CURRICULUM VITAE

I. Personal Data:

Name: Leslie C. Costello
Place of Birth: New York, New York

II. Education:

Degree	Institution	Field	Minor
B.S.	University of MD	Zoology	Chemistry
M.S.	University of MD	Zoology	Biochemistry
Ph.D.	University of MD	Physiology	Biochemistry

III. Appointments:

1995 - present: Professor, Division of Oncology, Dental School, University of Maryland, Baltimore.
1995 – present: Professor of Physiology and Endocrinology, University of Maryland Greenebaum Cancer Center
1980 -1995 : Chairman & Professor, Department of Physiology, Dental School, University of Maryland, Baltimore, Maryland.
1977 - 1980: Adjunct appointment: Professor, Department of Oncology, Howard University, Director of Endocrinology Cancer Section of the Cancer Research Center.
1975 - 1979: Professor and Chairman, Department of Physiology & Biophysics, College of Medicine, Howard University, Washington, D.C.
1970 - 1980: Professor, Department of Physiology & Biophysics, College of Medicine, Howard University, Washington, D.C.
1968 - 1974: Part-time appointment as Research Associate, Cystic Fibrosis Center, Children's Hospital, Washington, D.C.
1967 - 1970: Associate Professor, Department of Physiology & Biophysics, College of Medicine, Howard University, Washington, D.C.
1964 - 1967: Professor & Head, Department of Anatomy & Physiology, School of Pharmacy, University of Maryland, Baltimore, Maryland.

IV. Membership in Professional Organizations:

American Physiology Society
Endocrine Society
Sigma IX
American Association for the Advancement of Science
Maryland Biological Society (President, 1960 - 1961)
Rho Chi (Honor Society)
Maryland Academy of Science
Society Experimental Biology and Medicine (Maryland Chapter)
American Society of Parasitologists
American Society of Zoologists
American Association of Dental Science
Society for Basic Urological Research

V. Professional Activities (Selected, not complete list)

Serve on study sections for NIH prostate research grants.
Serve on study section for VA prostate research programs.
Serve on Army (DOD) grant review committees
Member of NCI Clinical Cancer Program and Cancer Center Support Review Committee
Member Site Visit Team for National Cancer Institute (NIH).
Serve on evaluating Committee for National Science Foundation Grant Proposals.
Director of Endocrinology Unit for the Cancer Research Institute at Howard University.
Serve on Council for the Cancer Research Center at Howard University.
Referee for numerousl scientific journals including Journal of Cellular and Comparative Physiology, Science, Journal of Experimental Zoology, The Prostate, Cancer Research , Endocrinology, Mitochondria, Cancer Research, others
Director of the Endocrine-Cell Metabolism Unit at Howard University College of Medicine.
Director of Graduate Studies, Dept. Physiology and Biophysics, Howard University College of Medicine (1968-1972).
Executive Board UMAB-UMBC Task Force on Graduate School

VI. Honors: (Partial listing)

Elected to Rho Chi Honor Society
Elected to Sigma XI Society
Howard University Outstanding Scientist Certificate (1975)
Howard University Outstanding Scientist Award (1977)
Nominated for Membership on Clinical Cancer Program and Cancer Center Support Review Committee (NCI, NIH) 1979 - Elected June 1979-1983
Invited Participant in First Pan American Congress of Andrology, Caracas, Venzuela, 1979; and Second Congress, Mexico City, 1980
Recipient of Lederle Faculty Award and evaluated as Outstanding Lecturer at the University of Maryland, School of Pharmacy
Cited as Outstanding Teacher by Student Body on each occasion of evaluation of teaching at Howard University College of Medicine
Invited Participant 2nd NIADDK (NIH) Benign Prostatic Hyperplasia Symposium, Washington, D.C., 1985. Topic:Prostate Citrate Metabolism and Regulation
Invited Speaker, 1992 International Symposium on Biology Of Prostate Growth, NIDDK Topic: Prolactin Regulation Of The Prostate
Invited Major Speaker at the AUA Summer Conference on Advances in Cell Biology, 1992, Houston. Topic:The Energy Metabolism Of Prostate Malignancy
Invited Major Speaker at the AUA/SBUR National Meeting, 1998, Dallas. Topic: The role of zinc in the pathogenesis of prostate cancer.
Invited Speaker for NIH Mitochondrial Program, 2000: Topic: Metabolic Alterations In Prostate Malignancy. The presentation is archived for access by internet.
Invited Speaker at Zinc Signals 2003 International Conference; Grand Caymen. "The role of zinc in the pathogenesis of prostate cancer: A cause? A cure?"
Invited Speaker at the 2002 International Conference on Molecular Mechanisms as Targets in Prostate Diseases, Liverpool, England. "Zinc and altered citrate metabolism in the Pathogenesis of Prostate Cancer"

Invited Speaker for the International Conference on Molecular Mechanisms as Targets in Prostate Diseases ,2002. Liverpool, England. Topic "Zinc and altered citrate metabolism in the Pathogenesis of Prostate Cancer"

Invited "Warburg" Speaker; 4th International Meeting on Tumor Metabolism, 2006. Louisville, Ky. Topic: Altered Citrate Metabolism: The Metabolic Transformation Requirement in Prostate Malignancy."

