

บรรณานุกรม



1. G.J. Gores. Cholangiocarcinoma: current concepts and insights. *Hepatology*. 37:961-969 (2003).
2. K.N. Lazaridis and G.J. Gores. Cholangiocarcinoma. *Gastroenterology*. 128:1655-1667 (2005).
3. C.C. Conaway, Y.M. Yang, and F.L. Chung. Isothiocyanates as cancer chemopreventive agents: their biological activities and metabolism in rodents and humans. *Curr Drug Metab.* 3:233-255 (2002).
4. J. Jakubikova, Y. Bao, and J. Sedlak. Isothiocyanates induce cell cycle arrest, apoptosis and mitochondrial potential depolarization in HL-60 and multidrug-resistant cell lines. *Anticancer Res.* 25:3375-3386 (2005).
5. D. Xiao, K.L. Lew, Y. Zeng, H. Xiao, S.W. Marynowski, R. Dhir, and S.V. Singh. Phenethyl isothiocyanate-induced apoptosis in PC-3 human prostate cancer cells is mediated by reactive oxygen species-dependent disruption of the mitochondrial membrane potential. *Carcinogenesis*. 27:2223-2234 (2006).
6. D. Trachootham, Y. Zhou, H. Zhang, Y. Demizu, Z. Chen, H. Pelicano, P.J. Chiao, G. Achanta, R.B. Arlinghaus, J. Liu, and P. Huang. Selective killing of oncogenically transformed cells through a ROS-mediated mechanism by beta-phenylethyl isothiocyanate. *Cancer Cell*. 10:241-252 (2006).
7. H. Zhang, D. Trachootham, W. Lu, J. Carew, F.J. Giles, M.J. Keating, R.B. Arlinghaus, and P. Huang. Effective killing of Gleevec-resistant CML cells with T315I mutation by a natural compound PEITC through redox-mediated mechanism. *Leukemia*. 22:1191-1199 (2008).
8. N. Somparn, U. Kukongviriyapan, W. Tassaneeyakul, A. Jetsrisuparb, and V. Kukongviriyapan. Modification of CYP2E1 and CYP3A4 activities in haemoglobin E-beta thalassemia patients. *Eur J Clin Pharmacol*. 63:43-50 (2007).
9. S.T. Smiley, M. Reers, C. Mottola-Hartshorn, M. Lin, A. Chen, T.W. Smith, G.D. Steele, Jr., and L.B. Chen. Intracellular heterogeneity in mitochondrial membrane potentials revealed by a J-aggregate-forming lipophilic cation JC-1. *Proc Natl Acad Sci U S A*. 88:3671-3675 (1991).

สำนักงานคณะกรรมการวิจัยแห่งชาติ	
ท่องเที่ยวและสันัต្ត	
วันที่.....	02.๗.๖๘ 2555
เลขที่แบบฝึกหัด.....	248105
เลขประจำตัวผู้ใช้.....	
เลขประจำหนังสือ.....	

10. J.E. Chipuk and D.R. Green. Dissecting p53-dependent apoptosis. *Cell Death Differ.* 13:994-1002 (2006).
11. K.L. Cheung, T.O. Khor, S. Yu, and A.N. Kong. PEITC induces G1 cell cycle arrest on HT-29 cells through the activation of p38 MAPK signaling pathway. *Aaps J.* 10:277-281 (2008).

ภาคผนวก

ก. ประวัติผู้วิจัย

ชื่อ นางสาว เอื้อมเดือน ประวाप (หัวหน้าโครงการ)

ตำแหน่ง อ้างารย์ ระดับ 7

คุณวุฒิ ปริญญาเอก (เกสัชวิทยา)

ความชำนาญ/ความสนใจพิเศษ drug metabolism and pharmacogenetics, cancer research

สถานที่ติดต่อ ภาควิชาเภสัชวิทยา คณะแพทยศาสตร์ มหาวิทยาลัยขอนแก่น

โทรศัพท์/โทรสาร 043-363148, 043-348397

อีเมล์ peuam@kku.ac.th

งานวิจัยคีพินพ์

- Suphim B, **Prawan A**, Kukongviriyapan U, Kongpetch S, Buranrat B, Kukongviriyapan V. Redox Modulation and Human Bile Duct Cancer Inhibition by Curcumin. *Food Chem Toxicol.* 2010 May 24. [Epub ahead of print]
- Buranrat B, **Prawan A**, Kukongviriyapan U, Kongpetch S, Kukongviriyapan V. Dicoumarol enhances gemcitabine-induced cytotoxicity in high NQO1-expressing cholangiocarcinoma cells. *World J Gastroenterol* 2010 May 21; 16(19): 2362-70.
- Prawan A**, Saw CL, Khor TO, Keum YS, Yu S, Hu L, Kong AN. Anti-NF-kappaB and anti-inflammatory activities of synthetic isothiocyanates: Effect of chemical structures and cellular signaling. *Chem Biol Interact.* 2009 May 15; 179(2-3): 202-11. Epub 2008 Dec 30.
- Prawan A**, Buranrat B, Kukongviriyapan U, Sripa B, Kukongviriyapan V. Inflammatory cytokines suppress NAD(P)H:quinone oxidoreductase-1 and induce oxidative stress in cholangiocarcinoma cells. *J Cancer Res Clin Oncol.* 2009 Apr; 135(4): 515-22. Epub 2008 Sep 27.
- Tin Oo Khor, Mou-Tuan Huang, **Auemduan Prawan**, Yue Liu, Xingpei Hao, Siwang Yu, William Ka Lung Cheung, Jefferson Y. Chan, Bandaru S. Reddy, Chung S. Yang, and Ah-Ng Kong. Increased Susceptibility of Nrf2 Knockout Mice to Colitis-Associated Colorectal Cancer. *Cancer Prev Res (Phila Pa)*. 2008 Aug; 1(3): 187-91. Epub 2008 Mar 31.
- Khor TO, Cheung WK, **Prawan A**, Reddy BS, Kong AN. Chemoprevention of familial

- adenomatous polyposis in Apc(Min^{+/}) mice by phenethyl isothiocyanate (PEITC). *Mol Carcinog* 2008 May; 47(5): 321-5.
7. **Prawan A**, Keum YS, Khor TO, Yu S, Nair S, Li W, Hu L, Kong AN. Structural Influence of Isothiocyanates on the Antioxidant Response Element (ARE)-Mediated Heme Oxygenase-1 (HO-1) Expression. *Pharm Res* 2008 Apr; 25(4): 836-44. Epub 2007 Jul 27.
 8. Kukongviriyapan V, Somparn N, Senggunploi L, **Prawan A**, Kukongviriyapan U, Jetsrisuparb A. Endothelial Dysfunction and Oxidant Status in Pediatric Patients with Hemoglobin E-beta Thalassemia. *Pediatr Cardiol* 2008 Jan; 29(1): 130-5. Epub 2007 Sep 22.
 9. Buranrat B, **Prawan A**, Sripa B, Kukongviriyapan V. Inflammatory cytokines suppress arylamine N-acetyltransferase 1 in cholangiocarcinoma cells. *World J Gastroenterol* 2007 Dec 14; 13(46): 6219-25.
 10. **A. Prawan**, T.O. Khor, W. Li and A.-N.T. Kong. Application of Pharmacogenomics to Dietary Cancer Chemoprevention. *Current Pharmacogenomics* 2007 Sep; 5(3): 190-200. Review.
 11. **Prawan A**, Kundu JK, Surh YJ. Molecular basis of heme oxygenase-1 induction: implications for chemoprevention and chemoprotection. *Antioxid Redox Signal* 2005 Nov-Dec; 7(11-12): 1688-703. Review.
 12. **Prawan A**, Kukongviriyapan V, Tassaneeyakul W, Pairojkul C, Bhudhisawasdi V. Association between genetic polymorphisms of *CYP1A2*, *Arylamine N-acetyltransferase-1* and 2 and susceptibility to Cholangiocarcinoma. *Eur J Cancer Prev* 2005 Jun; 14(3): 245-50.
 13. Kukongviriyapan V, Senggunploi L, **Prawan A**, Gaysornsiri D, Kukongviriyapan U, Aiemsaaard J. Salivary caffeine metabolic ratio in alcohol-dependent subjects. *Eur J Clin Pharmacol* 2004 Apr; 60(2): 103-7. Epub 2004 Mar 12.
 14. Kukongviriyapan V, **Prawan A**, Warasiha B, Tassaneeyakul W, Aiemsaaard J. Polymorphism of *N*-acetyltransferase 1 and Correlation Between Genotype and Phenotype in a Thai population. *Eur J Clin Pharmacol* 2003 Aug; 59(4): 277-81. Epub 2003 Jul 19.
 15. Kukongviriyapan V, **Prawan A**, Tassaneeyakul W, Aiemsaaard J, Warasiha B. *Arylamine N-acetyltransferase-2* genotypes in the Thai population. *Br J Clin Pharmacol* 2003 Mar; 55(3): 278-81.

