Stephen J. Beebe, J Cell Sci Ther 2011, 2:4
doi: http://dx.doi.org/10.4172/2157-7013.S1.02

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cell Science & Stem Cell Research

29 Nov - 1 Dec 2011 Philadelphia Airport Marriott, USA

Nanosecond Pulsed Electric Fields (nsPEFs) induce Apoptosis via Mitochondrial Intrinsic Pathway in Jurkat cells

Stephen J. Beebe
Old Dominion University, USA

Nanosecond pulsed electric field (nsPEF) ablation induces apoptosis markers in several cell types, but cell death pathways have not been fully defined. To define extrinsic or intrinsic apoptosis mechanisms we investigated wildtype human Jurkat cells (WT) and mutants with deficiencies in FADD or caspase-8. While Fas receptor activation resulted in cell death in WT only, nsPEFs induced cell death (~90%) in these clones with identical electric field dependences. Under lethal conditions there were immediate (≤1 min) increases in propidium iodide uptake, Annexin-V-binding, calcium mobilization and a decrease in mitochondria membrane potential ($\Delta\Psi m$). The $\Delta\Psi m$ occurred even with absences of calcium or sodium ions and was insensitive to overexpression of Bcl-2 or Bcl-xl. Bid cleavage, but not cytochrome c release, was attenuated by inhibition of caspases and calpains. Caspase isozymes were selectively activated (-9>-3>>-8) and late appearances of Histone 2AX phosphorylation and TUNEL-positive cells were caspase-dependent. Electric field-dependent cell death was attenuated in APAF-1 deficient Jurkat cells, which did not express active caspase-9 or -3 or exhibit DNA damage, but was unaffected by cathepsin B inhibitors. Taken together, these data indicate that mitochondria are primary targets of nsPEFs, which immediately decrease $\Delta\Psi m$, leading to cytochrome c release, intrinsic apoptosome-mediated caspase activation with down-stream calpain- and caspase-mediated Bid cleavage and caspase-dependent DNA damage. These results indicate an unabated impact of nsPEFs on Jurkat cell mitochondria and caspase-dependent cell demise at lower electric fields with additional, undefined cell death mechanisms at higher electric fields. These findings have important implication for nsPEF ablation of cancer.

Biography

Stephen J. Beebe received his PhD (1982) in Medical Sciences from the Medical College of Ohio, (now University of Toledo- College of Medicine). He was a post-doctoral fellow at the Howard Hughes Medical Institute and Department of Molecular Physiology and Biophysics at Vanderbilt University, Nashville. He was Fulbright and Marshall Scholar at the University of Oslo, Department of Medical Biochemistry and National Hospital before becoming an Assistant and Associate Professor in Department of Physiological Sciences and Pediatrics 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.