



Biological effect of the 50 Hz Magnetic Field in a three-dimension (3D) in vitro experimental model of SH-SY5Y human neuroblastoma cells

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Extended Abstract

The culturing of primary neurons and neuronal-like cancer cells on conventional two-dimensional (2D) surfaces is the mainly used in vitro experimental model for both oncologic and neurodegenerative disorders. The limitations of such growing conditions are recently emerging, as 2D cultures lack the complex anatomical and functional connectivity of the neuronal network [1-3]. To provide a more physiological structural and biochemical system that more closely resemble the in vivo environment, different three-dimensional (3D) matrices have been exploited, including microporous polystyrene scaffolds, fibrin matrices, agarose, matrigel and collagen hydrogels [4-6]. Comparisons of cell growth in standard 2D monolayer cultures and 3D matrix have shown clear phenotypic differences in cellular surface area, stress fiber distribution, cellular migration and adhesions, neurite growth and dimensions, protein and gene expression, and epigenetics [7,8]. We here characterized the response to the extremely low frequency (ELF) magnetic field (MF, 50 Hz, 1 mT) of SH-SY5Y human neuroblastoma cells, cultured in a three-dimensional (3D) Alvetex® scaffold compared to conventional two-dimensional (2D) monolayers.

We proved that the growing phenotype of proliferating SH-SY5Y cells is not affected by the culturing conditions, as morphology, cell cycle distribution, proliferation/differentiation genes expression of 3D-cultures overlap what reported in 2D plates. In response to 72h exposure to 50 Hz MF, we demonstrated that no proliferation change and apoptosis activation occur in both 2D and 3D cultures. Consistently, no modulation of Ki67, MYCN, CCDN1 and Nestin, of neo-angiogenesis-controlling genes (HIF-1 α and VEGF), and of microRNA epigenetic signature (miR-21-5p, miR-222-3p and miR-133b) is driven by ELF exposure. Conversely, intracellular glutathione content and SOD1 expression are exclusively impaired in 3D-cultures cells in response to the MF, whereas no change of such redox modulators is observed in SH-SY5Y cells if grown on 2D monolayers.

Moreover, ELF-MF synergizes with the differentiating agents to stimulate neuroblastoma differentiation into a dopaminergic (DA) phenotype in the 3D-scaffold culture only, as growth arrest and induction of p21, TH, DAT and GAP43 are reported in ELF-exposed SH-SY5Y cells exclusively if grown on 3D scaffolds.

As overall, our findings prove that 3D culture is a more reliable experimental model for studying SH-SY5Y response to ELF-MF if compared to 2D conventional monolayer, and put the bases for promoting 3D systems in future studies addressing the interaction between electromagnetic fields and biological systems

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