

References

1. **Alqahtani S, and Kaddoumi A.** Vitamin E transporters in cancer therapy. *The AAPS journal* 17: 313-322, 2015.
2. **Andersen MH, Svane IM, Becker JC, and Straten PT.** The universal character of the tumor-associated antigen survivin. *Clinical cancer research : an official journal of the American Association for Cancer Research* 13: 5991-5994, 2007.
3. **Bao Y, Yin M, Hu X, Zhuang X, Sun Y, Guo Y, Tan S, and Zhang Z.** A safe, simple and efficient doxorubicin prodrug hybrid micelle for overcoming tumor multidrug resistance and targeting delivery. *J Control Release* 235: 182-194, 2016.
4. **Behrens P, Rothe M, Wellmann A, Krischler J, and Wernert N.** The Ets-1 transcription factor is up-regulated together with MMP 1 and MMP 9 in the stroma of pre-invasive breast cancer. *J Pathol* 194: 43-50, 2001.
5. **Bissonauth V, Shatenstein B, and Ghadirian P.** Nutrition and breast cancer among sporadic cases and gene mutation carriers: an overview. *Cancer Detect Prev* 32: 52-64, 2008.
6. **Blackburn JS, Rhodes CH, Coon CI, and Brinckerhoff CE.** RNA interference inhibition of matrix metalloproteinase-1 prevents melanoma metastasis by reducing tumor collagenase activity and angiogenesis. *Cancer research* 67: 10849-10858, 2007.
7. **Brinckerhoff CE, Rutter JL, and Benbow U.** Interstitial collagenases as markers of tumor progression. *Clinical cancer research : an official journal of the American Association for Cancer Research* 6: 4823-4830, 2000.
8. **Butt AM, Mohd Amin MC, and Katas H.** Synergistic effect of pH-responsive folate-functionalized poloxamer 407-TPGS-mixed micelles on targeted delivery of anticancer drugs. *Int J Nanomedicine* 10: 1321-1334, 2015.
9. **Cao N, and Feng SS.** Doxorubicin conjugated to D-alpha-tocopheryl polyethylene glycol 1000 succinate (TPGS): conjugation chemistry, characterization, in vitro and in vivo evaluation. *Biomaterials* 29: 3856-3865, 2008.
10. **Cappetta D, De Angelis A, Sapiro L, Prezioso L, Illiano M, Quaini F, Rossi F, Berrino L, Naviglio S, and Urbanek K.** Oxidative Stress and Cellular Response to Doxorubicin: A Common Factor in the Complex Milieu of Anthracycline Cardiotoxicity. *Oxidative medicine and cellular longevity* 2017: 1521020, 2017.
11. **Cappetta D, Rossi F, Piegari E, Quaini F, Berrino L, Urbanek K, and De Angelis A.** Doxorubicin targets multiple players: A new view of an old problem. *Pharmacological research* 127: 4-14, 2018.
12. **Chen W, Park SK, Yu W, Xiong A, Sanders BG, and Kline K.** Synthesis and screening of novel vitamin E derivatives for anticancer functions. *European journal of medicinal chemistry* 58: 72-83, 2012.
13. **Chen Y, Jungsuwadee P, Vore M, Butterfield DA, and St Clair DK.** Collateral damage in cancer chemotherapy: oxidative stress in nontargeted tissues. *Mol Interv* 7: 147-156, 2007.
14. **Chen ZP, Li M, Zhang LJ, He JY, Wu L, Xiao YY, Duan JA, Cai T, and Li WD.** Mitochondria-targeted drug delivery system for cancer treatment. *Journal of drug targeting* 24: 492-502, 2016.
15. **Chou TC, Motzer RJ, Tong Y, and Bosl GJ.** Computerized quantitation of synergism and antagonism of taxol, topotecan, and cisplatin against human teratocarcinoma cell growth: a rational approach to clinical protocol design. *J Natl Cancer Inst* 86: 1517-1524, 1994.
16. **Chou TC, and Talalay P.** Quantitative analysis of dose-effect relationships: the combined effects of multiple drugs or enzyme inhibitors. *Adv Enzyme Regul* 22: 27-55, 1984.
17. **Curtin NJ.** PARP inhibitors for cancer therapy. *Expert Rev Mol Med* 7: 1-20, 2005.
18. **D'Andrea GM.** Use of antioxidants during chemotherapy and radiotherapy should be avoided. *CA: a cancer journal for clinicians* 55: 319-321, 2005.

