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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 impacts like this in evolutionary history, they can exhibit unique intracellular responses that are noteworthy and remarkable. Under high NPS conditions tumor cells undergo programmed cell death (PCD) and innate and adaptive immune mechanisms are activated. Under low NPS levels cells can be stimulated and activated. The transition of this technology from physics scenarios to biological and medical landscapes uniquely combines expertise from engineers, physicists, biologists and physicians.

NPS strategy for cancer treatment uses 60-100 ns pulse durations and electric field strengths up to 50 kV/cm. When orthotopic mouse mammary and rat hepatocellular carcinoma tumors are eliminated by NPS, animals are protected by an immune-mediated, vaccine-like effect against exposure to 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 subsets of CD8+ natural killer cells and NKT-cells expressing the 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, an abscopal effect occurs including reduced spontaneous distant metastases and eradication of second untreated lesions.

Non-lethal NPS can activate DCs. NPS attenuates respiration in dendritic cells (DCs) and other cells by affecting complexes I and IV in the electron transport chain (ETC) increasing levels of superoxide anions in mitochondria, which presumably activate DCs as indicated by expression of 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 are 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 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).

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