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Pulse power ablation of melanoma and hepatocellular carcinoma with nanosecond pulsed electric fields

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Pulsed power technology with nanosecond pulsed electric fields (nsPEFs) ablates tumors by instantaneously releasing high power (~180MW), low energy (mJ/cc) stored electric fields into cells or tissues. Different than conventional electroporation, this technology uses 20-100ns pulses and electric fields of 50-60 kV/cm. NsPEFs eradicated B16f10 melanoma (95-100%) and Hepa1-6 hepatocellular carcinoma (HCC) (75%) in ectopic mouse models and N1S1 HCC (90-100%) in a rat orthotopic model; however, mechanisms of tumor death require closer analysis. Three to six hours after treatment, there were transient peaks of tumor cells that exhibited active caspases, H2AX phosphorylation, TUNEL and pyknotic nuclei. Although large DNA fragments were present, fragmentation by DNA ladder formation was not readily observed. Clearly, apoptosis in tumor cell masses cannot be equivalent to apoptosis during homeostasis. Tumor weight and volume decreased progressively after the first day due in part to apoptosis induction, anti-vascular effects and tumor infarction. One week post-pulse, levels of VEGF and PD-ECGF were significantly reduced. In addition, vessel numbers as surrogate for microvascular density dramatically decreased as did VEGF and down-stream microvascular density markers, CD31, CD35 and CD105, all indicating anti-vascular effects as a significant detriment to tumorigenesis and metastasis. The activation of caspase-associated apoptosis, anti-vascular effects, tumor infarction and inhibition of revascularization demonstrate that nsPEFs recruit at least two dominant cancer therapeutic targets with a single treatment modality and explain, at least in part, the success of nsPEF application for tumor treatment in vivo as a new cancer therapeutic modality.

Biography

Stephen J. Beebe, molecular cell biologist / biochemist received his PhD in 1982 from the Medical College of Ohio, (now the Medical School at University of Toledo) in Medical Sciences (Pharmacology/ Biochemistry). He was a post-doctoral fellow at the Howard Hughes Medical Institute and Department of Molecular Physiology and Biophysics at Vanderbilt University, Nashville Tennessee. He was Fulbright Scholar at the University of Oslo, Norway at the National Hospital and Department of Medical Biochemistry before taking a position as Assistant Professor in the Jones Institute for Reproductive Medicine and then an Associate Professor in the Department of Physiological Science and the Center for Pediatric Research at Eastern Virginia Medical School in Norfolk, Virginia. He is now a Professor at Old Dominion University in the Frank Reidy Research Center for Bioelectrics in Norfolk Virginia.

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