Invited Speaker for the Fujihara Seminar, Osaka, Japan, Oct, 2010: Zinc signal and cellular functions. Topic: Role of zinc and altered metabolism in the development and progression of prostate malignancy.

VIII. Publications (list from ~175 peer reviewed papers)

Most recent publications

Costello LC, Franklin RB (2016) Plasma Citrate Homeostasis: How It Is Regulated; And Its Physiological and Clinical Implications. An Important, But Neglected, Relationship in Medicine. J Hum Endocrinol 1: 005.

Costello LC, Franklin RB. Decreased zinc in the development and progression of malignancy: an important common relationship and potential for prevention and treatment of carcinomas. Expert opinion on therapeutic targets. 2017;21(1):51-66.

Costello LC, Franklin RB. A comprehensive review of the role of zinc in normal prostate function and metabolism; and its implications in prostate cancer. Arch Biochem Biophys. 2016 Dec 1;611:100-112

Costello LC, Zou J, Franklin RB. In situ clinical evidence that zinc levels are decreased in breast invasive ductal carcinoma. Cancer causes & control : CCC. 2016;27(6):729-735.

Costello LC, Zou J, Franklin RB. In situ clinical evidence that zinc levels are decreased in breast invasive ductal carcinoma. Cancer Causes Control. 2016 Jun;27(6):729-35.

Franklin RB, Zou J, Zheng Y, Naslund MJ, Costello LC. Zinc Ionophore (Clioquinol) Inhibition of Human ZIP1-Deficient Prostate Tumor Growth in the Mouse Ectopic Xenograft Model: A Zinc Approach for the Efficacious Treatment of Prostate Cancer. Int J Cancer Clin Res January 9, 2016.

Costello LC, Chellaiah MA, Zou J, Reynolds MA, Franklin RB. In vitro BMP2 stimulation of osteoblast citrate production in concert with mineralized bone nodule formation. J Regen Med Tissue Eng. 2015;4. pii: 2

Desouki MM, Franklin RB, Costello LC, Fadare O. Persistent low expression of hZip1 in mucinous carcinomas of the ovary, colon, stomach and lung. J Ovarian Res. 2015 Jun 17;8(1):40.

Costello LC, Franklin RB, Zou J, Naslund MJ. Evidence that Human Prostate Cancer is a ZIP1-Deficient Malignancy that could be Effectively Treated with a Zinc Ionophore (Clioquinol) Approach. Chemotherapy (Los Angel). 2015 Jun;4(2). pii: 152.

Franklin RB, Zou J, Costello LC. The cytotoxic role of RREB1, ZIP3 zinc transporter, and zinc in human pancreatic adenocarcinoma. Cancer Biol Ther. 2014 Oct;15(10):1431-7.

Costello LC, Franklin RB. The status of zinc in the development of hepatocellular cancer: an important, but neglected, clinically established relationship. Cancer Biol Ther. 2014 Apr;15(4):353-60.

Franklin RB, Chellaiah M, Zou J, Reynolds MA, Costello LC. Evidence that Osteoblasts are Specialized Citrate-producing Cells that Provide the Citrate for Incorporation into the Structure of Bone. Open Bone J. 2014;6:1-7.

Costello LC, Chellaiah M, Zou J, Franklin RB, Reynolds MA. The status of citrate in the hydroxyapatite/collagen complex of bone; and Its role in bone formation. J Regen Med Tissue Eng. 2014;3:4.

Partial List of Early Publications (From 1980-2013)

Toghrol, F., Franklin, R.B. and Costello, L.C. Citrate synthesis in rat ventral prostate from fatty acids and amino acids. Enzyme 25:372-376, 1980.

Costello, L.C. and Franklin, R.B. Citrate production by rat ventral prostate and its regulation by testosterone. Invited Paper in Symposium "Male Accessory Organs". Pan Amer. Cong. Andrology, January 1981.

Costello, L.C. and Franklin, R.B. Aconitase activity, citrate oxidation and zinc inhibition in rat ventral prostate. Enzyme 26:281-287, 1981.

Franklin, R.B., Brandly, R.L. and Costello, L.C. Mitochondrial aspartate, amino-transferase and the effect of testosterone on citrate production in rat ventral prostate. J. Urol. 127:798-802, 1982.

Franklin, R.B., Brandly, R.L. and Costello, L.C. Effect of inhibitors of RNA and protein synthesis on mitochondrial aspartate aminotransferase response to testosterone in rat ventral prostate. The Prostate 3(6):637-642, 1982.

