BIOGRAPHICAL SKETCH

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NAME Mercola, Dan	POSITION TITLE Professor of Pathology and Laboratory Medicine
eRA COMMONS USER NAME Dan Mercola	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
University of Southampton, England	B.M.	1981	Medicine
University of California, Los Angeles,	Ph.D.	1969	Biophysics
University of California, Los Angeles,	M.S.	1967	Biophysics
University of California, Los Angeles	B.A.	1963	Psychology

A. Personal statement. The major focus of my research over the past 9 years has been on prostate cancer and in particular the identification of gene signatures useful for diagnosis, prognosis, and the understanding of mechanism. The approach has been to combine previous training and research in biophysics with previous training and practice of pathology to utilize high throughput bioinformatics to exploit gene expression data at the RNA and protein level to find multigene signatures. These signatures have been developed for diagnosis, prognosis, aging, and residual disease. The overall interest is the empirical application of these signatures as tests and in the assumption that the gene composition of these signatures involves a subset of genes that are function in generating the phenotype of prostate adenocarcinoma cells and in contributing to degrees of aggression of the tumors. The use of the results in clinical testing requires an active interest in translation and several partnerships under licensing agreements have been made with established specialty companies (Althea Biotechnologies Inc., Proveri Inc.) to speed the development of translation. Current research is focused on analysis of which genes have functional roles through the use of cell models, expression analysis, and chip-on-chip and chip-sequencing studies. Current research on test development is to carry out preclinical and clinical trial validation in a CLIA setting to facilitate FDA applications to support PMA/510K approval either for local application in the UCI CLIA lab as a reference lab, i.e. LDT, or to facilitate partnering and co-development.

Positions and Employment

1969-1973 University of Oxford, postdoctoral fellow with Prof. Dorothy Hodgkin (Nobel Laureate)
1974-1979 University of Oxford, Member of Faculty of Agricult. & Biol. Sci., (M.A., 1974) and Wolfson College
1982-pres. California State Medical License, M.D., No. A 40362; DEA No. BM3561467
1981-1985 Resident, Pathology, University of California at San Diego, Board Certification: 1985; F.C.A.P
1985-1991 Assistant Clinical Professor, University of California at San Diego, Pathology Department
1985-1995 Associate Adjunct Professor, University of California at San Diego, Pathology Department
1985-1997 Staff Physician, DVAMC, San Diego, CA
1993-2005 Professor, Sidney Kimmel Cancer Center, University of California, San Diego, San Diego, CA
2005- pres Professor, Pathology & Laboratory Medicine, University of California, Irvine, Irvine, CA
2005- pres Director, Translational Cancer Biology, University of California, Irvine, Irvine, CA

Other Experience and Professional Memberships

1995- Member, NIH Site Visit Review Committee, Program Project Grant Application
1992- Editorial Boards: Antisense and Nucleic Acid Drug Development; Cancer Gene Therapy
1992-1997 Member, Organizing Committee of the Am. Assoc. Clin. Chem. Annual San Diego Conference
1993- NIH Ad Hoc Reviewer, Study Section, RFA: "Cancer Therapy with Biological Response Modifiers"
1993-1998 Member, Grants Review subcomm. for Oncology, 9/93-10/99, U.S. Dept. of Veterans Affairs
1999- pres. Associate Member, UCSD Cancer Center
2004 NIH Study Section member, ZCA1, June 7-8, 2004, Dr. T. Meeker, SRA.
2004 NIH site visit to NIH Cancer and Cell Biology Branch, Sept. 21-23, 2004, M. Johnson, Exec. Sec.

2004-2006 NIH, member, Research Evaluation Panel, The NCI CPCTR, Canc. Diag. Prog.
2004-2005 NIH study section, 'EDRN: Biomarkers Development Laboratory', Review panel.
2005 NIH Study Section member, ZCA1 SRRB-E, CMCAR, 6/20/05, Tim Meeker, SRA.
2006 Department of Defense, Breast Cancer, Study Section.
2008 Department of Defense, Prostate Cancer, Study Section, Panel for Molecular Biology
2008 Department of Defense/USAMRRC, Prostate Cancer Study Section, 9/8/08, H. Schwartz, SRA.
2009 Department of Defense, Breast Cancer Grants Review Panel, CBY-1, B. DiVenney, SRA.
2010 Department of Defense, Breast Cancer Grants Review Panel, CBY-1, Moira Hitchens, SRA.

Honors 1972: Science Citation Classic, Blundell et al, Insulin, its structure, biology, and activity. The Proteins; 1974,
1974: Oxford University, M.A. status;
2004; Named San Diego Padres "Medical All-Star for 2004" presented by M. Milkin.

