REFERENCES

- [1]. Siegel R, Naishadham D and Jemal A, "Cancer statistics, 2013", <u>CA: a cancer</u> journal for clinicians. 63, 1. (2013): 11-30.
- [2]. Steeg PS and Theodorescu D, "Metastasis: a therapeutic target for cancer", <u>Nat</u> <u>Clin Pract Oncol.</u> 5, 4. (2008): 206-19.
- [3]. Simpson CD, Anyiwe K and Schimmer AD, "Anoikis resistance and tumor metastasis", <u>Cancer letters</u>. 272, 2. (2008): 177-85.
- [4]. Frisch SM and Screaton RA, "Anoikis mechanisms", <u>Curr Opin Cell Biol</u>. 13, 5.(2001): 555-62.
- [5]. Choochuay K, Chunhacha P, Pongrakhananon V, Luechapudiporn R and Chanvorachote P, "Imperatorin sensitizes anoikis and inhibits anchorageindependent growth of lung cancer cells", <u>Journal of natural medicines</u>. 67, 3. (2013): 599-606.
- [6]. Wongpankam E, Chunhacha P, Pongrakhananon V, Sritularak B and Chanvorachote P, "Artonin E mediates MCL1 down-regulation and sensitizes lung cancer cells to anoikis", <u>Anticancer research</u>. 32, 12. (2012): 5343-51.
- [7]. Powan P, Saito N, Suwanborirux K and Chanvorachote P, "Ecteinascidin 770, a tetrahydroisoquinoline alkaloid, sensitizes human lung cancer cells to anoikis",
 <u>Anticancer research</u>. 33, 2. (2013): 505-12.
- [8]. Pongrakhananon V, Nimmannit U, Luanpitpong S, Rojanasakul Y and Chanvorachote P, "Curcumin sensitizes non-small cell lung cancer cell anoikis through reactive oxygen species-mediated Bcl-2 downregulation", <u>Apoptosis</u>. 15, 5. (2010): 574-85.

- [9]. Galante JM, Mortenson MM, Bowles TL, Virudachalam S and Bold RJ, "ERK/BCL-2 pathway in the resistance of pancreatic cancer to anoikis", <u>The</u> <u>Journal of surgical research</u>. 152, 1. (2009): 18-25.
- [10]. Lin D, Feng J and Chen W, "Bcl-2 and caspase-8 related anoikis resistance in human osteosarcoma MG-63 cells", <u>Cell biology international</u>. 32, 10. (2008): 1199-206.
- [11]. Halim H, Chunhacha P, Suwanborirux K and Chanvorachote P, "Anticancer and antimetastatic activities of Renieramycin M, a marine tetrahydroisoquinoline alkaloid, in human non-small cell lung cancer cells", <u>Anticancer research</u>. 31, 1. (2011): 193-201.
- [12]. Stan RV, "Structure of caveolae", <u>Biochimica et biophysica acta</u>. 1746, 3.
 (2005): 334-48.
- [13]. Moon KC, Lee GK, Yoo SH, Jeon YK, Chung JH, Han J, et al., "Expression of caveolin-1 in pleomorphic carcinoma of the lung is correlated with a poor prognosis", <u>Anticancer research</u>. 25, 6c. (2005): 4631-7.
- [14]. Yoo SH, Park YS, Kim HR, Sung SW, Kim JH, Shim YS, et al., "Expression of caveolin-1 is associated with poor prognosis of patients with squamous cell carcinoma of the lung", <u>Lung cancer (Amsterdam. Netherlands)</u>. 42, 2. (2003): 195-202.
- [15]. Nam KH, Lee BL, Park JH, Kim J, Han N, Lee HE, et al., "Caveolin 1 expression correlates with poor prognosis and focal adhesion kinase expression in gastric cancer", <u>Pathobiology : journal of immunopathology</u>. molecular and cellular <u>biology</u>. 80, 2. (2013): 87-94.

- [16]. Ho CC, Huang PH, Huang HY, Chen YH, Yang PC and Hsu SM, "Up-regulated caveolin-1 accentuates the metastasis capability of lung adenocarcinoma by inducing filopodia formation", <u>The American journal of pathology</u>. 161, 5. (2002): 1647-56.
- [17]. Fiucci G, Ravid D, Reich R and Liscovitch M, "Caveolin-1 inhibits anchorageindependent growth, anoikis and invasiveness in MCF-7 human breast cancer cells", <u>Oncogene</u>. 21, 15. (2002): 2365-75.
- [18]. Ravid D, Maor S, Werner H and Liscovitch M, "Caveolin-1 inhibits anoikis and promotes survival signaling in cancer cells", <u>Advances in enzyme regulation</u>.
 46. (2006): 163-75.
- [19]. Halim H, Luanpitpong S and Chanvorachote P, "Acquisition of anoikis resistance up-regulates caveolin-1 expression in human non-small cell lung cancer cells", <u>Anticancer research</u>. 32, 5. (2012): 1649-58.
- [20]. Rungtabnapa P, Nimmannit U, Halim H, Rojanasakul Y and Chanvorachote P, "Hydrogen peroxide inhibits non-small cell lung cancer cell anoikis through the inhibition of caveolin-1 degradation", <u>American journal of physiology Cell</u> <u>physiology</u>. 300, 2. (2011): C235-45.
- [21]. Li L, Ren CH, Tahir SA, Ren C and Thompson TC, "Caveolin-1 maintains activated Akt in prostate cancer cells through scaffolding domain binding site interactions with and inhibition of serine/threonine protein phosphatases PP1 and PP2A", <u>Molecular and cellular biology</u>. 23, 24. (2003): 9389-404.

