

BIOGRAPHICAL SKETCH

Andreas I. Constantinou, Professor

EDUCATION

INSTITUTION AND LOCATION	DEGREE	YEAR	FIELD
National University of Athens, Greece	B. S.	1975	BIOLOGY
University of Toledo, Toledo, OH	M. S.	1980	BIOLOGY
Medical College of Ohio, Toledo, OH	Ph. D.	1985	BIOCHEMISTRY

PROFESSIONAL EXPERIENCE

1980 - 1984	Predoctoral Fellow, Department of Biochemistry, Medical College of Ohio, Toledo, Ohio
1984 - 1986	Postdoctoral Fellow, Department of Molecular Biology, Northwestern University Medical School, Chicago, Illinois
1986 - 1990	Postdoctoral Appointee, Division of Biological and Medical Research, Argonne National Laboratory, Argonne, Illinois
1990 - 1992	Research Biologist, IIT Research Institute, Chicago, Illinois
1992 - 1994	Assistant Professor, Specialized Cancer Center and Department of Genetics, School of Medicine, University of Illinois at Chicago, Chicago, Illinois
1994 - 1997	Assistant Professor, Department of Surgical Oncology and Department of Genetics, University of Illinois at Chicago, Chicago, Illinois
1997 - 2002	Associate Professor, Department of Surgical Oncology, Department of Genetics and Department of Pharmacology, University of Illinois at Chicago, Chicago, Illinois
2000 - 2002	Associate Professor, Medicinal Chemistry/Pharmacognosy, College of Pharmacy, University of Illinois at Chicago, Chicago, Illinois
2000 - 2002	Director of Research, Functional Foods for Health (FFH) Program
2004 - 2006	Chairman, Department of Biological Sciences, University of Cyprus
2006 - 2008	Dean, Faculty of Pure and Applied Sciences, University of Cyprus
2009 - 2012	Chairman, Department of Biological Sciences, University of Cyprus
2002 - present	Professor of Molecular Biology, University of Cyprus.

PROFESSIONAL ACTIVITIES

1997 – present	Associate Editor for <i>Nutrition and Cancer, an International Journal</i>
2002 – present	Member, Editorial Board, <i>in vivo</i> .

ADVISORY COMMITTEE MEMBERSHIP

1994 - 1996	Member, Army Breast Cancer Research Projects (CTB-5A).
1995 - 1998	Ad Hoc Member, NIH/NCI, Contracts Technical Review Group.
2000 - 2002	Ad Hoc Member, NIH/NCI, Interdisciplinary Research Teams for Molecular Targets.
2000 - 2006	Member, NIH/NCI, Special Emphasis Panel, Cancer Prevention Research Small Grants.
2001 – 2006	Ad Hoc Member, ACS-National, CNE Study Section.

RESEARCH INTERESTS

- Role of nutrition in carcinogenesis; cancer chemoprevention
- Application of systems biology in cancer chemoprevention
- Phytoestrogens and Selective Estrogen Receptor Modulators (SERMs).
- Cell death mechanisms
- Tumor targets