Khan, M.A., Seibel, W., Franklin, R.B., Provenza D. Vincent and Costello, L.C. Growth pattern and citrate production in organ cultures of rat ventral prostate. The Prostate 3:391-403, 1982.

Franklin, R.B., Khan, M.A. and Costello, L.C. Testosterone stimulation of mitochondrial aspartate aminotransferase in organ cultures of rat ventral prostate. J. Steroid. Biochem. 20:709-713, 1984.

Franklin, R.B. and Costello, L.C. Glutamate dehydrogenase in rat ventral prostate and a proposed aspartate-glutamate pathway of citrate synthesis. J. Urol. 132:1239-1243, 1984.

Franklin, R.B., Costello, L.C. and Kukoyi, B. On the mechanism of action of testosterone regulation of prostate citrate production: Testosterone stimulation of mitochondrial

aspartate. Invited participant of 2nd NIADDK Benign Prostatic Hyperplasia Symposium, May 1985.

Franklin, R.B., Kahng, M.W., Akuffo, V. and Costello, L.C. The effect of testosterone on citrate synthesis and citrate oxidation and a proposed mechanism for regulation of net citrate production in prostate. Horm. Metabol. Res. 18:177-181, 1986.

Franklin, R.B., Kukoyi, B., Akuffo, V. and Costello, L.C. Testosterone stimulation of mitochondrial aspartate amino-transferase levels and biosynthesis in rat ventral prostate. J. Steroid Biochem. 28:247-256, 1987.

Costello, L.C., Akuffo, V. and Franklin, R.B. Net citrate production by isolated prostate epithelial cells. Enzyme 39:125-133, 1988.

Costello, L.C., Kahn, M.A., Franklin, R.B. Preliminary studies on the cultivation and characterization of minipig prostate epithelial cells. Cell Biology 12:637-646, 1988.

Costello, L.C., Akuffo, V., and Franklin, R.B. Testosterone stimulates net citrate production from aspartate by prostate epithelial cells. Horm. Metabol. Res. 20:252-253, 1988.

Costello and Franklin. Prostate epithelial cells utilize glucose and aspartate as the carbon sources for net citrate production. The Prostate 15:335-342, 1989.

Franklin, Qian, Costello. Regulation of aspartate aminotransferase messenger RNA level by testosterone. J. Steroid Biochem. 35:569-574, 1990.

Franklin, Lao, Costello. Evidence for two aspartate transport systems in prostate epithelial cells. The Prostate 16:137-146, 1990.

Franklin and Costello. Prolactin directly stimulates citrate production and mAAT of prostate epithelial cells. The Prostate 17:13-18, 1990.

Costello and Franklin. Concepts of citrate production and secretion by prostate. 1. Metabolic relationships. The Prostate 18:25-46, 1991.

Costello and Franklin. Concepts of citrate production and secretion by prostate. 2. Hormone relationships in normal and neoplastic prostate. The Prostate 19: 181-205, 1991.

Franklin, Ekiko, Costello. Prolactin stimulates transcription of aspartate aminootransferase in prostate cells. Mol. Cell Endocrinol. 90: 27-32, 1992.

Costello and Franklin. Effects of prolactin on the prostate: Invited paper for the main program, 1992 International Symposium on Biology of Prostate Growth, sponsored by DKUHD/NIDDK/NIH, Sept. 1992.

Lao, Franklin, Costello. A high affinity L-aspartate transporter in prostate epithelial cells which is regulated by testosterone. The Prostate 22: 53-63, 1993.

Qian, Franklin, Costello. Testosterone regulates mitochondrial aspartate aminotransferase gene expression and mRNA stability in prostate. J. Steroid Biochem. Mol. Biol. 44: 13-19,

1993.

Costello and Franklin. Testosterone regulates pyruvate dehydrogenase activity of prostate mitochondria. Horm. Metab. Res. 25: 268-270, 1993.

Costello, Lao, Franklin. Citrate modulation of highBaffinity aspartate transport in prostate epithelial cells. Cell. Mol. Biol. 39: 515-524, 1993.

Costello and Franklin. Effect of prolactin on the prostate. The Prostate 24: 162-166, 1994.

Costello, Franklin, Liu. Testosterone regulates pyruvate dehydrogenase E1α in prostate. Endocrine J. 2: 147-151, 1994.

Costello and Franklin. The bioenergetic theory of prostate malignancy. The Prostate 25: 162-166, 1994.

Costello, Franklin, Liu. Prolactin specifically increases PDH E1α in rat lateral prostate epithelial cells. The Prostate, 26: 189-193, 1995.

Juang, Costello, Franklin. Androgen modulation of multiple transcription start sites of the mAAT gene in rat prostate. J. Biol. Chem., 270: 12629-12634, 1995.

Costello, Liu, Franklin. Testosterone stimulates the biosynthesis of m-aconitase in prostate epithelial cells. Cell. Mol. Endocrinol., 112: 45-51, 1995.

Franklin, Juang, Zou, Costello. Regulation of citrate metabolism by androgen in human prostate carcinoma cells. Endocrine J., 3: 603-607, 1995.

Franklin, Zou, Costello: Effect of zinc on proliferation of human prostate cancer cells.1st World Congress on Basic Urological Research, Rotterdam, 1995.

Liu, Costello, Franklin: Prolactin specifically regulates citrate oxidation and m-aconitase of prostate epithelial cells. Metabolism: 45:442-449, 1996.

Liu Y, Costello LC, Franklin RB: Prolactin and testosterone regulation of mitochondrial zinc in prostate epithelial cells. Prostate 1997;30:26-32.

Costello, Liu, Franklin: Testosterone and prolactin stimulation of m-aconitase in pig prostate epithelial cells. Urology 1996.

Costello LC, Franklin RB: Citrate metabolism of normal and malignant prostate epithelial cells. Urol 1997;50:3-12.

Franklin RB and Costello LC: Intermediary energy metabolism of normal and malignant prostate epithelial cells. In "Prostate: Basic and Clinical Aspects." Naz RK (ed), New York, CRC Press, pp 115-150, 1997.

Costello LC, Liu Y, Franklin RB, Kennedy MC: Zinc inhibition of mitochondrial aconitase and its importance in citrate metabolism of prostate epithelial cells. J Biol Chem 1997;272:28875-28881.

Franklin RB, Zou J, Gorski E, Yang YH, Costello LC: Prolactin regulation of mAAT andPKC in human prostate cancer cells. Mol Cell Endocrinol 1997;127:19-25.

Franklin R B, Zou J, Costello L C: Effect of zinc on proliferation of human prostate cancer cells. Urological Res 1995;23:266.

Costello LC, Franklin RB: The novel role of zinc in the intermediary metabolism of prostate epitelial cells and its implications in prostate malignancy. Prostate 1998;35:285-296.

Costello LC, Franklin RB, Narayan P: Citrate in the diagnosis of prostate cancer. Prostate 1999;38:237-245.

Costello LC, Liu Y, Zou J, Franklin RB: Evidence for a zinc uptake transporter in human prostate cancer cells which is regulated by prolactin and testosterone. JBC 274:17499-17504, 1999.

Gorski E, Zou J, Costello LC, Franklin RB: Protein kinase C mediates prolactin regulation of mitochondrial aspartate aminotransferase gene expression in prostate cells. Molecular Urol 3: 17-23, 1999.

Liang, Liu, Zou, Franklin, Costello, Feng: Inhibitory effect of zinc on human prostatic carcinoma cell growth. Prostate 40:200-207, 1999.

Costello, Liu, Zou, Franklin: Evidence for a zinc uptake transporter in human prostate cancer cells which is regulated by prolactin and testosterone. J Biol Chem 274:17499-17504, 1999.

Costello, Franklin, Narayan: Citrate in the diagnosis of prostate cancer. Prostate 38:237-245, 1999.

Costello, Franklin, Kennedy: Zinc causes a shift toward citrate at equilibrium of the m-aconitase reaction of prostate motochondria. J Inorg Biochem 78:161-165, 2000.

Feng, P., Liang,J-Y, Li, T-L., Guan, Z-X., Zou, J., Franklin, R.B., Costello, L.C. Zinc induces mitochondria apoptogenesis in prostate cells. Mol. Urology 4:31-36, 2000.

Costello, L.C., Liu, Y., Zou, J., Franklin, R.B. The pyruvate dehydrogenase E1 alpha gene is testosterone and prolactin regulated in prostate epithelial cells. Endocrine Research 26:23-39, 2000.

Franklin, R.B., Zou, J., Ma, J. Costello, L.C. Protein kinase C epsilon and AP-1 mediate prolactin regulation of mitochondrial aspartate aminotransferase expression in the rat lateral prostate. Mol. and Cell. Endocrin.170:153-161,2000.

Costello, L.C., Franklin, R.B. The intermediary metabolism of the prostate: A key to understanding the pathogenesis and progression of prostate malignancy. Oncology.59:269-282,2001.

Costello LC, Franklin RB. The metabolism of prostate malignancy: Insights into the pathogenesis of prostate cancer and new approaches for its diagnosis and treatment.

Oncology Spectrums 2:452-457,2001.

Costello LC, Franklin RB. Mitochondrial aspartate aminotransferase. In Encycl Molec Med Vol 5 (Wiley & Sons, Inc)pp 270-272, 2002.

Costello, L., Franklin, RB., Kurhanewicz, J. The metabolic characterization of prostate malignancy by magnetic resonance spectroscopy. In: Encyclopedia of Cancer, Academic Press, , 2002.

Costello LC, Franklin RB. Testosterone and prolactin regulation of metabolic genes and citrate metabolism of prostate spithelial cells.Horm Metabol Res 34:417-424, 2002.