B. Selected peer-reviewed publications (Selected from 128; in chronological order)

7. Blundell, T.L.; Cutfield, J.F.; Cutfield, S.M.; Dodson, E.J.; Dodson, G.G.Hodgkin, D.C.; Mercola, D.A. and Vijayan, M.: Atomic Positions in Rhombohedral 2-zinc Insulin Crystals, Nature, 231, 506-511 (1971).
8. Mercola, D.A.; Morris, J.W.S. and Arquilla, E.: Use of Resonance Interaction in the Study of the Chain Folding of Insulin in Solution, Biochemistry, 11, 3860-3874 (1972).
9. Hodgkin, D. and Mercola, D. A.: The Secondary and Tertiary Structure of Insulin, in Handbook of Physiology: Endocrinology, Vol. 1, Sect. 7, D. Steiner (ed.), pp. 139-57, Am. ,Physiol. Soc., Washington, D. C. (1972).
18. Bentley G; Dodson E; Hodgkin D; Mercola, D. (1976) The Structure of Insulin in 4-zinc Insulin. Nature, 261:166-168.
91. Virolle, T., Adamson, E.D., Baron, V., Birle, D., Mercola, D., Mustelin, T., and de Belle., I. PTEN is directly Tran activated in vivo by Egr-1 during irradiation-induced signaling" Nature Cell Biol. 2001;3:1124-1128.

Prostate Cancer:

96. Krones-Herzig, A., Adamson, E., and Mercola, D. EGR1, a novel upstream gatekeeper of the p53 tumor suppressor, controls replicative senescence. PNAS (USA) 2003:100:3233-3238.
97. Baron, V., De Gregorio, G., Krones-Herzig, A., Virolle, T., Calogero, A., Urcis, R., and Mercola, D. Inhibition of Egr-1 Expression Reverses Transformation of Prostate Cancer Cells In Vitro And In Vivo. Oncogene 2003:22(27):4194-204.
98. Virolle, T., Krones-Herzig, A., Baron, V., De Gregorio, G., Adamson, E., and Mercola, D. Egr1 promotes growth & survival of prostate cancer cells: identification of novel Egr1 target genes. JBC. 2003:278;11802-10.
103. Stuart, R., Wachsman, W., Berry, C.C., Arden, K., Goodison, S., Klacansky, I., McClelland, M., Wang-Rodriquez, J., Wasserman, L., Tarin, D., Mercola, D. In silico dissection of cell-type associated patterns of gene expression in prostate cancer. Proc. Natl. Acad. Sci U.S.A. 2004:101;615-620.
106. Hayakawa, J., Mittal, S., Wang, Y., Korkmaz, K., Adamson, A., English, C., Ohmichi, M., McClelland, M., Mercola, D. Identification of Promoters Bound by c-Jun/ATF2 During Rapid Large-scale Gene Activation Following Genotoxic Stress. Molecular Cell, 2004;16:521-535.
108. Anja Krones-Herzig, Shalu Mittal, Kelly Yule, Hongyan Liang, Chris English, Rafael Urcis, Tarun Soni, Eileen Adamson, & Dan Mercola. Early Growth Response 1 Acts as a Tumor Suppressor In vivo & In Vitro via Regulation of p53. Cancer Research. 2005;65(12):5133-43.
109. Yipeng Wang, Qiuju Yu, Ann Cho, Shalu Mittal, Gaelle Rondeau, Dan Mercola, John Welsh, Michael McClelland, Optimization of high-throughput methylation analysis using human promoter microarray. Neoplasia 2005;8:748-760.
115. Krajewska M, Olson AH, Mercola D, Reed JC, Krajewski S. Claudin-1 immunohistochemistry for distinguishing malignant from benign epithelial lesions of prostate. Prostate. 2007;15;67(9):907-10.
117. Maryla Krajewska, Shinichi Kitada, Jane N. Winter, Daina Variakojis, Alan Lichtenstein, Dayong Zhai, Michael Cuddy, Xianshu Huang, Frederic Luciano, Cheryl H. Baker, Hoguen Kim6, Eunah Shin7, Susan Kennedy, Allen H. Olson, Andrzej Badzio, Jacek Jassem, Ivo Meinhold-Heerlein, Michael J. Duffy, Aaron D. Schimmer, Ming Tsao3, Ewan Brown, Anne Sawyers, Michael Andreeff, Dan Mercola, Stan Krajewski & John C. Reed. Bcl-B Expression in Human Epithelial and Nonepithelial Malignancies Clin.l Canc. Res. 2008;14: 3011-3021,
116. Jia, Zhenyu, Tang, Sha, Mercola, Dan, & Xu, Shizhong. Detection of Quantitative Trait Associated Genes Using Cluster Analysis. *In* Evolutionary Computation, Machine Learning, & Data Mining in Bioinformatics,