PUBLICATIONS

ORIGINAL FULL PAPERS

1. Chakraborty I, **Constantinou AI**, McCorquodale M. Monoclonal antibodies to sperm surface antigens. *Animal Reprod. Science*, 9: 101-109, 1985.
2. **Constantinou AI**, Squinto, SP, Jungmann, JA. The phosphoform of regulatory subunit RII of cyclic AMP-dependent protein kinase possesses intrinsic topoisomerase activity. *Cell*, 43: 429-437, 1985.
3. Jungmann RA, **Constantinou AI**, Squinto SP, Kwast-Welfeld J, Schweppe JJ. Regulation of lactate dehydrogenase gene expression by cyclic AMP-dependent protein kinase subunits. *Ann. N.Y. Acad. Sci.* 478: 147-161, 1986.
4. **Constantinou AI**, Voelkel-Meiman K, Sternglanz R, McCorquodale M, McCorquodale J. Involvement of host DNA gyrase in growth of bacteriophage T5. *J. Virology* 57: 875-882. 1986.
5. **Constantinou AI**, Henning-Chubb C, Huberman E. Novobiocin and Phorbol 12-Myristate 13-acetate-induced differentiation of human leukemia cells associated with a reduction in topoisomerase II activity. *Cancer Res.* 49: 1110-1117, 1989.
6. Hunzicker-Dunn M., Meizels ET, Kern LC, Ekstrom RC, **Constantinou AI**. Separation of the complexes formed between the regulatory and catalytic subunits of cyclic adenosine monophosphate-dependent protein kinase and topoisomerase I activity in preovulatory follicle-enriched immature rat ovaries. *Molecul. Endocrinol.* 3: 780-789, 1989.
7. **Constantinou AI**, Kiguchi K, Huberman E. Induction of differentiation and DNA strand breakage in human HL-60 and K-562 leukemia cells by genistein. *Cancer Res.*, 50: 2618-2624, 1990.
8. Kiguchi K, Constantinou AI, Huberman E. Genistein-induced cell differentiation and protein-linked DNA strand breakage in human melanoma cells. *Cancer Communications* 2: 271-278, 1990.
9. Ganapathi R, Kamath N, **Constantinou AI**, Grabowski D, Ford J, Anderson A. Effect of the calmodulin inhibitor trifluoperazine on phosphorylation of p-glycoprotein and topoisomerase II: Relationship to modulation of subcellular distribution, DNA damage and cytotoxicity of doxorubicin in multidrug resistant L1210 mouse leukemia cells. *Biochemical Pharm.* 41: 21-26, 1991.
10. **Constantinou AI**, Grdina D, Kiguchi K, Huberman E. The effect of topoisomerase inhibitors on the expression of differentiation markers and cell cycle progression in human K-562 leukemia cells. *Exp. Cell Res.* 203: 100-103, 1992.
11. Ganapathi R, Zwelling L, **Constantinou A**, Ford J, Grabowski D. Altered phosphorylation, biosynthesis and degradation of the 170 kDa form of topoisomerase II as a determinant of amsacrine resistance in human leukemia cells. *Biochem. Biophys. Res Commun.* 192 (3): 1274-1280, 1993.
12. Grdina DJ, **Constantinou AI**, Shigematsou N. Inhibition of topoisomerase II activity in CHO K1 cells by 2-[(aminopropyl)amino]ethanethiol (WR-1065). *Radiation Res.*, 138: 44-52, 1994.
13. Mehta RG, Liu J, **Constantinou AI**, Hawthorne M, Pezzuto J, Moon R, Moriarty R. Structure-activity relationships of brassinin in preventing the development of carcinogen-induced mammary lesions in organ culture. *Anticancer Res.* 14:1209-1214, 1994.
14. Constantinou AI, Huberman E. Genistein, an inducer of tumor cell differentiation: possible mechanisms of action. *Proc. Soc. Exper. Biol. Med.* 208:109-115, 1995.
15. Mehta RG, Moriarty RM, Liu J, **Constantinou AI**, Thomas C, Hawthorne M, Pezzuto J, Moon R. Brassinin, a phytoalexin from cabbage: synthesis and activity as cancer chemopreventive agent. *Carcinogenesis* 16: 399-404, 1995.