α-Tocopheryl Succinate Sensitizes the Human Breast Cancer Cells to Doxorubicin and Reduces Doxorubicin Induced Cardiotoxicity

19. **Dumont N, Bakin AV, and Arteaga CL.** Autocrine transforming growth factor-beta signaling mediates Smad-independent motility in human cancer cells. *The Journal of biological chemistry* 278: 3275-3285, 2003.
20. **Ferreira AR, Metzger-Filho O, Sarmento RMB, and Bines J.** Neoadjuvant Treatment of Stage IIB/III Triple Negative Breast Cancer with Cyclophosphamide, Doxorubicin, and Cisplatin (CAP Regimen): A Single Arm, Single Center Phase II Study (GBECAM 2008/02). *Frontiers in Oncology* 7: 2018.
21. **Fini MA, Monks J, Farabaugh SM, and Wright RM.** Contribution of Xanthine Oxidoreductase to Mammary Epithelial and Breast Cancer Cell Differentiation In Part Modulates Inhibitor of Differentiation-1. *Mol Cancer Res* 2011.
22. **Fini MA, Orchard-Webb D, Kosmider B, Amon JD, Kelland R, Shibao G, and Wright RM.** Migratory activity of human breast cancer cells is modulated by differential expression of xanthine oxidoreductase. *J Cell Biochem* 105: 1008-1026, 2008.
23. **Frankfurt OS, and Krishan A.** Identification of apoptotic cells by formamide-induced dna denaturation in condensed chromatin. *J Histochem Cytochem* 49: 369-378, 2001.
24. **Gava FN, Zacché E, Ortiz EMG, Champion T, Bandarra MB, Vasconcelos RO, Barbosa JC, and Camacho AA.** Doxorubicin induced dilated cardiomyopathy in a rabbit model: An update. *Research in Veterinary Science* 94: 115-121, 2013.
25. **Gharib MI, and Burnett AK.** Chemotherapy-induced cardiotoxicity: current practice and prospects of prophylaxis. *Eur J Heart Fail* 4: 235-242, 2002.
26. **Ghigo A, Li M, and Hirsch E.** New signal transduction paradigms in anthracycline-induced cardiotoxicity. *Biochim Biophys Acta* 1863: 1916-1925, 2016.
27. **Gogvadze V, Norberg E, Orrenius S, and Zhivotovsky B.** Involvement of Ca²⁺ and ROS in alpha-tocopherol succinate-induced mitochondrial permeabilization. *International journal of cancer Journal international du cancer* 127: 1823-1832, 2010.
28. **Hao T, Chen D, Liu K, Qi Y, Tian Y, Sun P, Liu Y, and Li Z.** Micelles of d-alpha-Tocopheryl Polyethylene Glycol 2000 Succinate (TPGS 2K) for Doxorubicin Delivery with Reversal of Multidrug Resistance. *ACS Appl Mater Interfaces* 7: 18064-18075, 2015.
29. **Hastak K, Alli E, and Ford JM.** Synergistic chemosensitivity of triple-negative breast cancer cell lines to poly(ADP-Ribose) polymerase inhibition, gemcitabine, and cisplatin. *Cancer research* 70: 7970-7980, 2010.
30. **Hayot C, Debeir O, Van Ham P, Van Damme M, Kiss R, and Decaestecker C.** Characterization of the activities of actin-affecting drugs on tumor cell migration. *Toxicol Appl Pharmacol* 211: 30-40, 2006.
31. **Herr I, Wilhelm D, Bohler T, Angel P, and Debatin KM.** Activation of CD95 (APO-1/Fas) signaling by ceramide mediates cancer therapy-induced apoptosis. *The EMBO journal* 16: 6200-6208, 1997.
32. **Hortobagyi GN.** Chemotherapy of breast cancer: a historical perspective. *Semin Oncol* 24: S17-11-S17-14, 1997.
33. **Ireland DJ, Kissick HT, and Beilharz MW.** Alpha-Tocopheryl succinate: toxicity and lack of anti-tumour activity in immuno-competent mice. *Food and chemical toxicology : an international journal published for the British Industrial Biological Research Association* 46: 508-512, 2008.
34. **Israel K, Yu W, Sanders BG, and Kline K.** Vitamin E succinate induces apoptosis in human prostate cancer cells: role for Fas in vitamin E succinate-triggered apoptosis. *Nutr Cancer* 36: 90-100, 2000.
35. **Janoff AS, Kurtz CL, Jablonski RL, Minchey SR, Boni LT, Gruner SM, Cullis PR, Mayer LD, and Hope MJ.** Characterization of cholesterol hemisuccinate and alpha-tocopherol hemisuccinate vesicles. *Biochim Biophys Acta* 941: 165-175, 1988.
36. **Jha K, Shukla M, and Pandey M.** Survivin expression and targeting in breast cancer. *Surgical oncology* 21: 125-131, 2012.
37. **Johnstone CN, Smith YE, Cao Y, Burrows AD, Cross RSN, Ling X, Redvers RP, Doherty JP, Eckhardt BL, Natoli AL, Restall CM, Lucas E, Pearson HB, Deb S, Britt KL, Rizzitelli A, Li J, Harmey JH, Pouliot**