- [22]. Chunhacha P, Pongrakhananon V, Rojanasakul Y and Chanvorachote P, "Caveolin-1 regulates Mcl-1 stability and anoikis in lung carcinoma cells", <u>Am J</u> <u>Physiol Cell Physiol</u>. 302, 9. (2012): C1284-92.
- [23]. Valastyan S and Weinberg RA, "Tumor metastasis: molecular insights and evolving paradigms", <u>Cell</u>. 147, 2. (2011): 275-92.
- [24]. Lim SK, Choi YW, Lim IK and Park TJ, "BTG2 suppresses cancer cell migration through inhibition of Src-FAK signaling by downregulation of reactive oxygen species generation in mitochondria", <u>Clinical & experimental metastasis</u>. 29, 8. (2012): 901-13.
- [25]. Pongrakhananon V, Chunhacha P and Chanvorachote P, "Ouabain suppresses the migratory behavior of lung cancer cells", <u>PloS one</u>. 8, 7. (2013): e68623.
- [26]. Akkarawut K, Pithi C, Boonchoo S and Varisa P, "Moscatilin Inhibits Lung Cancer Cell Motility and Invasion via Suppression of Endogenous Reactive Oxygen Species", <u>BioMed Research International</u>. 2013. (2013).
- [27]. Mitra SK, Hanson DA and Schlaepfer DD, "Focal adhesion kinase: in command and control of cell motility", <u>Nature reviews Molecular cell biology</u>. 6, 1. (2005): 56-68.
- [28]. Sieg DJ, Hauck CR and Schlaepfer DD, "Required role of focal adhesion kinase (FAK) for integrin-stimulated cell migration", <u>Journal of cell science</u>. 112 (Pt 16). (1999): 2677-91.
- [29]. Sanuphan A, Chunhacha P, Pongrakhananon V and Chanvorachote P, "Long-Term Nitric Oxide Exposure Enhances Lung Cancer Cell Migration", <u>BioMed</u> <u>Research International</u>. 2013. (2013): 9.

- [30]. Larsen M, Tremblay ML and Yamada KM, "Phosphatases in cell-matrix adhesion and migration", <u>Nature reviews Molecular cell biology</u>. 4, 9. (2003): 700-11.
- [31]. Nobes CD and Hall A, "Rho, rac, and cdc42 GTPases regulate the assembly of multimolecular focal complexes associated with actin stress fibers, lamellipodia, and filopodia", <u>Cell.</u> 81, 1. (1995): 53-62.
- [32]. Sritularak B and Likhitwitayawuid K, "New Bisbibenzyls from Dendrobium falconeri", <u>Helvetica Chimica Acta</u>. 92, 4. (2009): 740-4.
- [33]. Pore MM, Hiltermann TJ and Kruyt FA, "Targeting apoptosis pathways in lung cancer", <u>Cancer letters</u>. 332, 2. (2013): 359-68.
- [34]. Jemal A, Bray F, Center MM, Ferlay J, Ward E and Forman D, "Global cancer statistics", <u>CA: a cancer journal for clinicians</u>. 61, 2. (2011): 69-90.
- [35]. Parkin DM, Bray F, Ferlay J and Pisani P, "Global cancer statistics, 2002", <u>CA: a</u> <u>cancer journal for clinicians</u>. 55, 2. (2005): 74-108.
- [36]. Herbst RS, Heymach JV and Lippman SM, "Lung cancer", <u>The New England</u> journal of medicine. 359, 13. (2008): 1367-80.
- [37]. Rosell R, Felip E, Maestre J, Sanchez JM, Sanchez JJ, Manzano JL, et al., "The role of chemotherapy in early non-small-cell lung cancer management", <u>Lung</u> <u>cancer (Amsterdam. Netherlands)</u>. 34 Suppl 3. (2001): S63-74.
- [38]. Haura EB, "Treatment of advanced non-small-cell lung cancer: a review of current randomized clinical trials and an examination of emerging therapies", <u>Cancer control : journal of the Moffitt Cancer Center</u>. 8, 4. (2001): 326-36.

- [39]. Clegg A, Scott DA, Hewitson P, Sidhu M and Waugh N, "Clinical and cost effectiveness of paclitaxel, docetaxel, gemcitabine, and vinorelbine in nonsmall cell lung cancer: a systematic review", <u>Thorax</u>. 57, 1. (2002): 20-8.
- [40]. Ray MR and Jablons D. Hallmarks of Metastasis. In: Keshamouni V, Arenberg D,
 Kalemkerian G, editors. Lung Cancer Metastasis: Springer New York; 2010. p.
 29-46.
- [41]. Geiger TR and Peeper DS, "Metastasis mechanisms", <u>Biochimica et biophysica</u> <u>acta</u>. 1796, 2. (2009): 293-308.
- [42]. Ananthakrishnan R and Ehrlicher A, "The forces behind cell movement", International journal of biological sciences. 3, 5. (2007): 303-17.
- [43]. Zhao X and Guan JL, "Focal adhesion kinase and its signaling pathways in cell migration and angiogenesis", <u>Advanced drug delivery reviews</u>. 63, 8. (2011): 610-5.
- [44]. Thodeti C and Ghosh K. Mechanisms of Tumor Cell Migration and Invasion in Lung Cancer Metastasis. In: Keshamouni V, Arenberg D, Kalemkerian G, editors. Lung Cancer Metastasis: Springer New York; 2010. p. 93-109.
- [45]. Nagano M, Hoshino D, Koshikawa N, Akizawa T and Seiki M, "Turnover of focal adhesions and cancer cell migration", <u>International journal of cell biology</u>.
 2012. (2012): 310616.
- [46]. Zhong J, Paul A, Kellie SJ and O'Neill GM, "Mesenchymal migration as a therapeutic target in glioblastoma", Journal of oncology. 2010. (2010): 430142.
- [47]. Golubovskaya VM and Cance WG, "FAK and p53 protein interactions", <u>Anti-</u> <u>cancer agents in medicinal chemistry</u>. 11, 7. (2011): 617-9.

- [48]. Hall JE, Fu W and Schaller MD, "Focal adhesion kinase: exploring Fak structure to gain insight into function", <u>International review of cell and molecular</u> <u>biology</u>. 288. (2011): 185-225.
- [49]. Lal H, Verma SK, Foster DM, Golden HB, Reneau JC, Watson LE, et al.,
 "Integrins and proximal signaling mechanisms in cardiovascular disease",
 <u>Frontiers in bioscience (Landmark edition)</u>. 14. (2009): 2307-34.
- [50]. Calderwood DA, Zent R, Grant R, Rees DJ, Hynes RO and Ginsberg MH, "The Talin head domain binds to integrin beta subunit cytoplasmic tails and regulates integrin activation", <u>J Biol Chem</u>. 274, 40. (1999): 28071-4.
- [51]. Li S and Hua ZC, "FAK expression regulation and therapeutic potential", Advances in cancer research. 101. (2008): 45-61.
- [52]. Owen JD, Ruest PJ, Fry DW and Hanks SK, "Induced focal adhesion kinase (FAK) expression in FAK-null cells enhances cell spreading and migration requiring both auto- and activation loop phosphorylation sites and inhibits adhesion-dependent tyrosine phosphorylation of Pyk2", <u>Molecular</u> and <u>cellular biology</u>. 19, 7. (1999): 4806-18.
- [53]. Cance WG, Harris JE, Iacocca MV, Roche E, Yang X, Chang J, et al., "Immunohistochemical analyses of focal adhesion kinase expression in benign and malignant human breast and colon tissues: correlation with preinvasive and invasive phenotypes", <u>Clinical cancer research : an official journal of the</u> <u>American Association for Cancer Research</u>. 6, 6. (2000): 2417-23.
- [54]. Sood AK, Coffin JE, Schneider GB, Fletcher MS, DeYoung BR, Gruman LM, et al., "Biological significance of focal adhesion kinase in ovarian cancer: role in

migration and invasion", <u>The American journal of pathology</u>. 165, 4. (2004): 1087-95.

- [55]. Akasaka T, van Leeuwen RL, Yoshinaga IG, Mihm MC, Jr. and Byers HR, "Focal adhesion kinase (p125FAK) expression correlates with motility of human melanoma cell lines", <u>The Journal of investigative dermatology</u>. 105, 1. (1995): 104-8.
- [56]. Cary LA, Chang JF and Guan JL, "Stimulation of cell migration by overexpression of focal adhesion kinase and its association with Src and Fyn", <u>Journal of cell science</u>. 109 (Pt 7). (1996): 1787-94.
- [57]. Ridley AJ, "Rho GTPases and cell migration", <u>Journal of cell science</u>. 114, Pt15. (2001): 2713-22.
- [58]. Malliri A and Collard JG, "Role of Rho-family proteins in cell adhesion and cancer", <u>Current opinion in cell biology</u>. 15, 5. (2003): 583-9.
- [59]. Raftopoulou M and Hall A, "Cell migration: Rho GTPases lead the way", <u>Developmental biology</u>. 265, 1. (2004): 23-32.
- [60]. Allen WE, Jones GE, Pollard JW and Ridley AJ, "Rho, Rac and Cdc42 regulate actin organization and cell adhesion in macrophages", <u>Journal of cell science</u>.
 110 (Pt 6). (1997): 707-20.
- [61]. Hall A, "Small GTP-binding proteins and the regulation of the actin cytoskeleton", <u>Annual review of cell biology</u>. 10. (1994): 31-54.
- [62]. Guadamillas MC, Cerezo A and Del Pozo MA, "Overcoming anoikis--pathways to anchorage-independent growth in cancer", <u>Journal of cell science</u>. 124, Pt 19. (2011): 3189-97.

- [63]. Taddei ML, Giannoni E, Fiaschi T and Chiarugi P, "Anoikis: an emerging hallmark in health and diseases", <u>The Journal of pathology</u>. 226, 2. (2012): 380-93.
- [64]. Mehlen P and Puisieux A, "Metastasis: a question of life or death", <u>Nature</u> reviews Cancer. 6, 6. (2006): 449-58.
- [65]. Elmore S, "Apoptosis: a review of programmed cell death", <u>Toxicologic</u> <u>pathologv</u>. 35, 4. (2007): 495-516.
- [66]. Raffray M and Cohen GM, "Apoptosis and necrosis in toxicology: a continuum or distinct modes of cell death?", <u>Pharmacology & therapeutics</u>. 75, 3. (1997): 153-77.
- [67]. Golstein P and Kroemer G, "Cell death by necrosis: towards a molecular definition", <u>Trends in biochemical sciences</u>. 32, 1. (2007): 37-43.
- [68]. Chiarugi P and Giannoni E, "Anoikis: a necessary death program for anchoragedependent cells", <u>Biochemical pharmacology</u>. 76, 11. (2008): 1352-64.
- [69]. Grossmann J, "Molecular mechanisms of "detachment-induced apoptosis— Anoikis", <u>Apoptosis</u>. 7, 3. (2002): 247-60.
- [70]. "Anoikis Resistance: An Essential Prerequisite for Tumor Metastasis", International journal of cell biology. 2012. (2012).
- [71]. Youle RJ and Strasser A, "The BCL-2 protein family: opposing activities that mediate cell death", <u>Nature reviews Molecular cell biology</u>. 9, 1. (2008): 47-59.
- [72]. Oltvai ZN, Milliman CL and Korsmeyer SJ, "Bcl-2 heterodimerizes in vivo with a conserved homolog, Bax, that accelerates programmed cell death", <u>Cell</u>. 74, 4. (1993): 609-19.

- [73]. Adams JM and Cory S, "The Bcl-2 apoptotic switch in cancer development and therapy", <u>Oncogene</u>. 26, 9. (2007): 1324-37.
- [74]. Reddig PJ and Juliano RL, "Clinging to life: cell to matrix adhesion and cell survival", <u>Cancer metastasis reviews</u>. 24, 3. (2005): 425-39.
- [75]. Neutzner A, Li S, Xu S and Karbowski M, "The ubiquitin/proteasome systemdependent control of mitochondrial steps in apoptosis", <u>Seminars in cell &</u> <u>developmental biology</u>. 23, 5. (2012): 499-508.
- [76]. Boisvert-Adamo K, Longmate W, Abel EV and Aplin AE, "Mcl-1 is required for melanoma cell resistance to anoikis", <u>Molecular cancer research : MCR</u>. 7, 4. (2009): 549-56.
- [77]. Parton RG and Simons K, "The multiple faces of caveolae", <u>Nature reviews</u> <u>Molecular cell biology</u>. 8, 3. (2007): 185-94.
- [78]. Okamoto T, Schlegel A, Scherer PE and Lisanti MP, "Caveolins, a family of scaffolding proteins for organizing "preassembled signaling complexes" at the plasma membrane", <u>The Journal of biological chemistry</u>. 273, 10. (1998): 5419-22.
- [79]. Yang G, Truong LD, Timme TL, Ren C, Wheeler TM, Park SH, et al., "Elevated expression of caveolin is associated with prostate and breast cancer", <u>Clinical</u> <u>cancer research : an official journal of the American Association for Cancer</u> <u>Research.</u> 4, 8. (1998): 1873-80.
- [80]. Sunaga N, Miyajima K, Suzuki M, Sato M, White MA, Ramirez RD, et al., "Different roles for caveolin-1 in the development of non-small cell lung cancer versus small cell lung cancer", <u>Cancer research</u>. 64, 12. (2004): 4277-85.

- [81]. Lloyd PG and Hardin CD, "Caveolae in cancer: two sides of the same coin? Focus on "Hydrogen peroxide inhibits non-small cell lung cancer cell anoikis through the inhibition of caveolin-1 degradation"", <u>American journal of</u> <u>physiology Cell physiology</u>. 300, 2. (2011): C232-4.
- [82]. Carver LA and Schnitzer JE, "Caveolae: mining little caves for new cancer targets", <u>Nat Rev Cancer</u>. 3, 8. (2003): 571-81.
- [83]. Williams TM and Lisanti MP, "Caveolin-1 in oncogenic transformation, cancer, and metastasis", <u>Am J Physiol Cell Physiol</u>. 288, 3. (2005): C494-506.
- [84]. Fresno Vara JA, Casado E, de Castro J, Cejas P, Belda-Iniesta C and Gonzalez-Baron M, "PI3K/Akt signalling pathway and cancer", <u>Cancer treatment reviews</u>.
 30, 2. (2004): 193-204.
- [85]. Pal I and Mandal M, "PI3K and Akt as molecular targets for cancer therapy: current clinical outcomes", <u>Acta pharmacologica Sinica</u>. 33, 12. (2012): 1441-58.
- [86]. Franke TF, "PI3K/Akt: getting it right matters", <u>Oncogene</u>. 27, 50. (2008): 6473-88.
- [87]. Bellacosa A, Kumar CC, Di Cristofano A and Testa JR, "Activation of AKT kinases in cancer: implications for therapeutic targeting", <u>Advances in cancer</u> <u>research</u>. 94. (2005): 29-86.
- [88]. Scheid MP and Woodgett JR, "PKB/AKT: functional insights from genetic models", <u>Nature reviews Molecular cell biology</u>. 2, 10. (2001): 760-8.

- [89]. Diaz-Montero CM, Wygant JN and McIntyre BW, "PI3-K/Akt-mediated anoikis resistance of human osteosarcoma cells requires Src activation", <u>European</u> journal of cancer (Oxford. England : 1990). 42, 10. (2006): 1491-500.
- [90]. Cardone MH, Roy N, Stennicke HR, Salvesen GS, Franke TF, Stanbridge E, et al., "Regulation of cell death protease caspase-9 by phosphorylation", <u>Science</u> (<u>New York. NY</u>). 282, 5392. (1998): 1318-21.
- [91]. Datta SR, Katsov A, Hu L, Petros A, Fesik SW, Yaffe MB, et al., "14-3-3 proteins and survival kinases cooperate to inactivate BAD by BH3 domain phosphorylation", <u>Molecular cell</u>. 6, 1. (2000): 41-51.
- [92]. Khwaja A, "Akt is more than just a Bad kinase", <u>Nature</u>. 401, 6748. (1999): 33-4.
- [93]. Eastman A, "The formation, isolation and characterization of DNA adducts produced by anticancer platinum complexes", <u>Pharmacology & therapeutics</u>.
 34, 2. (1987): 155-66.
- [94]. Brozovic A, Ambriovic-Ristov A and Osmak M, "The relationship between cisplatin-induced reactive oxygen species, glutathione, and BCL-2 and resistance to cisplatin", <u>Critical reviews in toxicology</u>. 40, 4. (2010): 347-59.
- [95]. Kelland L, "The resurgence of platinum-based cancer chemotherapy", <u>Nature</u> reviews Cancer. 7, 8. (2007): 573-84.
- [96]. Goodsell DS, "The molecular perspective: cisplatin", <u>The oncologist</u>. 11, 3.(2006): 316-7.
- [97]. Reedijk J and Lohman PH, "Cisplatin: synthesis, antitumour activity and mechanism of action", <u>Pharmaceutisch weekblad Scientific edition</u>. 7, 5. (1985): 173-80.

- [98]. Wang D and Lippard SJ, "Cellular processing of platinum anticancer drugs", <u>Nature reviews Drug discovery</u>. 4, 4. (2005): 307-20.
- [99]. Matsushima H, Yonemura K, Ohishi K and Hishida A, "The role of oxygen free radicals in cisplatin-induced acute renal failure in rats", <u>The Journal of laboratory and clinical medicine</u>. 131, 6. (1998): 518-26.
- [100]. Baek SM, Kwon CH, Kim JH, Woo JS, Jung JS and Kim YK, "Differential roles of hydrogen peroxide and hydroxyl radical in cisplatin-induced cell death in renal proximal tubular epithelial cells", <u>The Journal of laboratory and clinical</u> <u>medicine</u>. 142, 3. (2003): 178-86.
- [101]. Itoh T, Terazawa R, Kojima K, Nakane K, Deguchi T, Ando M, et al., "Cisplatin induces production of reactive oxygen species via NADPH oxidase activation in human prostate cancer cells", <u>Free radical research</u>. 45, 9. (2011): 1033-9.
- [102]. Kim HJ, Lee JH, Kim SJ, Oh GS, Moon HD, Kwon KB, et al., "Roles of NADPH oxidases in cisplatin-induced reactive oxygen species generation and ototoxicity", <u>The Journal of neuroscience : the official journal of the Society</u> <u>for Neuroscience</u>. 30, 11. (2010): 3933-46.
- [103]. Kawai Y, Nakao T, Kunimura N, Kohda Y and Gemba M, "Relationship of intracellular calcium and oxygen radicals to Cisplatin-related renal cell injury", <u>Journal of pharmacological sciences</u>. 100, 1. (2006): 65-72.
- [104]. van Maanen JM, Retel J, de Vries J and Pinedo HM, "Mechanism of action of antitumor drug etoposide: a review", <u>Journal of the National Cancer Institute</u>.
 80, 19. (1988): 1526-33.

- [105]. Pommier Y and Marchand C, "Interfacial inhibitors: targeting macromolecular complexes", <u>Nature reviews Drug discovery</u>. 11, 1. (2012): 25-36.
- [106]. Wu CC, Li TK, Farh L, Lin LY, Lin TS, Yu YJ, et al., "Structural basis of type II topoisomerase inhibition by the anticancer drug etoposide", <u>Science (New</u> <u>York. NY)</u>. 333, 6041. (2011): 459-62.
- [107]. Burden DA, Kingma PS, Froelich-Ammon SJ, Bjornsti MA, Patchan MW, Thompson RB, et al., "Topoisomerase II.etoposide interactions direct the formation of drug-induced enzyme-DNA cleavage complexes", <u>The Journal of biological chemistry</u>. 271, 46. (1996): 29238-44.
- [108]. Karpinich NO, Tafani M, Rothman RJ, Russo MA and Farber JL, "The course of etoposide-induced apoptosis from damage to DNA and p53 activation to mitochondrial release of cytochrome c", <u>The Journal of biological chemistry</u>. 277, 19. (2002): 16547-52.
- [109]. Sinha BK, "Topoisomerase inhibitors. A review of their therapeutic potential in cancer", <u>Drugs</u>. 49, 1. (1995): 11-9.
- [110]. Nitiss JL, "Targeting DNA topoisomerase II in cancer chemotherapy", <u>Nature</u> reviews Cancer. 9, 5. (2009): 338-50.
- [111]. Chen CA, Chen CC, Shen CC, Chang HH and Chen YJ, "Moscatilin induces apoptosis and mitotic catastrophe in human esophageal cancer cells", <u>Journal</u> <u>of medicinal food</u>. 16, 10. (2013): 869-77.
- [112]. Chanvorachote P, Chunhacha P and Pongrakhananon V, "Anoikis: a potential target to prevent lung cancer metastasis?", <u>Lung Cancer Management</u>. 2, 3. (2013): 169-71.