Proceeding of the 6th European Conference, EvoBIO 2008, Naples, Italy, March 2008, E, Marchiori & J. H. Moorte, *Eds*., Springer-Verlag, Germany.
118. M. Krajewska, S. Kitada, J. N. Winter, D. Variakojis, A. Lichtenstein, D. Zhai, M. Cuddy, X. Huang, F. Luciano, C. H. Baker, H. Kim, E. Shin, S. Kennedy, A. H. Olson, A. Badzio, J. Jassem, I. Meinhold-Heerlein, M. J. Duffy, A. D. Schimmer, M. Tsao3, E.Brown, A. Sawyers, M. Andreeff1, Dan Mercola, S. Krajewski & John C. Reed. Bcl-B Expression in Human Epithelial & Nonepithelial Malignancies Clin.Canc.Res. 2008;14:3011-3021.
119. Yu J, Zhang SS, Saito K, Williams S, Arimura Y, Ma Y, Ke Y, Baron V, Mercola D, Feng GS, Adamson E, Mustelin T. PTEN regulation by Akt-EGR1-ARF-PTEN axis. EMBO J. 2009 Jan 7;28(1):21-33. Epub 2008 Dec.
120. Koziol JA, Feng AC, Jia Z, Wang Y, McClelland M, Mercola D. The Wisdom of the Commons: Ensemble Tree Classifiers for Prostate Cancer Prognosis. *Bioinformatics.* 2008; 25:54-60.
125. Simoneau AR (AS), Liao WX, Yi G, Hope CJ, Xie J, Holcombe RF (GFS), Jurnak FA, Mercola D (CA), Hoang, BH (GFS), Zi X (CA), Li S, Liu F (AS), Tang Y: WIF1, a Wnt pathway inhibitor, regulates SKP2 and c-myc expression leading to G1 arrest and growth inhibition of human invasive urinary bladder cancer cells. Mol Cancer Ther 8, 458-68.
126. Jia Z, Wang Y, Ye K, Li Q, Tang S, Xu S, Mercola D. Association Study between Gene Expression and Multiple Relevant Phenotypes with Cluster Analysis. Lect Notes Comput Sci. 2009;5483:1-12. PubMed PMID: 19655036; PubMed Central PMCID:PMC2719899.
129. Major JM, Klonoff-Cohen HS, Pierce JP, Slymen DJ, Saltzstein SL, Macera, C., Mercola, Dan, Kattan M.W.. Prostate Cancer Postoperative Nomogram Scores and Obesity. *PLoS ONE. 2011;*6(2):e17382. 137.
124. Yipeng Wang, Xiao-Qin Xia, Zhenyu Jia, Anne Sawyers, Huazhen Yao, Jessica Wang-Rodriquez, Michael McClelland, **Dan Mercola***. In silico estimates of tissue components in surgical samples based on expression profiling data. Cancer Research. Cancer Res; 70(16); July 27, 2010. PMID: 20663908 . *these two authors contributed equally.
125. Zhenyu Jia, Yipeng Wang, Anne Sawyers, Huazhen Yao, Farahnaz Rahmatpanah, Xiao-Qin Xia, Qiang Xu, Rebecca Pio, Tolga Turan, James A. Koziol, Stephen Goodison, Philip Carpenter, Jessica Wang-Rodriquez, Anne Simoneau, Frank Meyskens, Manuel Sutton, Waldemar Lernhardt, Thomas Beach, Michael McClelland* and **Dan Mercola*** Diagnosis of Prostate Cancer Using Differentially Expressed Genes in Stroma. Cancer Research, 2011;71(7):2476-2487. PMID: 21459804. *Contributed equally.
126. Chen, Xin; Shizhong Xu, Yipeng Wang, Michael McClelland, Zhenyu Jia, and Dan **Mercola**. Identification of Biomarkers for Prostate Cancer Prognosis Using a Novel Two-Step Cluster Analysis M. Loog et al. (Eds.): vol. Pattern Recognition in Bioinformatics; series Lecture Notes in Bioinformatince 7036; Springer-Verlag Berlin Heidelberg 2011.
131. Zhenyu Jia, Yipeng Wang, Yuanjie Hu, Christine McLaren, Yingyan Yu, Kai Ye, Xiao-Qin Xia, James A. Koziol, Waldemar Lernhardt, Michael McClelland, Dan Mercola. A Sample Selection Strategy to Boost the Statistical Power of Signature Detection in Cancer Expression Profile Studies Anti-Cancer AGENTS IN Medicinal Chemistry 2012;(in press)(http://www.benthamscience.com/cmcaca/MSandI.htm).
132. Jia, Zhenyu; Farahnaz Rahmatpanah, Xin Chen, Waldemar Lernhardt, Yipeng Wang, Xiao-Qin Xia, Michael McClelland , Dan Mercola. Prognosis of Prostate Cancer Using Gene Expression Changes in Stroma. *PloSone* (in press June 2012).

