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Molecular effects of therapeutic ultrasound: Novel mechanisms and potential applications

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Therapeutic ultrasound has been in clinical practice for more than half a century. Original treatments involved lower energy exposures for healing in physical therapy. Today, focused ultrasound (FUS) exposures are being employed for thermal ablation of solid tumors. More recently, pulsed exposures have been investigated where heating is minimalized and nonthermal mechanisms generate mechanical effects that can enhance tissue permeability for improving the delivery of drugs and genes. In the majority of cases, investigations to develop these applications have involved gross morphology and histopathology. More recently investigators have been looking at molecular effects. Our investigations have moved forward for both FUS and non-FUS exposures. For FUS, upregulation of genes in tumors that could be associated with promoting metastasis and also be beneficial for immunotherapy has been identified. In skeletal muscle, enhanced levels of pro-inflammatory cytokines, trophic factors and adhesion molecules in response to treatments were characterized. Subsequently, showed how these effects can increase targeting of endothelial precursor cells to enhance perfusion in a model of peripheral arterial disease. A mechanism of mechano transduction mediated through localized strain, generated by a transfer of momentum has been proposed. For lower energy, non-FUS exposures, a novel mechanism based on the formation of gaps between lipid leaflets of cellular membranes due to pressure differentials of propagating sound waves is proposed. These may perturb transmembrane receptors and initiate signal transduction pathways. In this presentation, these mechanisms will be discussed, as well as potential new applications based on these unique interactions of ultrasound energy and biological tissues.

Biography

Victor Frenkel completed his PhD at the Technion, Israel Institute of Technology in 1999. After a post-doctoral fellowship at the University of Maryland Biotechnology Institute in Baltimore, he served as a staff scientist at the Dept. of Radiology and Imaging Sciences at the Clinical Center of the National Institutes of Health in Bethesda, Maryland. His research is focused on the understanding of ultrasound interactions with biological tissue, and using this knowledge to propose novel applications in oncology, cardiovascular disease and cellular therapy.

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