Cell membrane poration by microbubble oscillation

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Despite the great potential of sonoporation as a promising drug delivery technique in medicine, its applications have been limited mostly by the lack of understanding the underlying biophysical mechanism.

We introduced a new method for capturing real time highly magnified images of cell–microbubble interaction and present an analytical analysis of the interaction.

Key words: Sonoporation, Drug delivery, Cell membrane, Microbubble

Ultrasound contrast agent microbubbles have contributed as an important tool in different areas of diagnostic ultrasound. Among newly emerging areas of therapeutic ultrasound, one of the most interesting has been ultrasound-microbubble assisted drug/gene delivery. Combination of ultrasound and contrast agent microbubbles is believed to alter the cell membrane permeability [1], causing transient formation of pores in the membrane, known as sonoporation [2]. Increased uptake of drug/gene by insonated cells at the presence of microbubbles has led to intensive acoustical and optical study of microbubble behavior in different ultrasound intensity levels. Although little is known about the biological mechanism of sonoporation, it is generally accepted that nonlinear oscillation/inertial cavitation of microbubbles under high acoustic pressures can produce jet phenomenon which causes damages in the cell membrane of the sonicated cells [3]. Microstreaming of microbubbles oscillation has been suggested as a favorite mechanism for sonoporation [4,5].

Despite the great potential of sonoporation as a promising drug delivery technique in medicine, its applications have been limited mostly by the lack of understanding the underlying biophysical mechanism, partly due to the inadequacy of the existing models for coupling with highly sensitive imaging techniques to directly observe the actual precursor events of cell–microbubble interaction under low intensity ultrasound.

We introduced a new in-vitro method utilizing capillary-microgripping system and micro-transducer to achieve the maximum level of experimental flexibility for capturing real time highly magnified images of cell–microbubble interaction [6]. Insonation of single cells and microbubbles parallel with high speed microphotography and fluorescence microscopy allowed us to identify dynamic responses of cell-membrane/microbubble in correlation with sonoporation. Our results showed that linear bubble oscillation in close contact with the cell membrane can cause local deformation and transient porosity in the cell membrane without rupturing it.

References


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