

### Anti-tumor effect of sanguinarine in SW480, human colon cancer cell

Jiwon Park, Soh-Hyun Lee, Hana Kim and Tae-Lin Huh

Department of Genetic Engineering, collage of Natural Sciences, Kyungpook National University, Daegu 702-701, Korea

Sanguinarine has been reported to possess anti-microbial, anti-inflammatory, and anti-tumor activity. In a recent report, sanguinarine decreased reduced glutathione (GSH) in several human cancer cell lines. Mitogen-activated protein kinases (MAPKs) have been known to be activated under oxidative stress. So we hypothesized that sanguinarine may induce ROS generation, which might cause decreasing GSH level and induce cell death through activation of MAPK. To test this hypothesis, we evaluated that the effect of sanguinarine on ROS level, GSH level and MAPKs activities in human colon tumor cell, SW480. Sanguinarine induced ROS generation and MAPK activation. Sanguinarine-induced cell death was inhibited by N-Acetyl-L-Cysteine (NAC). We concluded, therefore, that sanguinarine treatment induces generation of ROS and sanguinarine-induced cell death is caused by activation of MAPK through increased ROS level.

### Apoptosis by sanguinarine in C6 glioma cells was associated with up-regulation of the Bax/Bcl-2 ratio and activation of caspases

Min Ho Han<sup>1,2</sup>, Woo Young Choi<sup>1,2</sup>, Gi-Young Kim<sup>3</sup>, Won Ho Lee<sup>2</sup>, Yeong-Min Park<sup>4</sup>, and Yung Hyun Choi<sup>1,5</sup>

<sup>1</sup>Dept Biochemistry and Biomaterial Control, Dongeui Univ College of Oriental Medicine, <sup>2</sup>Dept Biology, Pusan Natl Univ, <sup>3</sup>Faculty of Applied Marine Science, Cheju Natl Univ, <sup>4</sup>Dept Microbiology & Immunology and Lab Dendritic Cell Differentiation & Regulation, Pusan Natl Univ College of Medicine

Sanguinarine, derived from *Sanguinaria canadensis* and other species, is known to exhibit antimicrobial, antiinflammatory and antioxidant properties. Sanguinarine could induce cell cycle arrest and apoptosis in various cancer cell lines. However, the mechanism by which sanguinarine induces apoptosis is not completely understood. To investigate the underlying pathways, its potential to induce apoptosis in C6 glioma cells was investigated. Exposure of C6 cells to sanguinarine resulted in growth inhibition and induction of apoptosis in a dose-dependent manner as measured by MTT assay, fluorescence microscopy, agarose gel electrophoresis and flow cytometry analysis. Sanguinarine treatment induced the levels of tumor suppressor p53 and Cdk inhibitor p21. The increase in apoptosis was associated with the induction of Bax and inhibition of Bcl-2 expression. Sanguinarine treatment also activated caspases and DFF45/ICAD, which were associated with concomitant degradation of PARP and PLC- $\gamma$ 1 protein and DNA fragmentation. Taken together, it is suggested that sanguinarine can be a promising chemopreventive agent and changes in Bcl-2 family expression and caspase activity may play critical roles in sanguinarine-induced apoptosis in C6 cells.

### Caffeic acid protects WI 38 human lung fibroblast cells against hydrogen peroxide induced cell damage

Kyoung Ah Kang<sup>a</sup>, Kyoung Hwa Lee<sup>a</sup>, Rui Zhang<sup>a</sup>, Meijing Piao<sup>a</sup>, Sungwook Chae<sup>a</sup>, Kil Nam Kim<sup>b</sup>, You Jin Jeon<sup>b</sup>, Doek Bae Park<sup>c</sup>, Ho Jin You<sup>d</sup>, Jin Sook Kim<sup>e</sup>, and Jin Won Hyuna,\*<sup>111</sup>

<sup>a</sup>Department of Biochemistry, College of Medicine and Applied Radiological Science Research Institute, Cheju National University, Jeju-si 690-756, Korea <sup>b</sup>Department of Food Science and Technology, Cheju National University, Jeju-si 690-756, Korea <sup>c</sup>Department of Histology, College of Medicine, Cheju National University, Jeju-si 690-756, Korea <sup>d</sup>Department of Pharmacology, College of Medicine, Chosun University, 375 Seosuk-dong, Gwangju 501-759, Korea <sup>e</sup>Department of Herbal Pharmaceutical Development, Korea Institute of Oriental Medicine, Daejeon City 305-811, Korea

Cytoprotective effect of caffeic acid (3, 4-dihydroxy cinnamic acid) on human lung fibroblast (WI 38) cells against hydrogen peroxide induced damage was investigated. Caffeic acid was found to scavenge intracellular reactive oxygen species, and 1,1-diphenyl-2-picrylhydrazyl radical, and thus prevented lipid peroxidation. The radical scavenging activity of caffeic acid protected cell damage of WI 38 cells exposed to hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>), via the activation of extracellular signal regulated kinase protein. Caffeic acid increased the activity of catalase and its protein expression. Hence, from the present study, it is suggestive that caffeic acid protects WI 38 cells against H<sub>2</sub>O<sub>2</sub> damage by enhancing the cellular antioxidant activity.

### Cardioprotective effect of ARC against hypoxic injury in transgenic mice

Jong-Ok Pyo<sup>1</sup>, SungMin Song<sup>2</sup>, Jae-Woong Chang<sup>2</sup>,Yeon-Mi Hong<sup>3</sup>, Hyo-Jin Kim<sup>2</sup>, Dong-Gyu Jo<sup>4</sup>, Hyung-Ryung Kim<sup>2</sup>, YoungKeun Ahn<sup>6</sup> and Yong-Keun Jung<sup>12</sup>

Bio-Max Institute<sup>1</sup>, Dept. of Life Science<sup>2</sup>, Dept. of Animal Biotech., College of Agriculture and Life science<sup>3</sup>, Seoul Natl. Univ., Seoul 151-747, Korea, Lab. of Neuroscience, GRC, NIA, 5600, Nathan Shock Drive, Baltimore, MD 21224<sup>4</sup>, Wonkwang Univ., Jeonbuk, 570-749, Korea<sup>5</sup>and Dept.Cardiovascular medicine, Chonnam Natl.Univ. Hospt. Gwangju, Korea<sup>6</sup>

ARC is a caspase recruitment domain-containing molecule that plays an important role in the regulation of apoptosis. We have previously shown that ARC suppressed hypoxia-induced neuronal cell death or calcium-mediated cell death by interfering with caspase-8. To test whether ARC protects against hypoxic injury in the heart, we generated cardiac-specific transgenic mice overexpressing different levels of ARC under the control of mouse MHC promoter. Compared to control, ARC expression in mouse heart significantly suppressed the appearance of hypoxia-induced TUNEL-positive cells. By use of a Langendoff preparation, hearts from ARC transgenic mice showed improved recovery of contractile performance during reperfusion after ischemia. Also, cultured cardiomyocytes from neonatal ARC transgenic mice showed resistance to the hypoxic injury. Further, ectopic expression of ARC or the C-terminus of ARC protected the cardiomyocytes from hypoxic cell death. Our data demonstrate that ARC expression protects the cardiomyocyte against hypoxic injury via the C-terminus, thus providing new insight into therapeutic target for the protection of cardiac damage.