16. **Constantinou A**, Stoner GD, Young-Han, Mehta RG, Runyan C, Moon R. The dietary anticancer agent ellagic acid is a potent inhibitor of human DNA topoisomerases. *Nutr. Cancer.* 1995, 23:121-130
17. Constantinou A, Mehta, RG, Runyan C, Rao RVN, Vaughan A, Moon, R C. Plant flavonoids as DNA topoisomerase antagonists and poisons: structure-activity relationships. *J. Natural Products*, 58: 217-225, 1995.
18. Mehta RG, Mehta RR, **Constantinou AI**, Moon RC. Distribution of epidermal growth factor receptors in normal and neoplastic mammary tissues. *Oncology Reports* 2: 281-284, 1995.
19. Gerhauser C, Woonghon, M, Lee SK, Suh N, Yingde L, Kosmeder J, Luyengi L, Fong HH, Kinghorn DA, Moriarty RM, Mehta RG, **Constantinou AI**, Moon RC, Pezzuto JM. Rotenoids mediated potent cancer chemopreventive activity through transcriptional regulation of ornithine decarboxylase. *Nature Med.*, 1:260-266, 1995.
20. Ganapathi R, **Constantinou AI**, Kamath N, Dubyak G, Grabowski D, Krivacic K. Resistance to etoposide in human leukemia HL-60 cells: reduction in drug induced DNA cleavage associated with hypophosphorylation of topoisomerase II phosphopeptides. *Molecular Pharmacol.* 50: 243-248, 1996.
21. **Constantinou AI**, Vaughan A, Yamasaki H, Kamath N. Commitment to differentiation in mouse erythroleukemia cells is controlled by alterations in topoisomerase II alpha phosphorylation. *Cancer Res.* 56:4192-4196, 1996.
22. **Constantinou AI**, Mehta RG, Vaughan A. Inhibition of N-methyl-N-nitrosourea-Induced Mammary Tumors in Rats by the Soybean Isoflavones. *Anticancer Res.*, 16: 3293-3298, 1996.
23. Mehta RG, Moriarty RM, Mehta RR, Penmasta R, Lazzaro G, **Constantinou AI**, Knutson JC, Guo L. Prevention of preneoplastic mammary lesion development by a novel vitamin D analog 1alpha(hydroxy)vitamin D5. *J. Natl. Cancer Inst.*, 89: 212-218, 1997.
24. Krygier A, Murley JS, Mehta RR, **Constantinou AI**. Induction of human adenocarcinoma cell differentiation by the phytoestrogen genistein is independent to its antiestrogenic function. *Int J. Oncol.* 10:753-757, 1997.
25. **Constantinou AI**, Runyan C, Grdina D, Murley J. Apoptosis and cell cycle delay in G2-M phase introduced by the phytoestrogen genistein. *Phytomedicine (supplement 1)* 3: 124-125, 1997.
26. Hesser P, Larsen PE, **Constantinou AI**, Schram KH, Weber JM. Isolation of isoflavones from soy-based fermentations of the erythromycin-producing bacterium *Saccharopolyspora erythraea*. *Appl. Microbiol. Biotechnol* 47: 398-404, 1997.
27. Khodarev NA, Narayanna A, **Constantinou AI**, Vaughan ATM. Topologically constrained domains of supercoiled DNA in eukaryotic cells. *DNA and Cell Biology* 16: 1051-1058, 1997.
28. Murley JS, **Constantinou AI**, Grdina DJ. WR-1065, an active metabolite of the cytoprotector amifostine, affects phosphorylation of topoisomerase II α leading to changes in enzyme activity and cell cycle progression in CHO AA8 cells. *Cell Proliferation*, 30: 283-294, 1997.
29. Krygier A, Mehta RR, **Constantinou AI**. Genistein induces maturation of human breast cancer cells and prevents tumor growth in nude mice. *Am. J. Clin. Nutr.* 68 (supl):1426S-30S, 1998.
30. **Constantinou AI**, Kamath N, Murley JA. Genistein inactivates bcl-2, delays G2/M phase of the cell cycle, and induces apoptosis of human breast adenocarcinoma MCF-7 cells. *Eur. J. Cancer*, 34: 1927-1934, 1998.
31. Boddie AW, **Constantinou AI**, Williams C, Reed A. Nitrogen mustard up-regulates Bcl-2 and GSH and increases NTP and PCr in HT-29 colon cancer cell line. *Br. J. Cancer*, 77:1395-1404, 1998.
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Solubilization and stabilization of carotenoids using micelles: Delivery of lycopene to cells in culture. *Lipids*, 34: 1031-1036, 1999.

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39. Pisha E, Lui X, **Constantinou AI**, Bolton J. Evidence that a metabolite of equine estrogens, 4-Hydroxyequilenin, induces cellular transformation in vitro. *Chem. Res. Toxicol.* 14:82-90, 2001.
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44. **Constantinou AI**, Rossi H, Lantvit D, Hawthorn M, Xu X, Nho C-W, Jefferey EH, Christov K, van Breemen R, Pezzuto J. Soy protein isolate prevents chemically induced rat mammary tumors. *Pharmaceutical Biology* 40: 24-34, 2002.
45. Block KI, **Constantinou A**, Hilakivi-Clarke L, Hughes C, Tripathy D, Tice JA. Point-counterpoint: soy intake for breast cancer patients. *Integr Cancer Ther*, 1: 90-100, 2002.
46. Burdette JE, Chen SN, Lu ZZ, Xu H, White BE, Fabricant DS, Liu J, Fong HH, Farnsworth NR., **Constantinou AI**, Van Breemen RB, Pezzuto JM, Bolton JL. Black cohosh (*Cimicifuga racemosa* L.) protects against menadione-induced DNA damage through scavenging of reactive oxygen species: bioassay-directed isolation and characterization of active principles. *J Agric Food Chem*, 50: 7022-7028, 2002.
47. **Constantinou AI**, Husband, A. Phenoxodiol (2H-1-benzopyran-7-0,1,3-(4-hydroxyphenyl)), a novel isoflavone derivative, inhibits DNA topoisomerase II by stabilizing the cleavable complex. *Anticancer Res*, 22: 2581-2585, 2002.
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49. **Constantinou, A. I.**, Mehta, R., and Husband A. Phenoxodiol, a novel isoflavone derivative, inhibits dimethylbenz[a]anthracene (DMBA)-induced mammary carcinogenesis in female Sprague-Dawley rats. *Eur J Cancer*, 39: 1012-1018, 2003.
50. Gentile MS, Vasu C, Green A, Murillo G, Das Gupta TK, **Constantinou AI**, Prabhakar BS, Salti GI. Targeting colon cancer cells with genistein-17.1A immunoconjugate. *Int J Oncol*, 22: 955-959,

2003.

51. Tonetti DA, Rubenstein R, DeLeon M, Zhao H, Pappas SG, Bentrem DJ, Chen B, **Constantinou A**, Jordan CV. Stable transfection of an estrogen receptor beta cDNA isoform into MDA-MB-231 breast cancer cells. *J Steroid Biochem Mol Biol*, 87: 47-55, 2003.
52. Guo JY, Li X, Browning JD Jr, Rottinghaus GE, Lubahn DB, **Constantinou A**, Bennink M, MacDonald RS, Dietary soy isoflavones and estrone protect ovariectomized ERalphaKO and wild-type mice from carcinogen-induced colon cancer. *J Nutr*, 134: 179-182, 2004.
53. Punj V, Bhattacharyya S, Saint-Dic D, Vasu C, Cunningham EA, Graves J, Yamada T, **Constantinou AI**, Christov K, White B, Li G, Majumdar D, Chakrabarty AM, Das Gupta TK. Bacterial cupredoxin azurin as an inducer of apoptosis and regression in human breast cancer. *Oncogene*, 23: 2367-2378, 2004.
54. Murillo G, Choi, J, Pan O, **Constantinou A**, Mehta R. Garbanzo bean flour is as effective as soy bean flour in suppressing the formation of aberrant crypt in the colons of CF-1 mice. *Anticancer Res*. 24:3049-55 2004.
55. Constantinou AI, White BEP, Tonetti D, Yang Y, Liang W, Li W, van Breemen RB. The soy isoflavone daidzein improves the capacity of tamoxifen to prevent mammary tumors. *European J Cancer*, 41: 647-654, 2005
56. Tonetti DA, Zhang Y, Zhao H, Lim SB, **Constantinou AI**. The effect of the phytoestrogens genistein, daidzein, and equol on the growth of tamoxifen-resistant T47D/PKC alpha. *Nutr Cancer* 58:222-229, 2007
57. Constantinou C, Papas A and **Constantinou AI**. Vitamin E and Cancer: An insight into the anticancer activities of vitamin E isomers and analogues. *Int J Cancer*, 123:739-52, 2008
58. Georgaki S, Skopeliti M, Tsiatas M, Nicolaou KA, Husband AI, Bamias A, **Constantinou AI**, Tsitsilonis OE. Phenoxodiol, an anticancer isoflavene, induces immunomodulatory effects in vitro and in vivo. *J Cell Mol Med*. 20: 1-10, 2009
59. Batsi C, Markopoulou S, Kontargiris E, Charalambous C, Thomas C, Christoforidis S, Kanavaros P, **Constantinou AI**, Marcu KB, Kolettas E. Bcl-2 blocks 2-methoxyestradiol induced leukemia cell apoptosis by a p27(Kip1)-dependent G1/S cell cycle arrest in conjunction with NF-kappaB activation. *Biochem Pharmacol*. 78:33-44, 2009
60. Constantinou C, Papas KA, **Constantinou AI**. Caspase-independent pathways of programmed cell death: the unraveling of new targets of cancer therapy? *Curr Cancer Drug Targets* 9:717-28, 2009
61. Constantinou C, Hyatt JA, Vraka PS, Papas A, Papas KA, Neophytou C, Hadjivassiliou V, **Constantinou AI**. Induction of caspase-independent programmed cell death by vitamin E natural homologs and synthetic derivatives. *Nutr Cancer*: 61:864-74, 2009
62. Constantinou C, Neophytou CM, Vraka P, Hyatt JA, Papas KA, **Constantinou AI**. Induction of DNA Damage and Caspase-Independent Programmed Cell Death by Vitamin E. *Nutr Cancer*. 64:136-152 2012
63. Nicolaou KA, Liapis V, Evdokiou A, Constantinou C, Magiatis P, Skaltsounis AL, Koumas L, Costeas PA, **Constantinou AI**. Induction of discrete apoptotic pathways by bromo-substituted indirubin derivatives in invasive breast cancer cells. *Biochem Biophys Res Commun*. 425:76-82. 2012
64. Odiatou EM, Skaltsounis AL, Constantinou AI. Identification of the factors responsible for the in vitro pro-oxidant and cytotoxic activities of the olive polyphenols oleuropein and hydroxytyrosol. *Cancer Lett*. 330:113-21, 2013.
65. Charalambous C, Pitta C and Constantinou AI. Equol enhances tamoxifen's antitumor activity by induction of caspase-mediated apoptosis. *BMC Cancer*. 13:238-247, 2013.
66. Pitta C, Papageorgis P., Constantinou AI. Combination treatment with TSA and 5-aza-dc restores response to tamoxifen in tamoxifen resistant ER- β negative breast cancer cells. *Cancer Lett*. 337: 167-176, 2013
67. Cretu E, Karonen M, Salminen JP, Mircea C, Trifan A, Charalambous C, **Constantinou AI**, Miron

