Molecular bioeffects of low intensity ultrasound: apoptosis and gene expression

Kondo, Takashi\textsuperscript{1}, Tabuchi, Yoshiaki\textsuperscript{2}, Takasaki, Ichiro\textsuperscript{2}, Feril, Loreto B. Jr\textsuperscript{3}, Tachibana, Katsuro\textsuperscript{3}, Kudo, Nobuki\textsuperscript{2}, Zhao, Qing-Li\textsuperscript{1} and Ogawa, Ryohei\textsuperscript{1}

\textsuperscript{1}Department of Radiological Sciences, Graduate School of Medicine and Pharmaceutical Sciences, \textsuperscript{2}Division of Molecular Genetics, Life Science Research Center, University of Toyama, Toyama, Japan \textsuperscript{3}Department of Anatomy, Fukuoka University School of Medicine, Fukuoka, Japan,

\textsuperscript{4}Laboratory of Biomedical Instrumentation and Measurement, Graduate School of Information and Technology, Hokkaido University, Sapporo, Japan

Recently, we have reported that therapeutic ultrasound (US) (1 MHz, continuous waves) can induce apoptosis in human lymphoma U937 cells, and that extracellular reactive oxygen species due to inertial cavitation are not directly correlated with this event and intracellular calcium ions and reactive oxygen species play important roles in apoptosis induced by US [1, 2]. In addition, when change of gene expression was examined, v-jun avian sarcoma virus 17 oncogene homolog, and heme oxygenase 1 (HO-1) were identified as up-regulated genes and v-myb avian myeloblastosis viral oncogene homolog and cathepsin G as down-regulated genes [3]. However, the molecular mechanisms of apoptosis and change of gene expression induced by low-intensity pulsed US is not yet entirely clear. Here the molecular aspect induced by 1 MHz pulsed US modulated at 100 Hz (10% duty factor), on apoptosis and changes of gene expression in human leukemia cell lines were investigated. Free radical formation was used as an endpoint of inertial cavitation. Apoptosis was examined morphologically, biochemically, and flowcytometrically. Gene expressions were evaluated by using real-time polymerase chain reaction, and cDNA microarray analyses. Formation of hydroxyl radicals and hydrogen atoms was found in the solutions exposed to pulsed waves. The results showed that pulsed US can induce apoptosis at intensities where no free radical was detected. The striking up-regulation of HO-1, a gene usually associated with the oxidative stress was observed in human lymphoma U937 cells [4]. On the other hand, when the gene expression of human leukemia Molt-4 cells was examined after sonication, BCL-2 associated athanogene 3 (BAG 3) and genes of heat shock proteins (DNAJBJ1, HSPA1B, and HSPA6) showed increased levels of expression while isopentenyl-diphosphate delta isomerase (IDH) and 3-hydroxy-3-methylglutaryl-coenzyme A synthase 1 (HMGCS1) showed decreased levels in the cells 3h after treatment [5].

We show current data on the apoptosis induction and its mechanism, the enhancement of apoptosis in the presence of an echo-contrast agent, and the change of gene-expression and its mechanism involved, particularly those induced by low intensity pulsed US [6].

Keywords: apoptosis, gene expression, cavitation, mechanical effects


NOTE: Replace all text in this document and do not change any sections.