Mechanism of rat osteosarcoma cell apoptosis induced by a combination of low-intensity ultrasound and 5-aminolevulinic acid in vitro

Y.N. Li1, Q. Zhou2, B. Yang2, Z. Hu2, J.H. Wang2, Q.S. Li3* and W.W. Cao1,4*

1School of Life Science and Technology, Harbin Institute of Technology, Harbin, China
2Laboratory of Photo-and Sono-Theranostic Technologies and Condensed Matter Science and Technology Institute, Harbin Institute of Technology, Harbin, China
3Cardiovascular Institute, The First Affiliated Hospital of Dalian Medical University, Dalian, China
4Materials Research Institute, The Pennsylvania State University, State College, PA, USA

*These authors contributed equally to this study.

Corresponding author: W.W. Cao
E-mail: lyn1009@126.com / gaowenwu_gww@yeah.net

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ABSTRACT. We investigated the killing effect of low-intensity ultrasound combined with 5-aminolevulinic acid (5-ALA) on the rat osteosarcoma cell line UMR-106. Logarithmic-phase UMR-106 cells were divided into a control group, ultrasound group and 5-ALA group. The cell apoptotic rate, production of reactive oxygen species, and the change in mitochondrial membrane potential were analyzed by flow cytometry; ultrastructural changes were observed by transmission electron microscopy. Using low-intensity ultrasound at 1.0 MHz and 2.0 W/cm² plus 5-ALA at a concentration of 2 mM, the apoptotic rate of the sonodynamic therapy group was 27.2 ± 3.4% which was significantly higher than that of the control group, ultrasound group, and 5-ALA group (P < 0.05). The
production of reactive oxygen species was 32.6 ± 2.2% and the decrease in mitochondrial membrane potential was 39.5 ± 2.5%. The 33342 staining showed nuclear condensation and fragmentation in the ultrasound group and 5-ALA group. Structural changes in the cell membrane, mitochondria, Golgi apparatus, and other organelles observed by transmission electron microscopy included formation of apoptotic bodies. The killing effect of low-intensity ultrasound combined with 5-ALA on UMR-106 cells was significant. Cell apoptosis played a vital role in the killing effect, and the mitochondria pathway contributed to the apoptosis of UMR-106 cells.

**Key words:** 5-Aminolevulinic acid; Apoptosis; Sonodynamic therapy; UMR-106 cells