P23

Induction of Egr-1 is Associated with Anti-metastatic and Anti-invasive Ability of β-lapachone in Human Hepatocarcinoma Cells

Sung Ok Kim[1], Jae Im Kwon[2], Yong Kee Jeong[3], Gi Young Kim[4], Nam Deuk Kim[5], Won-Kyung Choe[6] and Yung Hyun Choi[1,2]*

[1]*Department of Biomaterial Control (BK21 program), Dongeui University Graduate School and*
[2]*Department of Biochemistry, Dongeui University College of Oriental Medicine and Busan 614-052;*
[3]*College of Natural Resources and Life Science, Dong-A University, Busan 604-714;*
[4]*Faculty of Applied Marine Science, Cheju National University, Jeju 690-756;*
[5]*Division of Pharmacy, Pusan National University, Busan 609-735;*
[6]*Department of Food & Nutrition, Gimcheon College, Gyeongsanbuk-do 740-704, South Korea*

β-lapachone, a quinone compound obtained from the bark of the lapacho tree (*Tabebuia avellanedae*), was reported to have anti-inflammatory and anti-cancer activities. In this study, we investigated novel functions of β-lapachone in terms of anti-metastasis and anti-invasion abilities using human hepatocarcinoma cell lines, HepG2 and Hep3B. β- lapachone dose-dependently inhibited cell viability and migration of both HepG2 and Hep3B cells, as determined by MTT assay and wound healing assay. RT-PCR and Western blot data revealed that β-lapachone dramatically induced the levels of protein, as well as mRNA expression of early growth response gene-1 (Egr-1) and thrombospondin-1 (TSP-1) at an early point in time, and then decreased in a time-dependent manner. In addition, the down-regulation of Snail and up-regulation of E-cadherin expression were observed in β-lapachone-treated HepG2 and Hep3B cells, which was associated with the decreased invasive ability as measured by matrigel invasion assay. Taken together, our results strongly suggest that β-lapachone may be expected to inhibit progression and metastasis of hepatoma cells, at least in part by inhibiting the invasive ability of the cells *via*up-regulation of the expression of the Egr-1, TSP-1, and E-cadherin.[This work was supported by the Korea Science and Engineering Foundation (KOSEF) grant funded by the Korea government(MOST) (R01-2006-000-11117-0).].

Key words: β-lapachone, Egr-1, metastasis, invasion

P24

Naringenin Induced Apoptosis in Human Leukemic THP-1 Cells through Inactivation of Akt and Mitochondria Dependent Activation of Caspase-3 Pathway

Joon Hee Park[1], Cheng-Yun Jin[2], Gi Young Kim[3], Yong Kee Jeong[4] and Yung Hyun Choi[4,5]

Departments of [1]Biology and [4]Oriental Medicine, Dongeui University and [5]Department of Biomaterial Control (BK21 program), Dongeui University Graduate School, Busan 614-052;
[2]*Division of Biological Sciences, Pusan National University, Busan 609-735;*
[3]*Faculty of Applied Marine Science, Cheju National University, Jeju 690-756*

Naringenin (NGEN), a flavonoid, has shown cytotoxicity in various human cancer cell lines and inhibitory effects on tumor growth. In this study, we investigated the apoptosis induced by NGEN via the activation of caspases and loss of mithocondrial potentiol in human leukemia THP-1 cells. Exposure to NGEN induced apoptosis dose-dependently up until 0.2 mM as demonstrated by a quantitative analysis of nuclear morphological change and flow cytometric analysis, but not in naringin (NGN). NGEN dose-dependently increased hyperpolarization of mitochondrial membrane potential. An extensive inhibitor for caspases, abolished the NGEN induced apoptosis. The apoptosis-triggering of NGEN was shown to markedly promote the activation of caspase-3, and cleavage of poly(ADP-ribose) polymerase (PARP). NGEN induced apoptosis caused by inhibition of Akt activation in time dependent manner. Pretreatment with LY294002, significantly increased NGEN induced apoptosis. This result indicates a common pathway to apoptosis by NGEN. One of the mechanisms by NGEN induced apoptosis may relate to the activation of caspase-3 and mitochondria dysfunctions that correlates with inactivation of Akt.

Key words: Naringenin, apoptosis, Akt, caspase-3, THP-1