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Enhanced inner ear drug delivery assisted by ultrasound-aided microbubbles

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Sensorineural Hearing Loss (SNHL) can result from multiple causes, including aging, infection, noise exposure, ototoxic drugs, and immune-mediated inflammation. Clinical therapeutic strategies for SNHL may involve pharmaceutical medications, acoustic sound amplification, or implantable surgical devices. Pharmaceutical approaches are always considered as the first choice in treating hearing disorders, and most of them are prescribed as systemic delivery. However, the systemic medication route has limitations because the blood–cochlea barrier can limit inner ear drug absorption or penetration and because undesirable systemic side effects are possible. One alternative to the systemic route is delivered via the Round Window Membrane (RWM), which, because of its exposure to the middle ear, can serve as a viable route for delivery of therapeutic medications to the inner ear via middle ear applications. Intratympanic injection therapies are now widely applied for the treatment of several hearing disorders; however, the therapeutic responses vary for ambiguous reasons. We have targeted the practical application of Ultrasound Microbubbles (US-MBs) to increase the RWM permeability, thereby facilitating medication delivery to the inner ear. Using guinea pigs as animal models, we showed that US-MB exposure can provide a 38-fold improvement of the inner ear absorption of biotin–FITC applied through the RWM when compared to spontaneous absorption. Cochlear hair cell uptake of gentamicin was also significantly enhanced using US-MBs. We also confirmed an increased permeability of the RWM in response to the acoustic cavitation effects of MBs by showing the passage of the tracer through the three-layered structure of the RWM. The US-MB approach did not damage the integrity of the RWM or cause any deterioration of the hearing thresholds, indicating a good safety margin. Our recent work now focuses on facilitating inner ear gene delivery using US-MBs. We believe that US-MB-mediated techniques have great potential for use in delivery of therapeutic medication or genes to the inner ear in future clinical applications.

Biography

Chih-Hung Wang is a professor of Otolaryngology-Head and Neck Surgery at the National Defense Medical Center, Taipei, Taiwan. He received his MD and PhD degrees from the National Defense Medical Center. After completing his doctoral degree, he completed a postdoctoral course with Prof Yehoash Raphael at Kresge Hearing Research Institute and a visiting fellowship course with Dr Steven A Telian at the Department of Otolaryngology-Head and Neck Surgery, University of Michigan, in 2003–2004. His main research interest is in otology, focusing on developing strategies for inner ear protection and repair, including stem cell and gene therapy topics. He has also previously served as the director of the Department of Otolaryngology-Head and Neck Surgery, Tri-Service General Hospital, Taipei, Taiwan. He was promoted to major general on 1st July 2016 and served as the director of Medical Affairs Division, Army Logistics Command, and ROCA...

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