Feng P, Li T-L, Guan Z-X, Franklin RB, Costello LC. Direct effect of zinc on mitochondrial apoptogenesis in prostate cells. Prostate 522:311-318,2002.

Guan, Kukoyu, Feng, Franklin, Costello. Kinetic identification of o mitochondrial zinc uptake transport process in prostate cells. J Inorg Biochem 97:199-206, 2003

Franklin, Ma, Zou, Guan, Kukoyi, Feng, Costello, Human Zip1 is a major zinc uptake transporter for accumulation of zinc in prostate cells. J Inorgan Biochem 96:435-442,2003.

Feng, Li, Guan, Franklin,Costello. Effect of zinc on prostate tumorigenicity in nude mice.Ann NY Acad Sci, in press,1010: 316-320, 2003

Leslie C. Costello*, Pei Feng*, Beatrice Milon*, Ming Tan, Renty B. Franklin. The Role of Zinc in the Pathogenesis and Treatment of Prostate Cancer: Critical Issues to Resolve. Prostate Cancer and Prostate Diseases. 2004,in press.**

Leslie C. Costello, Zhixin Guan, Renty B. Franklin, Pei Feng. Metallothionein Can Function as a Chaperone for Zinc Uptake Transport into Prostate and Liver Mitochondria. J Inorg Biochem. 98:664-666. 2004.

Franklin, R.B. Milon, B. Feng, P. Costello, L.C. Zinc and zinc transporter in normal prostate function and the pathogenesis of prostate cancer. Frontiers in Bioscience 10:2230-2239, 2005.

Costello LC, Feng P, Franklin RB: Mitochondrial Function, Zinc, and Intermediary Metabolism Relationships in Normal Prostate and Prostate Cancer. Mitochondrion 5: 143-153, 2005

Costello LC, Franklin RB, Feng P, Tan M, Bagasra O. Zinc and Prostate Cancer: A critical scientific, medical and public interest issue. Cancer Causes Control 16(8):901-915.2005

Costello LC, Franklin RB. "Why Do Tumor Cells Glycolyze?": From Glycolysis Through Citrate To Lipogenesis. Mol Cell Biochem 280:1-8, 2005.

Franklin RB, Feng P, Milon BC, Desouki MM, Singh KK, Kajdacsy-Balla A, Bagasra O, Costello LC. hZIP1 zinc uptake transporter down regulation and zinc depletion in prostate cancer. Mol Cancer. 4:32 pp1-13, 2005.

Dakubo GB, Parr RL, Costello LC, Franklin RB, Thayer RE. Altered metabolism and mitochondrial genome in prostate cancer. J. Clin. Pathol 59: 10–16, 2006.

Ziqiang Yu, Costello LC, Feng P, Franklin RB. Characterization of the mitochondrial aconitase promoter and the identification of transcription factor binding. Prostate:66:1061-9.2006.

Singh KK, Desouki MM, Franklin RB, Costello LC. Mitochondrial Aconitase and Citrate Metabolism in Malignant and Nonmalignant Human Prostate Tissues. Mol Cancer 5:14, 4 April 2006

Franklin RB, Zou J, Yu Z, Costello LC. EAAC1 is expressed in rat and human prostate epithelial cells; functions as a high-affinity L-aspartate transporter; and is regulated by prolactin and testosterone. BMC Biochemistry 7:10, 2006.

Costello LC, Franklin RB. The clinical relevance of the metabolism of prostate cancer; zinc and tumor suppression: connecting the dots. Mol Cancer 2006, 5:17, 2006.

Milon B, Wu Q, Zou J, Costello LC, Franklin RB. Histidine residues in the region between transmembrane domains III and IV of hZip1 are required for zinc transport across the plasma membrane in PC-3 cells. Biochim Biophys Acta-Biomembranes.1758:1696-1701, 2006.

Costello LC, Franklin RB. Tumor cell metabolism: the marriage of molecular genetics and proteomics with cellular intermediary metabolism; proceed with caution! Mol Cancer. 2006 Nov 7;5:59.

Franklin RB, Costello LC. Zinc as an anti-tumor agent in prostate cancer and in other cancers. Arch Biochem Biophys. 2007 Mar 16

Desouki MM, Geradts J, Milon B, Franklin RB, Costello LC. hZip2 and hZip3 zinc transporters are down regulated in human prostate adenocarcinomatous glands. Mol Cancer. Jun 5;6:37, 2007.

Feng P, Li T, Guan Z, Franklin RB, Costello LC. The Involvement of Bax in Zinc-Induced Mitochondrial Apoptogenesis in Malignant Prostate Cells. Mol Cancer 7:**25, 2008.**

Costello LC, Franklin RB. Prostatic Fluid Electrolyte Composition for the Screening of Prostate Cancer: A Potential Solution to a Major Problem. Prost Cancer Prostatic Dis 12(1):17-24, 2008.