C. Research Support: **Ongoing Research Support**

ACTIVE:

1 U01 CA152738-01 (PI: Mercola – PI 09/01/10 – 8/31/15
NIH/NCI 3.4 million
The Prostate Cancer Tumor Microenvironment Exhibits Differentially Expressed Genes Useful for Diagnosis"
The establishment of UCI as a "Biomarker Dectecion Laboratory" for the NCI EDRN and to develop a multisite prospective clinical validation trial of the multigene diagnositic signature for the diagnosis of prostate cancer from nontumor-containing biopsy tissue.

1R01CA122558-01A2 (Zi, Xiaolin – PI; Collaborator, D. Mercola) 12/1/2007-11/30/2012
NIH/NCI
Title:"**Chemoprevention of urinary bladder carcinogenesis by flavokawain A**"

(1) Determine flavokawain A's ability to inhibit bladder tumor development and progression in a) UPII-mutant Ha-ras transgenic mice that produce superficial papillary TCC and b) UPII-SV40T transgenic mice that produce CIS with progression to high-grade superficial papillary and invasive tumors. (2) Determine flavokawain A's efficacy in inhibiting bladder carcinogenesis in the OH-BBN-induced model of urinary bladder cancers in mice. (3) Investigate in vitro molecular mechanisms of flavokawain A leading to cell cycle arrests and apoptosis.

Completed.

1 U01 CA114810-01 (Mercola - P.I.) 07/01/05-06/30/10 3 MOS.
NIH/NCI 8.9 million
"Evaluation of Predictive Signatures of Prostate Cancer"
A multi-disciplinary, multi-institutional consortium assembled to develop a predictive signature of prostate cancer and to validate the signature in a prospective trial.

UCI CANCER RESEARCH INSTITUTE 6/1/08 – 5/31/11.
(Farahaz Rahmatpanah – PI; D. Mercola – Mentor/Sponsor)
"**Chip-on-chip analysis of gene regulation by HER2 in human breast cancer**"
This is a training grant position for support of postdoctoral fellow Farahnaz Rahmatpanah, Ph.D.

CANCER PROJECT OF WASHINGTON D.C. (Gordon Saxe – PI; D. Mercola UCI site PI) 9/1/08-8//31/11.
"**Identification of gene transcript levels that correlated with diet of newly diagnosed prostate cancer patients**"
UCI SPECS consented patients are also recruited by informed consent to complete and electronic diet questionnaire at the time of diagnosis of prostate cancer and to provide blood used for analysis of analyte that confirm the veracity of diet survey results. The diet questionnaire results are analyzed by the Viorcare Inc./Fred Hutch Cancer Research Institute algorithm to determine over 250 dietary values which are then correlated with gene expression as measure by Affymetrix U133 plus 2.0 arrays of fresh frozen prostate cancer tissue of the same patients collected by the UCI SPECS project.

BC050883 (Mercola - P.I.) 4/1/06 – 3/31/10 1.8 MOS.
Army Medical Research & Materiel Command $447,830
"Novel Array-Based Target Identification for Synergistic Sensitization of Breast Cancer to Herceptin"
"IDEA" award

NIH SBIR, (Waldemar Lernhardt, Ph.D., CEO, Proveri Inc. – PI) 9/30/09 – 9/29/10. 3 MOS.
NIH Phase I, $ 150,000.
"Development of an Antibody panels for the diagnosis and prognosis of prostate cancer."
SBIR Contract, nonreviewed phase II approval, $ 1,000,000.

BCTR65506 (Mercola - P.I.) 9/1/06-8/31/09 .6 MOS.
Susan G. Komen Foundation $250,000
"**Array-Based Identification of Genes Causing Chemotherapy Resistance by Breast Cancer**"

082-07 (Mercola- P.I.) 8/1/07-7/31/09 .2 MOS.
Mary Kay Ash Foundation $100,000
"Development of a Diagnostic Test for Breast Cancer Based on DNA Methylation Signature"

2P30 CA-62203-14 (Meyskens) 08/01/02-01/31/09…. 1.2 MOS.
NIH/NCI - University of California, Irvine $1,724,690
Cancer Center Support Grant