ข. การเผยแพร่ผลงานวิจัย

- นำเสนอผลงานในที่ประชุมวิชาการระดับชาติ แบบ poster presentation 1 ครั้ง

(การประชุมวิชาการประจำปี ครั้งที่ 32 สมาคมเภสัชวิทยาแห่งประเทศไทย 2552 เรื่อง

Chemotherapy 2010: Discovery and Development ระหว่างวันที่ 25-26 มี.ค. 2553 ณ

มหาวิทยาลัยธรรมศาสตร์ ศูนย์รังสิต)

- บทความ proceedings

1 เรื่อง

(Ornanong Tusskorn, Veerapol Kukongviriyapan, Auemduan Prawan, Upa Kukongviriyapan. PEITC inhibits cholangiocarcinoma via induction of mitochondrial dysfunction. *Thai J Pharmacol* 2010; 32(1): 76-81)



บทคัดย่อของบทความ proceedings เรื่อง PEITC Inhibits Cholangiocarcinoma via Induction of Mitochondrial Dysfunction

Phenethyl isothiocyanate (PEITC), a natural compound found abundantly in cruciferous and other vegetables, has been shown to possess cancer chemopreventive activity. The purpose of this investigation was to examine the cytotoxic effect of PEITC in cholangiocarcinoma cells (CCA). Cholangiocarcinoma cells, KKU-100 and human liver Chang cells were used for comparison in the study. Effects of PEITC on cell growth and induction of apoptosis was determined by fluorescent dye staining using acridine orange and ethidium bromide. Cultured cells were exposed to PEITC for 3, 12, 24 and 48 hours following assessment of cell viability and apoptotic cell death. PEITC can induce a large proportion of cells to undergo apoptosis in a dose-time dependent manner. The PEITC induced depletion of intracellular antioxidant GSH in the cell lines. Moreover, a rapid collapse of the mitochondrial transmembrane potential, as measured by JC-1 staining, was observed concurrently with an apparent apoptosis in both cells. Furthermore, Western blot analysis were used to examine the antioxidant and survival response related proteins. The results revealed that PEITC increased levels of Nrf2 and cyclin D1 in both cell lines, and Bax and Trx protein expression was up-regulated in KKU-100. The effect of PEITC on cell growth and apoptosis may contribute to cancer chemopreventive properties. In conclusion, our data lucidly evidence the chemopreventive merits of dietary phytochemical PEITC in suppression of cholangiocarcinoma

Keywords: *Phenylethyl isothiocyanate; Cholangiocarcinoma; Apoptosis; Cytotoxicity*