- [113]. Rivera E and Gomez H, "Chemotherapy resistance in metastatic breast cancer: the evolving role of ixabepilone", <u>Breast Cancer Res</u>. 12, Suppl 2. (2010): 1-12.
- [114]. Seruga B, Ocana A and Tannock IF, "Drug resistance in metastatic castrationresistant prostate cancer", <u>Nature reviews Clinical oncology</u>. 8, 1. (2011): 12-23.
- [115]. Hakansson A, Gustafsson B, Abdiu A, Krysander L and Hakansson L, "Bcl-2 expression in metastatic malignant melanoma. Importance for the therapeutic efficacy of biochemotherapy", <u>Cancer immunology. immunotherapv : CII</u>. 52, 4. (2003): 249-54.
- [116]. Koshikawa N, Maejima C, Miyazaki K, Nakagawara A and Takenaga K, "Hypoxia selects for high-metastatic Lewis lung carcinoma cells overexpressing Mcl-1 and exhibiting reduced apoptotic potential in solid tumors", <u>Oncogene</u>. 25, 6. (2006): 917-28.
- [117]. Kennedy SG, Kandel ES, Cross TK and Hay N, "Akt/Protein kinase B inhibits cell death by preventing the release of cytochrome c from mitochondria", <u>Molecular and cellular biology</u>. 19, 8. (1999): 5800-10.
- [118]. Chanvorachote P, Nimmannit U, Lu Y, Talbott S, Jiang BH and Rojanasakul Y, "Nitric oxide regulates lung carcinoma cell anoikis through inhibition of ubiquitin-proteasomal degradation of caveolin-1", <u>The Journal of biological</u> <u>chemistry</u>. 284, 41. (2009): 28476-84.
- [119]. Serrels B, Serrels A, Brunton VG, Holt M, McLean GW, Gray CH, et al., "Focal adhesion kinase controls actin assembly via a FERM-mediated interaction with the Arp2/3 complex", <u>Nature cell biology</u>. 9, 9. (2007): 1046-56.

- [120]. Tureckova J, Vojtechova M, Krausova M, Sloncova E and Korinek V, "Focal adhesion kinase functions as an akt downstream target in migration of colorectal cancer cells", <u>Translational oncology</u>. 2, 4. (2009): 281-90.
- [121]. Steffen A, Ladwein M, Dimchev GA, Hein A, Schwenkmezger L, Arens S, et al.,
 "Rac function is crucial for cell migration but is not required for spreading and focal adhesion formation", Journal of cell science. 126, Pt 20. (2013): 4572-88.





APPENDIX

APPENDIX TABLES OF EXPERIMENTAL RESULTS

Table 2 The percentage of H460 cell viability was determined by MTT assay after treatment with various concentrations of DF-A (0-100 μ M) for 24 h (concentration-dependency).

DF-A (μM)	Cell viability (%)
0	100.00 ± 0.00
0.5	99.90 ± 0.29
1	99.67 ± 0.26
2.5	96.06 ± 0.38
5	93.24 ± 1.03
10	77.84 ± 0.12*
25	62.33 ± 0.92*
50	50.60 ± 1.37*
100	9.33 ± 0.74*

Table 3 The percentage of HaCat cell viability was determined by MTT assay after treatment with various concentrations of DF-A (0-100 μ M) for 24 h (concentration-dependency).

DF-A (μM)	Cell viability (%)
0	100.00 ± 2.47
0.5	98.09 ± 1.11
1	96.12 ± 0.87
2.5	91.38 ± 0.33
5	91.83 ± 1.31
10	91.05 ± 2.26
25	81.72 ± 0.70
50	58.14 ± 0.34*
100	20.40 ± 0.18*
L	k

Table 4 The percentage of apoptotic H460 cells was determined by MTT assay after treatment with various concentrations of DF-A (0-100 μ M) for 24 h (concentration-dependency).

DF-A (µM)	Apoptotic cells (%)
0	0.00 ± 0.00
0.5	1.12 ± 0.29
1	0.84 ± 0.26
2.5	3.90 ± 0.38
5	6.58 ± 1.03
10	21.72 ± 20.90*
25	34.49 ± 0.92*
50	45.20 ± 2.77*
100	88.14 ± 0.74*

Table 5 The percentage of apoptotic HaCat cells was determined by MTT assay after treatment with various concentrations of DF-A (0-100 μ M) for 24 h (concentration-dependency).

DF-A (µM)	Apoptotic cells (%)
0	0.00 ± 0.708
0.5	1.90 ± 0.33
1	3.87 ± 0.38
2.5	8.61 ± 0.37
5	8.16 ± 0.40
10	8.94 ± 0.49
25	18.27 ± 0.58
50	41.85 ± 0.84*
100	75.59 ± 0.76*

Table 6 The percentage of H460 cell viability was determined by MTT assay after treatment with various non-concentrations of DF-A (0-5 μ M) for 0, 6, 9, 12 or 24 h (time- and concentration- dependency).

