allied academies

12th World Cancer Congress

July 23-25, 2018 | Moscow, Russia

Stephen J Beebe[1]

Brittany Lassiter[2]

Siqi Guo[3]

Old Dominion University, USA

Translational research with nanosecond pulse stimulation for Immuno-Oncology applications

Nano-Pulse Stimulation (NPS) is a technology based on pulsed power physics, used for decades in high-powered physics and military applications. Electrical energy is stored and released in nanosecond bursts, producing instantaneous high power and low, non-thermal energy. Since biological cells have not experienced NPS in evolutionary history, they can exhibit unique intracellular responses. At NPS levels cells undergo programmed cell death (PCD) and induce innate and adaptive immune mechanisms while at low NPS levels cells can be stimulated and activated. The transition of this technology from physics scenarios to biologic and medical landscapes uniquely combines expertise from engineers, physicists, biologists and physicians.

Our NPS strategy uses 60-100 ns pulse durations and electric fields up to 50 kV/cm. When orthotopic mouse mammary and rat liver tumors are eliminated by NPS, animals are protected by an immune-mediated, vaccine-like effect against the same cancer. Immune responses are dynamic on several therapeutic fronts. NPS directly eliminates primary tumors by inducing regulated form(s) of immunogenic cell death. This is accompanied by specific activation of natural killer cells and NKT-cells expressing NKG2D and CD161 activation receptors. In addition, dendritic cells (DCs), which are activated by dead and dying cancer cells, induce cytotoxic T-cells expressing adaptive memory phenotypes. Importantly, NPS eliminates immunosuppressive cells in the tumor microenvironment and blood. In the mouse model, a strong abscopal effect occurs including reduction of spontaneous distant metastases and eradication of second untreated lesions.

Non-lethal NPS can activate DCs. NPS attenuates respiration in DCs and other cells by affecting electron transport chain complexes I and IV increasing superoxide anions in mitochondria, which activate DCs that express activation markers and cytokine secretion. Higher NPS induces opening of the permeability transition pore and induces PCD. How these and other intracellular NPS-induced mechanisms lead to ablation-induced immune responses is under investigation.

Speaker Biography

Stephen J Beebe is a Research Professor in the Frank Reidy Research Center for Bioelectrics at Old Dominion University (ODU). He received his PhD in Medical Sciences (Pharmacology) at the University of Toledo College of Medicine in 1982 and was a post-doctoral fellow at the Howard Hughes Medical Institute, Department of Molecular Physiology and Biophysics, Vanderbilt University School of Medicine. He was a Fulbright and Marshall Scholar in Oslo, Norway. He is the author of 125 peer reviewed manuscripts and books chapters. He was awarded two NIH grants analyzing structure and function of Protein Kinase A and cAMP signal transduction. He now investigates mechanisms of NanoPulse Stimulation (NPS) in cancer and biology. He has trained over 30 graduate students and post-doctoral fellows, is a member of Editorial Boards for four journals and is the Chair of the ODU Institutional Animal Care and Use Committee (IACUC).

e: sbeebe@odu.edu

Notes: