Ligustilide induces reactive oxygen species-mediated apoptosis by targeting OSGIN1 expression in human osteosarcoma cells

Renn-Chia Lin[1, 2], Yi-Hsien Hsieh[3]
[1]Department of Orthopedics, Chung Shan Medical University Hospital
[2]School of Medicine, Chung Shan Medical University
[3]Institute of Medicine, Chung Shan Medical University
Email of Presenting Author: rennchia@gmail.com

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INTRODUCTION: Osteosarcoma (OS) is the most common malignant bone tumor in children and adolescents. The current standard therapeutic approaches include chemotherapy and local surgery to manage the primary lesions. However, the effectiveness of current treatments is often limited by chemoresistance. The development of novel natural compounds or therapeutic strategies is a critical area of research. Ligustilide (A), a major bioactive component found in several traditional Chinese medicinal herbs, has been reported to possess a wide range of pharmacological activities, such as anti-metastatic, anti-inflammatory, and pro-apoptotic effects. However, the anti-tumor activity of Ligustilide against human OS cells remains unclear.

METHODS: Cell viability in human OS cells was assessed using the MTT assay with various concentrations of Ligustilide. Cellular reactive oxygen species (ROS) were detected by staining with the fluorescent probe. The proteins expression were assessed through western blotting. RNA sequencing was employed to detect changes in gene expression in OS cell lines.

RESULTS SECTION: We demonstrated that Ligustilide effectively inhibited cell viability in a dose-dependent manner (B,C), and promotes apoptosis in human OS cell lines (E,F). Furthermore, Ligustilide treatment significantly increased the production of ROS and DNA damage (G,H.I). RNA sequencing analysis revealed that Ligustilide markedly upregulated both the mRNA and protein expression of oxidative stress-induced growth inhibitor 1 (OSGIN1) in human OS cells (M,N,O). Notably, treatment with N-acetylcysteine (NAC) reduced ROS levels (J,K,L) and suppressed the Ligustilide-induced OSGIN1 expression (P). Furthermore, treatment with NAC reduced apoptosis-related protein expression (P) and increased human OS cells viability that inhibited by Ligustilide (L).

DISCUSSION: Our findings suggest that Ligustilide induces ROS-mediated apoptosis through the upregulation of OSGIN1 expression in human OS cells.

SIGNIFICANCE/CLINICAL RELEVANCE: (1-2 sentences): These results provide new insights into the anti-tumor potential of Ligustilide and support its further investigation as a promising therapeutic agent for osteosarcoma.

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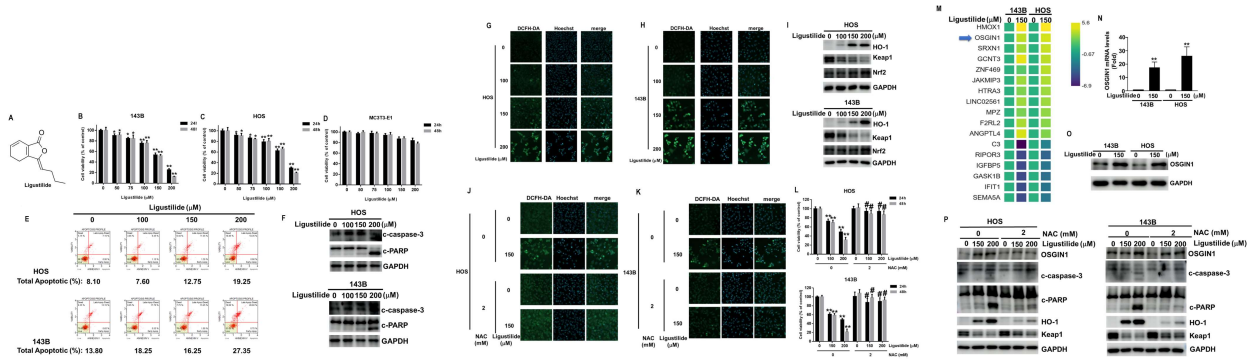

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