α-Tocopheryl Succinate Sensitizes the Human Breast Cancer Cells to Doxorubicin and Reduces Doxorubicin Induced Cardiotoxicity

- N, and Anderson RL.** Functional and molecular characterisation of EO771.LMB tumours, a new C57BL/6-mouse-derived model of spontaneously metastatic mammary cancer. *Dis Model Mech* 8: 237-251, 2015.
38. **Kalender Y, Yel M, and Kalender S.** Doxorubicin hepatotoxicity and hepatic free radical metabolism in rats. The effects of vitamin E and catechin. *Toxicology* 209: 39-45, 2005.
39. **Kim HS, Lee YS, and Kim DK.** Doxorubicin exerts cytotoxic effects through cell cycle arrest and Fas-mediated cell death. *Pharmacology* 84: 300-309, 2009.
40. **Kline K, Yu W, and Sanders BG.** Vitamin E and breast cancer. *J Nutr* 134: 3458S-3462S, 2004.
41. **Kogure K, Manabe S, Hama S, Tokumura A, and Fukuzawa K.** Potentiation of anti-cancer effect by intravenous administration of vesiculated alpha-tocopheryl hemisuccinate on mouse melanoma in vivo. *Cancer letters* 192: 19-24, 2003.
42. **Kogure K, Morita M, Nakashima S, Hama S, Tokumura A, and Fukuzawa K.** Superoxide is responsible for apoptosis in rat vascular smooth muscle cells induced by alpha-tocopheryl hemisuccinate. *Biochim Biophys Acta* 1528: 25-30, 2001.
43. **Krumova K, Friedland S, and Cosa G.** How lipid unsaturation, peroxy radical partitioning, and chromanol lipophilic tail affect the antioxidant activity of alpha-tocopherol: direct visualization via high-throughput fluorescence studies conducted with fluorogenic alpha-tocopherol analogues. *Journal of the American Chemical Society* 134: 10102-10113, 2012.
44. **Larkins TL, Nowell M, Singh S, and Sanford GL.** Inhibition of cyclooxygenase-2 decreases breast cancer cell motility, invasion and matrix metalloproteinase expression. *BMC Cancer* 6: 181, 2006.
45. **Lawson KA, Anderson K, Simmons-Menchaca M, Atkinson J, Sun L, Sanders BG, and Kline K.** Comparison of Vitamin E Derivatives {alpha}-TEA and VES in Reduction of Mouse Mammary Tumor Burden and Metastasis. *Exp Biol Med (Maywood)* 229: 954-963, 2004.
46. **Li PY, Lai PS, Hung WC, and Syu WJ.** Poly(L-lactide)-vitamin E TPGS nanoparticles enhanced the cytotoxicity of doxorubicin in drug-resistant MCF-7 breast cancer cells. *Biomacromolecules* 11: 2576-2582, 2010.
47. **Liu WH, and Chang LS.** Fas/FasL-dependent and -independent activation of caspase-8 in doxorubicin-treated human breast cancer MCF-7 cells: ADAM10 down-regulation activates Fas/FasL signaling pathway. *The international journal of biochemistry & cell biology* 43: 1708-1719, 2011.
48. **Lou PJ, Lai PS, Shieh MJ, MacRobert AJ, Berg K, and Bown SG.** Reversal of doxorubicin resistance in breast cancer cells by photochemical internalization. *International journal of cancer Journal international du cancer* 119: 2692-2698, 2006.
49. **Neuzil J.** Vitamin E succinate and cancer treatment: a vitamin E prototype for selective antitumour activity. *British journal of cancer* 89: 1822-1826, 2003.
50. **Neuzil J, Dong LF, Ramanathapuram L, Hahn T, Chladova M, Wang XF, Zobalova R, Prochazka L, Gold M, Freeman R, Turanek J, Akporiaye ET, Dyason JC, and Ralph SJ.** Vitamin E analogues as a novel group of mitocans: anti-cancer agents that act by targeting mitochondria. *Molecular aspects of medicine* 28: 607-645, 2007.
51. **Neuzil J, Tomasetti M, Mellick AS, Alleva R, Salvatore BA, Birringer M, and Fariss MW.** Vitamin E analogues: a new class of inducers of apoptosis with selective anti-cancer effects. *Curr Cancer Drug Targets* 4: 355-372, 2004.
52. **Neuzil J, Tomasetti M, Zhao Y, Dong LF, Birringer M, Wang XF, Low P, Wu K, Salvatore BA, and Ralph SJ.** Vitamin E analogs, a novel group of "mitocans," as anticancer agents: the importance of being redox-silent. *Mol Pharmacol* 71: 1185-1199, 2007.
53. **Neuzil J, Weber T, Schroder A, Lu M, Ostermann G, Gellert N, Mayne GC, Olejnicka B, Negre-Salvayre A, Sticha M, Coffey RJ, and Weber C.** Induction of cancer cell apoptosis by alpha-tocopheryl succinate: molecular pathways and structural requirements. *Faseb J* 15: 403-415., 2001.