Franklin RB, Costello LC. Re: Vitamin and mineral use and risk of prostate cancer: the case-control surveillance: Zhang et al. Cancer Causes Control. 2008 Dec 18 [Epub ahead of print].

Costello LC The effect of contemporary education and training of biomedical scientists on present and future medical research. Acad Med. 2009 Apr;84(4):459-63.

Franklin RB, Costello LC. The important role of the apoptotic effects of zinc in the

development of cancers. J Cell Biochem.106:750-757, 2009.

Costello LC. The effect of contemporary education and training of biomedical scientists on present and future medical research. Acad Med. 2009 Apr;84(4):459-63.

Pal R, Parker D, Costello LC. A europium luminescence assay of lactate and citrate in biological fluids. Org Biomol Chem.:1525-1528, 2009.
Milon BC, Agyapong A, Bautista R, Costello LC, Franklin Rb. Ras Responsive Element Binding Protein-1 (RREB-1) Down Regulates hZIP1 Expression in Prostate Cancer Cells. Prostate 70(3):288-296, 2010.

Costello LC, Franklin RB. Zinc is decreased in prostate cancer: an established relationship of prostate cancer! J Biol Inorg Chem. 16:3-8, 2011.

Costello LC, Fensaleu C Franklin RB. Evidence for Operation of the Direct Zinc Ligand Exchange Mechanism for Trafficking, Transport, and Reactivity of Zinc in Mammalian Cells. J Inorg Biochem105:589-599, 2011

Zou J, Milon B, Desouki, M, Costello, LC, Franklin,RB. ZIP1Q1ZincTransporterDown-Regulation in Prostate Cancer Involves the Overexpression of Ras Responsive Element Binding Protein-1 (RREB-1). Prostate 2011, [Epub ahead of print].

Franklin RB, Levy BA, Zou J, Hanna N, Desouki MM, Bagasra O, Johnson LA, Costello LC. ZIP14 Zinc Transporter Downregulation and Zinc Depletion in the Development and Progression of Hepatocellular Cancer. J Gastrointest Cancer. 2011 Mar 5.

Costello LC, Franklin RB, Zou J, Feng P, Bok R, Mark G S, Kurhanewicz J. Human prostate cancer ZIP1/zinc/citrate genetic/metabolic relationship in the TRAMP prostate cancer animal model. Cancer Biol Ther. 2011 Dec 15;12(12). [Epub ahead of print]

Costello LC, Franklin RB. The genetic/metabolic transformation concept of carcinogenesis. Cancer Metastasis Rev. 2011 Nov 23. [Epub ahead of print]

Costello LC, Franklin RB. Integration of molecular genetics and proteomics with cell metabolism: how to proceed; how not to proceed! Gene. 2011 Oct 15;486(1-2):88-93.

Costello LC, Levy BA, Desouki MM, Zou J, Bagasra O, Johnson LA, Hanna N, Franklin RB. Decreased zinc and downregulation of ZIP3 zinc uptake transporter in the development of pancreatic adenocarcinoma. Cancer Biol Ther. 2011 Aug 15;12(4):297-303.

Franklin RB, Costello LC . SLC39A1 (solute carrier family 39 (zinc transporter), member 1). Atlas Genet Cytogenet Oncol Haematol. October 2011 .

Costello LC, Franklin RB. Cytotoxic/tumor suppressor role of zinc for the treatment of cancer: an enigma and an opportunity. Expert Rev Anticancer Ther. 2012 Jan;12(1):121-8.

Costello LC, Zou J, Desouki MM, Franklin RB. Evidence for Changes in RREB-1, ZIP3, and Zinc in the Early Development of Pancreatic Adenocarcinoma. J Gastrointest Cancer. 2012 Mar 18. [Epub ahead of print]

Costello LC, Franklin RB, Chellaiah M, Reynolds MA. The important role of osteoblasts and citrate production in bone formation: "Osteoblast citration" as a new concept for an old relationship. The Open Bone J. 4: 27-34, 2012

Costello LC, Franklin RB. A review of the important central role of altered citrate metabolism during the process of stem cell differentiation. J Regen Med Tissue Engineer in press, 2013.

Early Publications (partial list)

Gold AJ, Onwochei M, Costello LC. Renal handling and utilization of citrate in starvation-induced hypocitricemia. Am J Physiol. 1979 Oct;237(4):F307-11. PubMed PMID: 495723.
Related citations

99:
Franklin RB, Costello LC. Isocitrate uptake and citrate production by rat ventral prostate fragments. Invest Urol. 1978 Jul;16(1):44-7. PubMed PMID: 689836.
Related citations

100:
Costello LC, Fadika G, Franklin R. Citrate and isocitrate utilization by rat ventral prostate mitochondria. Enzyme. 1978;23(3):176-81. PubMed PMID: 738255.
Cited in PMCRelated citations

101:
Costello LC, Fadika G, Stacey R. Hepatic citrate changes in surgical stress. J Surg Res. 1977 Feb;22(2):92-6. PubMed PMID: 839765.
Related citations

