMF exposure and has an evident potential to compromise genetic as well as epigenetic stability. Mitochondrial integrity, an important indicator of neuronal aging and degeneration will be investigated quantitatively.
To assess the impact of RF-EMF exposure on the composition and behavior of the differentiating neural cell population, gene expression profiling (transcriptome) of single cells before and after differentiation will be performed. Cluster analysis of gene expression profiles will describe the dynamics of the cell population and potentially result in the identification of target regions with altered epigenetic modifications. Target-specific quantitation of DNA methylation and histone modifications at regulatory elements (promoter, enhancer) of identified genes, markers of neural stem cell and the neuronal lineage will be analyzed by pyrosequencing of bisulfite-converted DNA and by chromatin immunoprecipitation (ChIP).
This project will provide a significant and critical insight into the adverse effects of exposure to modulated RF-EMF as used for mobile communication (GSM) on signaling cascades and physiology as well as on morphological and epigenetic characteristics of neural cells *in vitro*.