α-Tocopheryl Succinate Sensitizes the Human Breast Cancer Cells to Doxorubicin and Reduces Doxorubicin Induced Cardiotoxicity

54. **Nguyen TK, Nilakantan V, Felix CC, Khanna AK, and Pieper GM.** Beneficial Effect of α-Tocopheryl Succinate in Rat Cardiac Transplants. *The Journal of Heart and Lung Transplantation* 25: 707-715, 2006.
55. **Octavia Y, Tocchetti CG, Gabrielson KL, Janssens S, Crijns HJ, and Moens AL.** Doxorubicin-induced cardiomyopathy: from molecular mechanisms to therapeutic strategies. *Journal of molecular and cellular cardiology* 52: 1213-1225, 2012.
56. **Olson LE, Bedja D, Alvey SJ, Cardounel AJ, Gabrielson KL, and Reeves RH.** Protection from doxorubicin-induced cardiac toxicity in mice with a null allele of carbonyl reductase 1. *Cancer research* 63: 6602-6606, 2003.
57. **Pacher P, Liaudet L, Bai P, Virag L, Mabley JG, Hasko G, and Szabo C.** Activation of poly(ADP-ribose) polymerase contributes to development of doxorubicin-induced heart failure. *J Pharmacol Exp Ther* 300: 862-867, 2002.
58. **Pei D.** Matrix metalloproteinases target protease-activated receptors on the tumor cell surface. *Cancer Cell* 7: 207-208, 2005.
59. **Petrella BL, and Brinckerhoff CE.** Tumor cell invasion of von Hippel Lindau renal cell carcinoma cells is mediated by membrane type-1 matrix metalloproteinase. *Mol Cancer* 5: 66, 2006.
60. **Prochazka L, Dong LF, Valis K, Freeman R, Ralph SJ, Turanek J, and Neuzil J.** α-Tocopheryl succinate causes mitochondrial permeabilization by preferential formation of Bak channels. *Apoptosis : an international journal on programmed cell death* 15: 782-794, 2010.
61. **Savitskaya MA, and Onischenko GE.** α-Tocopheryl succinate affects malignant cell viability, proliferation, and differentiation. *Biochemistry (Moscow)* 81: 806-818, 2016.
62. **Savitskaya MA, Vildanova MS, Kisurina-Evgenieva OP, Smirnova EA, and Onischenko GE.** Mitochondrial Pathway of α-Tocopheryl Succinate-Induced Apoptosis in Human Epidermoid Carcinoma A431 Cells. *Acta naturae* 4: 88-94, 2012.
63. **Shi Y, Moon M, Dawood S, McManus B, and Liu PP.** Mechanisms and management of doxorubicin cardiotoxicity. *Herz* 36: 296-305, 2011.
64. **Shiau CW, Huang JW, Wang DS, Weng JR, Yang CC, Lin CH, Li C, and Chen CS.** α-Tocopheryl succinate induces apoptosis in prostate cancer cells in part through inhibition of Bcl-xL/Bcl-2 function. *The Journal of biological chemistry* 281: 11819-11825, 2006.
65. **Steelant WF, Kawakami Y, Ito A, Handa K, Bruyneel EA, Mareel M, and Hakomori S.** Monosialyl-Gb5 organized with cSrc and FAK in GEM of human breast carcinoma MCF-7 cells defines their invasive properties. *FEBS Lett* 531: 93-98, 2002.
66. **Teng XW, Davies NM, Fukuda C, Good RL, and Fariss MW.** Pharmacokinetics and tissue distribution of d-α-tocopheryl succinate formulations following intravenous administration in the rat. *Biopharmaceutics & drug disposition* 26: 195-203, 2005.
67. **Tiwary R, Yu W, Sanders BG, and Kline K.** α-TEA cooperates with MEK or mTOR inhibitors to induce apoptosis via targeting IRS/PI3K pathways. *British journal of cancer* 104: 101-109, 2011.
68. **Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, and Jemal A.** Global cancer statistics, 2012. *CA: a cancer journal for clinicians* 65: 87-108, 2015.
69. **Ueno M, Kakinuma Y, Yuhki K, Murakoshi N, Iemitsu M, Miyauchi T, and Yamaguchi I.** Doxorubicin induces apoptosis by activation of caspase-3 in cultured cardiomyocytes in vitro and rat cardiac ventricles in vivo. *J Pharmacol Sci* 101: 151-158, 2006.
70. **Voigt W.** Sulforhodamine B assay and chemosensitivity. *Methods in molecular medicine* 110: 39-48, 2005.
71. **Wahba HA, and El-Hadaad HA.** Current approaches in treatment of triple-negative breast cancer. *Cancer biology & medicine* 12: 106-116, 2015.