102:
Franklin RB, Costello LC, Littleton GK. Citrate uptake and oxidation by fragments of rat ventral prostate. Enzyme. 1977;22(1):45-51. PubMed PMID: 837893.
Cited in PMCRelated citations

103:
Gold AJ, Costello LC. RENAL HANDLING OF CITRATE DURING HEAT-INDUCED HYPOCITRICEMIA. Am J Physiol. 1976 Jul;231(1):84-6. PubMed PMID: 183513.
Related citations

104:
Costello LC, Franklin R, Stacey R. Mitochondrial isocitrate dehydrogenase and isocitrate oxidation of rat ventral prostate. Enzyme. 1976;21(6):495-506. PubMed PMID: 12937.
Cited in PMCRelated citations

105:

Stacey R, Costello LC, Franklin R. Hypocitricemic response to surgical stress in rats. J Surg Res. 1975 Dec;19(6):391-5. PubMed PMID: 1207121.
Related citations

106:
Gold AJ, Costello LC. Effects of semistarvation on rat liver, kidney, and heart mitochondrial function. J Nutr. 1975 Feb;105(2):208-14. PubMed PMID: 163302.
Related citations

107:
Gold AJ, Costello LC. Effects of altitude and semistarvation on heart mitochondrial function. Am J Physiol. 1974 Dec;227(6):1336-9. PubMed PMID: 4155249.
Related citations

108:
Franklin R, Costello LC, Stacey R, Stephens R. Calcitonin effects on plasma and urinary citrate levels in rats. Am J Physiol. 1973 Nov;225(5):1178-80. PubMed PMID: 4745218.
Related citations

109:
Costello LC, Balkissoon B, Stacey R. Hypocitricemic effect of surgical stress. J Surg Res. 1973 Sep;15(3):182-8. PubMed PMID: 4728348.

<u>Books/Book Chapters</u>

Co-editor and contributor:
MITOCHONDRIA AND CANCER; K. Singh and L. Costello, editors; Springer: 2009.
Chapters: Costello and Franklin: Integration of Genetic, Proteomic, and Metabolic Approaches in Tumor Cell Metabolism.
Franklin and Costello: Citrate Metabolism in Prostate and Other Cancers.

Invited contributor of two chapters in:
METHODS OF CANCER DIAGNOSIS,THERAPY, AND PROGNOSIS; M.A. Hayat. Editor: Springer: 2008.
Costello and Franklin: Metabolic Transformations of Malignant Cells (An Overview).
Franklin and Costello: Role of Altered Cellular Metabolism and Molecular Genetics in Prostate Carcinoma

Invited contributor
Encyclopedia of Cancer. Academic Press, 2000.
Costello, Franklin, Kurhanewicz: The metabolic diagnosis of prostate malignancy by magnetic resonance spectroscopy. In:

Invited contributor
Prostate: Basic and Clinical Aspects. Naz RK (ed), NewYork, CRC Press, 1997.
Franklin RB and Costello LC: Intermediary energy metabolism of normal and malignant prostate epithelial cells. In

Invited contributor
Endocrine Control in Neoplasia, Raven Press, New York, 1978.
Costello, L.C., Littleton, G.K. and Franklin, R.B. Citrate and related intermediary metabolism in normal and neoplastic prostate.

LESLIE C. COSTELLO—GRANTS RECEIVED

1962 - 1964: NIH Grant, Effects in vitro of Parathormone on Enzymes
1962 - 1964: NSF Grant, The Relationship of Metabolism to the Embryological Development of Ascaris lumbricoides
1963 - 1965: NSF Grant, Identification of Enzyme Systems Related to the Oxidative Metabolism of Developing Ascaris eggs
1963 - 1965: NASA Grant, Relationship of Biochemical Activity to Environment Adaptation and Development changes in Ascaris
1965 - 1969: NIH Grant, Parathormone, Oxidative, Metabolism and Phosphorylation
1966 - 1970: NIH Grant, Parathyroid Metabolism and Calcium
1968 - 1971: NIH Grant, Parathyroid Hormone Effects on Kidney Metabolism
1969 - 1972: Army Research Office, Effects of Hypoxia on Cellular Metabolism
1970 - 1974: NIH Grant, Surgical Stress Effects on Citrate Metabolism
1972 - 1974: Army Research Office, Altitude Effects on Cellular Energy Metabolism
1974 - 1976: NIH Grant, Surgical Stress Effects on Citrate Metabolism
1975 - 1979: NIH Grant, Graduate Training Grant in Physiology
1976 - 1980: NIH Grant, Effects of Calcitonin on Citrate Regulation
1977 - 1980: NIH Grant, Prostate Citrate Metabolism
1977 - 1980: NIH Grant, Citrate and Androgen Regulation in Prostate Cancer
1981 - 1985: NIH Grant, Testosterone Control of Prostate Citrate Production
1982 - 1985: NIH Grant, Aspartate Utilization and Citrate Production in Prostate
1986 - 1991: NIH Grant, Aspartate Utilization and Citrate Production in Prostate
1986 - 1989: NIH Grant, Testosterone Control of Prostate Citrate Production
1990 - 1993: NIH Grant, Testosterone Control of Prostate Citrate Production
1992 - 1996: NIH Grant, Prolactin Regulation of Prostate Citrate Production
1996 - 2000: NIH Grant, Testosterone Control of Prostate Citrate Production
1996 - 2000:* NIH Grant, Prolactin regulation of Prostate Citrate Production
1996 - 2000: NIH Grant, Regulation of Prostate mAconitase
1999 - 2003:* NIH Grant, Zinc Transport Relationships in Prostate Cancer Cells
2000 – 2003* DOD Grant, Genetic Alterations in Prostate Tumorigenicity
2000 - 2004:* NIH Grant, Hormone Regulation of Prostate Citrate Production
2000 - 2005: NIH Grant, Regulation of Prostate m-Aconitase
2003 - 2006: NIH Grant. Novel Aspartate Transport in Prostate Cells
2004 - 2009* NIH Grant, Zinc transport relationships in Prostate Cancer Cells
2005 - 2010* NIH Grant, Zinc effects on apoptosis in prostate cells
2007 – 2012* NIH Grant, Prolactin regulation of prostate metabolic genes
2013 – 2015 NIH Grant, Concept of bone "citration": an essential function of differentiated osteoblasts