Time			DF-A (µM)		
(h)	0	0.5	1	2.5	5
0	100.00 ± 0.18	100.00 ± 0.15	100.00 ± 0.22	100.00 ± 0.59	100.00 ± 0.22
6	72.19 ± 1.00	67.24 ± 0.77	65.03 ± 0.71	55.09 ± 0.50	34.43 ±0.62*
9	69.30 ± 1.00	60.62 ± 0.78	59.88 ± 0.67	47.49 ± 0.76*	38.66 ±0.61*
12	64.18 ± 0.93	57.20 ± 0.74	51.92 ± 0.83	44.80 ± 0.63*	36.44 ±0.58*
24	56.19 ± 0.68	43.32 ± 0.70	39.89 ± 0.64	36.93 ± 0.61*	26.06 ± 0.32*

Table 7 The percentage of apoptotic H460 cells was determined by MTT assay after treatment with various non-concentrations of DF-A (0-5 μ M) for 24 h (concentration-dependency).

DF-A (µM)	Apoptotic cells (%)
0	29.80 ± 0.68
0.5	37.67 ± 0.70
1	43.10 ± 0.64
2.5	57.06 ± 0.61
5	78.93 ± 0.32

Table 8 The percentage of HaCat cell viability was determined by MTT assay after treatment with various non-concentrations of DF-A (0-5 μ M) for 0, 6, 9, 12 or 24 h (time- and concentration- dependency).

Time			DF-A (µM)		
(h)	0	0.5	1	2.5	5
0	100 ± 0.23	100 ± 0.33	100 ± 0.10	101.88 ± 0.46	100 ± 0.32
6	12.10 ± 0.22	12.41 ± 0.16	13.99 ± 0.12	14.48 ± 0.20	14.86 ± 0.23
9	13.93 ± 0.13	13.75 ± 0.05	16.18 ± 0.03	15.02 ± 0.14	17.52 ± 0.23
12	14.47 ± 0.12	13.96 ± 0.09	16.01 ± 0.06	15.94 ± 0.17	14.93 ± 0.32
24	12.25 ± 0.21	12.14 ± 0.14	13.49 ± 0.09	12.92 ± 0.13	14.69 ± 0.22

Table 9 The percentage of relative sub G_0 fraction of H460 cells was determined by PI staining and flow cytometry after treatment with various non-concentrations of DF-A (0-5 μ M) for 24 h (concentration- dependency).

DF-A (µM)	Sub G ₀ fraction (%)
0	19.17 ± 0.26
0.5	19.40 ± 0.49
1	21.68 ± 0.92
2.5	24.47 ± 0.74
5	35.15 ± 0.58*

Values are means of 3 independent triplicate experiments \pm SE. * p<0.05 versus non-treated control. Determined by One-way ANOVA.

Table 10 The percentage of Colony size of H460 cells was determined by image analyzer after treatment with various non-concentrations of DF-A (0-5 μ M) for 2 weeks (concentration- dependency).

DF-A (µM)	Colony size (%)
0	100.00 ± 1.71
0.5	98.72 ± 1.70
1	72.39 ± 0.96*
2.5	61.07 ± 1.97*
5	19.25 ± 0.77*

Table 11 The percentage of Colony number of H460 cells was determined by image analyzer after treatment with various non-concentrations of DF-A (0-5 μ M) for 2 weeks (concentration- dependency).

DF-A (µM)	Colony size (%)
0	100.00 ± 2.00
0.5	94.17 ± 2.30
1	86.83 ± 3.85
2.5	54.43 ± 1.57*
5	37.97 ± 1.36*

Values are means of 3 independent triplicate experiments \pm SE. *p<0.05

versus non-treated control. Determined by One-way ANOVA.

Table 12 The relative protein of pAkt/Akt was determined by Western blot analysis after untreated or treated cells with DF-A 5 μ M for 0, 6, 12 or 24 h (time-dependency).

	Relative protein level	
	DF-A (µM)	
Time (h)	0	5
0	1.00 ± 0.00	1.00 ± 0.00
6	1.00 ± 0.03	0.85 ± 0.09
12	1.00 ± 0.08	0.41 ± 0.05*
24	1.00 ± 0.01	0.50 ± 0.03*

Table 13 The relative protein of Mcl-1 was determined by Western blot analysis after untreated or treated cells with DF-A 5 μ M for 0, 6, 12 or 24 h (time-dependency).

	Relative protein level	
	DF-A (μM)	
Time (h)	0	5
0	1.00 ± 0.00	1.00 ± 0.00
6	0.92 ± 0.04	0.81 ± 0.02
12	0.61 ± 0.07	0.56 ± 0.03
24	0.59 ± 0.01	0.50 ± 0.08

	Relative protein level DF-A (µM)		
Time (h)	0	5	
0	1.00 ± 0.00	1.00 ± 0.00	
6	1.00 ± 0.02	1.00 ± 0.01	
12	1.00 ± 0.08	0.95 ± 0.02	
24	1.00 ± 0.05	1.00 ± 0.07	

Table 14 The relative protein of Bax was determined by Western blot analysis after untreated or treated cells with DF-A 5 μ M for 0, 6, 12 or 24 h (time-dependency).

Table 15 The relative protein of Cav-1 was determined by Western blot analysis after untreated or treated cells with DF-A 5 μ M for 0, 6, 12 or 24 h (time-dependency).