α-Tocopheryl Succinate Sensitizes the Human Breast Cancer Cells to Doxorubicin and Reduces Doxorubicin Induced Cardiotoxicity

72. **Wang XF, Witting PK, Salvatore BA, and Neuzil J.** Vitamin E analogs trigger apoptosis in HER2/erbB2-overexpressing breast cancer cells by signaling via the mitochondrial pathway. *Biochem Biophys Res Commun* 326: 282-289, 2005.
73. **Wojtacki J, Lewicka-Nowak E, and Lesniewski-Kmak K.** Anthracycline-induced cardiotoxicity: clinical course, risk factors, pathogenesis, detection and prevention--review of the literature. *Med Sci Monit* 6: 411-420, 2000.
74. **Wyatt CA, Geoghegan JC, and Brinckerhoff CE.** Short hairpin RNA-mediated inhibition of matrix metalloproteinase-1 in MDA-231 cells: effects on matrix destruction and tumor growth. *Cancer research* 65: 11101-11108, 2005.
75. **Yang C, Qin Y, Tu K, Xu C, Li Z, and Zhang Z.** Star-shaped polymer of betacyclodextrin-g-vitamin E TPGS for doxorubicin delivery and multidrug resistance inhibition. *Colloids Surf B Biointerfaces* 169: 10-19, 2018.
76. **Yang C WT, Qi Y, Zhang Z.** Recent Advances in the Application of Vitamin E TPGS for Drug Delivery. *Theranostics* 8: 464-485, 2018.
77. **Yu W, Israel K, Liao QY, Aldaz CM, Sanders BG, and Kline K.** Vitamin E succinate (VES) induces Fas sensitivity in human breast cancer cells: role for Mr 43,000 Fas in VES-triggered apoptosis. *Cancer research* 59: 953-961, 1999.
78. **Yu W, Sanders BG, and Kline K.** RRR-alpha-tocopheryl succinate inhibits EL4 thymic lymphoma cell growth by inducing apoptosis and DNA synthesis arrest. *Nutr Cancer* 27: 92-101, 1997.
79. **Zaremba T, and Curtin NJ.** PARP inhibitor development for systemic cancer targeting. *Anticancer Agents Med Chem* 7: 515-523, 2007.
80. **Zaremba T, Thomas H, Cole M, Plummer ER, and Curtin NJ.** Doxorubicin-induced suppression of poly(ADP-ribose) polymerase-1 (PARP-1) activity and expression and its implication for PARP inhibitors in clinical trials. *Cancer chemotherapy and pharmacology* 66: 807-812, 2010.
81. **Zhang X, Peng X, Yu W, Hou S, Zhao Y, Zhang Z, Huang X, and Wu K.** Alpha-tocopheryl succinate enhances doxorubicin-induced apoptosis in human gastric cancer cells via promotion of doxorubicin influx and suppression of doxorubicin efflux. *Cancer letters* 307: 174-181, 2011.
82. **Zhu J, Zhang J, Xiang D, Zhang Z, Zhang L, Wu M, Zhu S, Zhang R, and Han W.** Recombinant human interleukin-1 receptor antagonist protects mice against acute doxorubicin-induced cardiotoxicity. *European journal of pharmacology* 643: 247-253, 2010.