(* Co-PI; PI on all others)

Some Important Pioneering discoveries: a) First to identify that zinc is a specific inhibitor of m-aconitase activity in prostate cells, which inhibits citrate oxidation and provides the mechanism for net citrate production and secretion; the major function of the human prostate gland. This zinc inhibition of citrate metabolism now has widespread implications in prostate and other malignant cells, in neurochemistry, and in other metabolic conditions. **b)** elucidated of the citrate metabolic pathway and the role of zinc in normal and malignant prostate provided the foundation for the development of in situ MRS imaging for the identification, localization, volume estimation of malignant loci in prostate gland based on decreased citrate levels and associated metabolites. Dr. Sillerud (leading pioneer in magnetic resonance spectroscopy) and colleagues (Averna et al 2006) "*Beginning in 1978 Costello et al confirmed and greatly extended these early citrate findings through biochemical studies, which provided overwhelming evidence that decreased citrate represents a vital biochemical marker that can be used in the diagnosis of prostate adenocarcinoma*. Dr. Kurhanewicz and colleagues (leading developer of MRSI) state that *"This unique and complex biochemistry of prostatic citrate production and secretion has been elegantly described by Costello et al based on animal models and human prostate tissue extracts*." Prostate MRSI is now employed in medical centers world-wide including UCSF, Sloan-Kettering, Johns Hopkins, and others. **c)** First to identify that testosterone and prolactin regulates prostate citrate production via regulation of the key regulatory enzymes and transporters and their respective gene expressions, and the intracellular signaling pathways involved. **d)** First to identify that ZIP1 zinc transporter in prostate cells is functionally and kinetically the major zinc transporter involved in the uptake and accumulation of cellular zinc; and is down regulated in prostate adenocarcinoma. ZIP1 is now recognized as a tumor suppressor gene in prostate cancer; has been confirmed by others; and is now identified as such in gene oncology data bases. **e)** First to identify zinc as a tumor-suppressor agent in prostate cancer, and now observed in other cancers by other investigators. **f)** First to identify that zinc under physiological levels is an inducer of apoptosis in mammalian cells (notably prostate), which has been confirmed by others in prostate and other mammalian cells. First to show that zinc induces apoptosis via its direct effects on mitochondria resulting in mitochondrial apoptogenesis. Prior to our reports, others had reported zinc acts only as an inhibitor of apoptosis in mammalian cells. **g)** First to identify the mechanism for zinc uptake transport by mitochondria in mammalian cells. His innovative and pioneering contributions regarding zinc and prostate cancer are reflected in the acknowledgement of Cortesi et al (Clinical assessment of the cancer diagnostic value of prostatic zinc: a comprehensive needle-biopsy study. Prostate. 68(9):994-1006, 2008 that "*It is interesting to note that the zinc depletion occurs not only in the cancerous tissue segments but also, though less pronouncedly, in the Non-Cancer components surrounding the lesion.... This observation is consistent with the conclusions of Costello et al. that the zinc depletion is an early step in the cancer proliferation process and that zinc depletion precedes the transformation of cells from normal to cancerous type. It is well possible that although PCa has not been observed by the pathologist in these regions, the cellular precursor for its appearance is already present...Such behavior does point at a global aspect of the premalignant and malignant processes in the peripheral zone."* **h**) First to discover that zinc is decreased in pancreatic adenocarcinoma; and identified ZIP14 as the important zinc transporter that is down-regulated in the malignant cells.