The anti-proliferative effects of RF EMF amplitude-modulated at tumor-specific frequencies are mediated by calcium


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Introduction

Whole body radiation of low-level radiofrequency electromagnetic fields, amplitude-modulated (AM RF EMF) at specific frequencies ranging from 400 Hz to 21 kHz has efficacy in advanced hepatocellular carcinoma (HCC) (Costa et al. 2011) and may be used for cancer diagnosis (Abstract # 15607). In vitro studies demonstrate that AM RF EMF treatment inhibits cancer cell growth in a tumor-specific manner (Zimmerman et al. 2012). RNA-seq and microRNA analysis of HCC cells treated with AM RF EMF reveal altered expression of several mRNAs belonging to the IP3/DAG signaling pathway. Given the central modulatory effect of calcium in this pathway, we hypothesized that calcium modulates the growth inhibitory effect of RF EMF.

Methods

AM RF EMF exposure in vivo: Cell lines were exposed to 27.12 MHz radiofrequency electromagnetic fields using exposure systems designed to replicate in vivo exposure levels. Experiments were conducted at an SAR of 0.03 and 0.4 W/kg. Cells were exposed for three hours daily, seven days in a row. Cells were exposed to tumor-specific modulation frequencies previously identified in patients with a diagnosis of Hepatocellular Carcinoma or modulation frequencies never identified in patients with a diagnosis of cancer (Zimmerman et al. 2012). Huh-7 cells were cultured in the presence or absence of BAPTA, a Ca$^{2+}$-chelator, for three consecutive hours daily, seven days in a row. Proliferation was measured by triptetamidine (TH) assay.

Anti-proliferative effects of HCC-specific AM RF EMF in the presence or absence of BAPTA. Huh-7 cells were treated with randomly-chosen or HCC-specific frequencies in the presence or absence of BAPTA. Randomly-chosen frequencies compared to HCC-specific group in the absence of BAPTA is statistically significant (p = 0.0001). HCC-specific compared to HCC-specific + BAPTA is statistically significant (p = 0.0034). Randomly-chosen frequencies compared to randomly-chosen frequencies + BAPTA was not significantly different (p= 0.0952). Quantification of tryptetricamidine incorporation assay shows the average of two different experiments. Statistical analysis was performed 2-way ANOVA; groups were compared using post-hoc pairwise comparison.

Conclusions

• IP3/DAG pathway is inhibited by tumor-specific AM RF EMF.
• S100B mRNA is significantly decreased in HCC cell lines exposed to HCC-specific AM RF EMF.
• Ca$^{2+}$-chelation abrogates the AM RF EMF induced proliferative inhibition of HCC cells.
• Ca$^{2+}$ signaling is involved in mediating the effect of AM RF EMF induced proliferative inhibition in Hepatocellular Carcinoma cell lines.
• The growth of Huh-7 tumor xenografts is significantly inhibited by HCC-specific AM RF EMF.
• There is no difference in the growth of Huh-7 xenografts exposed to randomly chosen frequencies or not exposed to any AM RF EMF.

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References