- A. *In vitro* study of the antioxidant activity of a polyphenol-rich extract from *Pinus brutia* bark and its fractions J Med Food 16:984-91, 2013
68. Neophytou CM, Constantinou C, Papageorgis P, Constantinou AI. D-alpha-tocopheryl polyethylene glycol succinate (TPGS) induces cell cycle arrest and apoptosis selectively in Survivin-overexpressing breast cancer cells. *Biochem Pharmacology*, 89:31-42, 2014.
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72. Neophytou CM and Constantinou AI. Drug delivery innovations for enhancing the anticancer Potential of Vitamin E isoforms and their derivatives. *BioMed Research International*, 1-16, 2015
73. Papageorgis P, Ozturk S, Lambert AW, Neophytou CM, Tzatsos A, Wong CK, Thiagalingam S and Constantinou AI. Targeting IL13Ralpha2 activates STAT6-TP63 pathway to suppress breast cancer lung metastasis. *Breast Cancer Research*, 17:98, 2015
74. Savva CG, Totokotsopoulos S, Nicolaou KC, Neophytou CM, Constantinou AI. Selective activation of TNFR1 and NF- κ B inhibition by a novel biyouyanagin analogue promotes apoptosis in acute leukemia cells. *BMC Cancer*. 16(1):279, 2016 (doi: 10.1186/s12885-016-2310-5).
75. Theophilou IC, Neophytou CM, Kakas A, Constantinou AI. Carob and its Components in the Management of Gastrointestinal Disorders. *J Hepatol Gastroenterol* 2017; 1:005

BOOK CHAPTERS/COMMENTARIES

76. Mehta RG, Steele V, Pierson H, **Constantinou AI**, Moon RC. Licorice: absorption, distribution, metabolism and cancer chemoprevention. In P. A. Lachance ed. *Neutraceuticals: Designer Foods III Garlic, Soy and Licorice*. (Food and Nutrition Press, Inc) 265-278, 1997.
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80. **Constantinou AI**. Induction of apoptosis by genistein: Potential applications in cancer prevention and treatment. In G. Sarwar and J. B. Anderson eds, *Phytoestrogens and Health*, Chapter 25: 470-487, 2002.
81. **Constantinou AI** and van Breemen RB. Lycopene, a Dietary Cancer Chemopreventive Agent In: Kelloff G, Hawk E and Sigman C, editors (Humana Press Inc). *Cancer Chemoprevention Volume 1: Promising Cancer Chemoprevention Agents*, Chapter 34: 525-535, 2004.
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CONFERENCE PAPERS

84. Kakas AC, Lazarou S, Neophytou CM, Constantinou AI. Logical Modeling of Cancer and Chemoprevention. *Learning and Discovery in Symbolic Systems Biology*. 36-54, 2012
85. Antoniadou A, Keane J, Aristodimou A, Philipou C, Constantinou AI, Georgousopoulos C, Tozzi F, Kyriacou K, Hadjisavvas A, Loizidou M, Demetriou C, Pattichis C. The effects of applying cell-suppression and perturbation to aggregated genetic data. *Bioinformatics & Bioengineering (BIBE)*, 12th International Conference 644-649, 2012
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