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Anti-tumor activity of the X-linked inhibitor of apoptosis (XIAP) inhibitor embelin in gastric cancer cells

Da-Guang Wang · Ya-Bin Sun · Fei Ye · Wei Li · Punyaram Kharbuja · Ling Gao · David Y. Zhang · Jian Suo

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Abstract This study investigated the anticancer effects of embelin in human gastric cancer cells and the underlying molecular mechanisms. Gastric cancer cells were treated with embelin and 5-FU for methyl-thiazolyl-tetrazolium bromide cell viability assay and flow cytometric detection of cell viability and apoptosis. Protein pathway array (PPA) and Western blot were used to investigate differentially expressed proteins in embelin-treated gastric cancer cells. Embelin reduced gastric cancer cell viability, induced apoptosis, and enhanced 5-FU antitumor activity in gastric cancer cells. Mechanistically, embelin induced cell cycle arrest at the S and G2/M phases. Molecularly, embelin downregulated expression of X-linked inhibitor of apoptosis and cell cycle-regulatory proteins, such as CDK1, CDC25B, CDC25C, cyclinB1, and CDK2. PPA analysis showed that embelin modulated several pathways that are associated with cell growth and apoptosis, such as PI3K/AKT, JAK/STAT, p38 MAPK, and p53. The data from the current study implied that reduction of gastric cancer cell viability after treatment with embelin was through cell cycle arrest at the S and G2/M phases and apoptosis.

Keywords Embelin · Gastric cancer · Apoptosis · XIAP · Ingenuity pathway analysis

Introduction

Gastric cancer is a significant health problem worldwide—the fourth most common cancer and the second most common cause of cancer-related death in the world [1]. Because of the advancements in early detection, the elimination of risk factors, and effective treatment of early lesions, the incidence of this disease is declining. However, while surgery is the only curative treatment for localized gastric cancer, most of the cases present are at an advanced stage. Chemotherapy for gastric cancer is not the standard of care because currently available agents are not very effective. Recurrence rates are high, and survival and prognosis are poor for advanced gastric cancer [2]. Thus, novel approaches are needed to understand the molecular mechanisms responsible for gastric cancer development and progression and to provide novel targets and strategies for its control.

The process by which a normal gastric epithelial cell transforms and develops into a malignant tumor requires several genetic and cellular alterations; dysregulation of canonical oncogenic pathways is known to occur with varying frequencies [3]. Evasion of apoptosis is a hallmark of human cancers, including gastric cancer, and defects in the regulators of apoptosis invariably accompany tumorigenesis

Da-Guang Wang and Ya-Bin Sun contributed equally to this work.

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D.-G. Wang · W. Li · P. Kharbuja · J. Suo (✉)
Department of General Surgery, The First Hospital, Jilin University, Changchun 130021, Jilin, China
e-mail: suojian42@gmail.com

Y.-B. Sun
Department of Ophthalmology, The First Hospital, Jilin University, Changchun 130021, Jilin, China

F. Ye · D. Y. Zhang (✉)
Department of Pathology, Mount Sinai School of Medicine, New York, NY 10029, USA
e-mail: david.zhang@mssm.edu

L. Gao
Department of Cancer Center, The First Hospital, Jilin University, Changchun 130021, Jilin, China

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