	Relative protein level			
DF-A (µM)				
Time (h)	0 5			
0	1.00 ± 0.00	1.00 ± 0.00		
6	0.92 ± 0.08	1.00 ± 0.02		
12	0.91 ± 0.01	0.20 ± 0.05		
24	0.92 ± 0.05	0.11 ± 0.03		

Relative protein lev		rotein level	
	DF-A (µM)		
Time (h)	0	5	
0	1.00 ± 0.00	1.00 ± 0.00	
6	1.00 ± 0.09	0.65 ± 0.05	
12	1.00 ± 0.02	0.63 ± 0.01	
24	0.70 ± 0.05	0.41 ± 0.06	

Table 16 The relative protein of Bcl-2 was determined by Western blot analysis after untreated or treated cells with DF-A 5 μ M for 0, 6, 12 or 24 h (time-dependency).

Table 17 The percentage of H460 cells proliferation was determined by MTT assay after treatment with various non-concentrations of DF-A (0-5 μ M) for 0-72 h at various time points.

Time	Relative cell proliferation				
(h)	0	0.5	1	2.5	5
24	100.00 ± 0.34	95.55 ± 2.02	97.53 ± 0.95	100.64 ± 1.67	97.24 ± 3.00
48	100.00 ± 0.19	97.32 ± 1.18	95.23 ± 2.04	95.36 ± 2.39	96.32 ± 3.21
72	100.00 ± 0.98	99.75 ± 0.63	101.59 ± 0.88	97.72 ± 0.19	96.70 ± 1.10

Values are means \pm SE from 3 independent experiments. *p<0.05 versus untreated control at each indicated time. Determined by One-way ANOVA.

Table 18 Relative cell migration (wound closure) of H460 cells was determined by wound healing assay after treatment with various non-concentrations of DF-A (0-5 μ M) for 24 h.

Time (h)	Relative cell migration (wound closure)				
	DF-A (μM)				
	0	0.5	1	2.5	5
24	1.00 <u>+</u> 0.00	0.79 <u>+</u> 0.03	0.77 <u>+</u> 0.02	0.77 <u>+</u> 0.03	0.70 ± 0.00*

Table 19 Relative cell migration (wound closure) of H460 cells was determined by wound healing assay after treatment with various non-concentrations of DF-A (0-5 μ M) for 24, 48 or 72 h.

Time (h)	Relative cell migration (wound-healing)		
	DF-A (µM)		
	0 5		
24	1.00 <u>+</u> 0.00	0.66 <u>+</u> 0.02	
48	1.61 <u>+</u> 0.03	1.20 ± 0.02*	
72	2.36 ± 0.03	1.85 ± 0.03*	

Values are means of 3 independent triplicate experiments \pm SE. *p<0.05 versus untreated control. Determined by One-way ANOVA.

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Table 20 The relative protein of p-FAK/FAK, Rho-GTP and Rac-GTP was determined by western blot analysis after treatment with various non-concentrations of DF-A (0-5 μ M) for 24 h (concentration-dependency).

	Relative protein level				
	DF-A (µM)				
Proteins	0	0.5	1	2.5	5
р-ҒАК/ҒАК	1.00 ± 0.00	0.92 <u>+</u> 0.02	0.83 ± 0.08	0.21 <u>+</u> 0.03*	0.28 ± 0.03*
Rho-GTP	1.00 <u>+</u> 0.00	1.00 ± 0.05	1.00 ± 0.01	1.00 <u>+</u> 0.06	0.76 ± 0.05*
Rac-GTP	1.00 <u>+</u> 0.00	1.00 ± 0.01	1.00 <u>+</u> 0.02	1.00 <u>+</u> 0.07	0.97 ± 0.03

Table 21 The percentage of H460 cell viability was determined by MTT assay after pre-treatment with various non-concentration of DF-A (0-5 μ M) prior to cisplatin treatment.

Treatment	Cell viability (%)
Control (DF-A 0 μM)	100.00 ± 0.00
DMSO 0.5 %	97.15 ± 0.22
Cisplatin 100 µM	47.23 ± 0.38*
Cisplatin 100 µM + DMSO 0.5 %	47.44 ± 1.05
Cisplatin 100 µM + DF-A 0.5 µM	45.12 ± 0.48
Cisplatin 100 µM + DF-A 1 µM	51.68 ± 0.03
Cisplatin 100 µM + DF-A 2.5 µM	46.92 ± 0.61
Cisplatin 100 µM + DF-A 5 µM	50.20 ± 0.76

Table 22 The percentage of H460 cell viability was determined by MTT assay after pre-treatment with various non-concentration of DF-A (0-5 μ M) prior to etoposide treatment.

Treatment	Cell viability (%)
Control (DF-A 0 µM)	100.00 ± 0.00
DMSO 0.5 %	98.01 ± 0.68
Etoposide 100 µM	73.46 ± 0.09*
Etoposide 100 µM + DMSO 0.5 %	70.28 ± 0.18
Etoposide 100 μM + DF-A 0.5 μM	71.22 ± 0.31
Etoposide 100 μM + DF-A 1 μM	73.63 ± 0.25
Etoposide 100 μM + DF-A 2.5 μM	72.71 ± 0.53
Etoposide 100 µM + DF-A 5 µM	71.81 ± 0.44

VITA

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