Mol Cell Biochem (2013) 384:229–237
DOI 10.1007/s11010-013-1802-8

Capsaicin induces apoptosis in human osteosarcoma cells through AMPK-dependent and AMPK-independent signaling pathways

Hui Ying · Zhi Wang · Yan Zhang · Tie-yi Yang · Zhi-hong Ding · Shu-yi Liu · Jin Shao · Yue Liu · Xin-bing Fan

Received: 7 June 2013 / Accepted: 23 August 2013 / Published online: 5 September 2013

Abstract Recent studies have focused on the anti-tumor activity of capsaicin. However, the potential effects of capsaicin in osteosarcoma cells and the underlying mechanisms are not fully understood. In the current study, we observed that capsaicin-induced growth inhibition and apoptosis in cultured osteosarcoma cells (U2OS and MG63), which were associated with a significant AMP-activated protein kinase (AMPK) activation. AMPK inhibition by compound C or RNA interference suppressed capsaicin-induced cytotoxicity, while AMPK activators (AICAR and A769662) promoted osteosarcoma cell death. For the mechanism study, we found that AMPK activation was required for capsaicin-induced mTORC1 (mTOR complex 1) inhibition, B cell lymphoma 2 (Bcl-2) down-regulation and Bax upregulation in MG63 cells. Capsaicin administration induced p53 activation, mitochondrial translocation and Bcl-2 killer association, such effects were dependent on AMPK activation. Interestingly, we observed a significant pro-apoptotic *c*-Jun NH2-terminal kinases activation by capsaicin in MG63 cells, which appeared to be AMPK independent. In conclusion, capsaicin possessed strong efficacy against human osteosarcoma cells. Molecular studies revealed that capsaicin activated AMPK-dependent and AMPK-independent signalings to mediate cell apoptosis. The results of this study should have significant translational relevance in managing this deadly malignancy.

Hui Ying and Zhi Wang contributed equally to this paper.

H. Ying · Z. Wang · Y. Zhang (✉) · T. Yang · Z. Ding · S. Liu · J. Shao · Y. Liu · X. Fan
Department of Orthopedics, Gongli Hospital of Pudong New District, No. 219, Miaopu Road, Pudong New District, Shanghai 200135, China
e-mail: yanzhangdr@126.com

Keywords Osteosarcoma · Capsaicin · Apoptosis · AMPK · mTOR · JNK · p53

Abbreviations

MTT	3-(4,5-Dimethyl-thiazol-2-yl)2,5-diphenyl tetrazolium bromide
AICAR	5-Aminoimidazole-4-carboxamide riboside
ACC	Acetyl-CoA carboxylase
AMPK	AMP-activated protein kinase
mTORC1	mTOR complex 1
Bak	B-cell lymphoma 2 (Bcl-2) killer

Introduction

Osteosarcoma, occurs predominantly in children and young adults, is the most common form of primary bone tumor. Osteosarcoma has a very high rate of metastasis, and patients identified as metastatic osteosarcoma experience a 5-year survival rate as low as 20 % [1, 2]. Recent studies have reported significant research advances in adjuvant chemotherapy of osteosarcoma. However, the prognosis for patients with metastatic osteosarcoma is generally poor [1, 2]. The search for more effective anti-osteosarcoma agents is necessary and urgent.

Studies have observed that capsaicin induces apoptosis in human breast cancer cells [3], hepatocarcinoma cells [4], glioma cells [5], prostate cancer cells [6], and human leukemia cells [7]. However, the potential effects of capsaicin in osteosarcoma cells and the underlying mechanisms are not known.

AMP-activated protein kinase (AMPK) is composed of two catalytic (α1 and α2) and five regulatory (β1–2 and