

BIOGRAPHICAL SKETCH

Provide the following information for each individual included in the Research & Related Senior/Key Person Profile (Expanded) Form.

NAME Mercola, Dan	POSITION TITLE Professor of Pathology and Laboratory Medicine		
eRA COMMONS USER NAME: Danmercola			
EDUCATION/TRAINING (<i>Begin with baccalaureate or other initial professional education, such as</i>)			
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

Research and Professional Experience

The major focus of our research over the past 16 years has been on prostate cancer and breast cancer 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 investigate molecular mechanisms of disease. Early studies used spectroscopy and protein crystallography to study the mechanism of insulin action and muscle contraction progressing to prostate and breast cancer. A novel analytical method was developed to resolving global gene expression data of prostate cancer into gene expression by the four major cell-type contributions, tumor cells, normal epithelial cells, stroma cells, and BPH cells. Another novel aspect has been the recognition that gene expression changes in the tumor adjacent stroma, a component necessary for tumor formation, may be used to develop highly accurate multigene profiles (classifiers) for diagnosis and for prognosis for patients treated by prostatectomy. Recently working with Dr. Kathleen McGuire, we have realized that hundreds of gene expression changes in the stroma of prostate cancer of African Americans is explaining the deficient immune response which may be related to the aggressive phenotype of prostate cancer in African Americans. A prognostic classifier for African Americans is being developed. To facilitate translation of the gene profiles, the Regents of the University of California have sponsored four patent filings one of which is issued and has provided a license to the biotechnology startup, Proveri Inc. for development of specific tests. Proveri Inc. has formed a co-development agreement with Koelis Inc., an MRI imaging company. The prostate cancer studies have led to the development of a prostate tissue biorepository and associated annotated database with over 2900 patients by informed consent, outcomes data, over 300 microarrays and a large TMA. Translational development of tests for African Americans is a major priority.

Positions

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) & Wolfson College
1982-pres. California State Medical License, M.D., No. A 40362; DEA No. FM6151055.
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 with tenure, Pathology & Laboratory Medicine, University of California, Irvine, Irvine, CA
2005- pres. Director, Translational Cancer Biology, University of California, Irvine, Irvine, CA
2006 –pres. Member, UCI Chao Family Compressive Cancer Center, 2010-2014, Senior Leadership Council; 2010-2014, Co-leader, Cancer Prognosis and Prevention.

Honors

1972 Science Citation Classic, Blundell *et al.*, Insulin, Its Structure, Biology, and Activity. The Proteins,
1974 Oxford University, provided M.A. status
2004 Named San Diego Padres “Medical All-Star for 2004” presented by M. Milkin

2011 Mentor of the Year award, UCI, Institute for Clinical and Translational Sciences (one of three).
2013 Veterans of Foreign Wars, \$16,000. for excellence in prostate cancer research

Editorships. Grant Review Panels

Editorial Boards, current, 7 peer-reviewing journals; Study Section member, 2 (NIH, Dept.; Veterans' Affairs), NIH site visits, 3; CDMRP/DOD *ad hoc* reviewer, 4; NIH *ad hoc* reviewer, 12.

Trainees

41 postdoctoral workers, 6 graduate students, and 45 undergraduate special study or intern students.

Selected pertinent peer-reviewed papers from a total of over 157 (complete list at:

<http://www.ncbi.nlm.nih.gov/sites/myncbi/dan.mercola.1/bibliography/46230471/public/?sort=date&direction=descending>.)

107. Jun Hayakawa, Shalu Mittal, Yipeng Wang, Kemal Korkmaz, Mashide Ohmichi, Eileen Adamson, Michael McClelland, Dan Mercola. Identification of promoters bound by c-Jun/ATF2 during rapid large-scale gene activation following genotoxic stress. *Molecular Cell* 2004;16:521-535. PMID: 1554661311

<http://www.ncbi.nlm.nih.gov/pubmed/15546613>.

122. J. Yu, 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 4. PubMed PMID: 19057511; PubMed Central PMCID: PMC2633077.

123. Yaxiong Tang, Anne R. Simoneau, Wu-xiang Liao, Guo Yi, Christopher Hope, Feng Liu, Shunqiang Li, Jun Xie, Randall F. Holcombe, Frances A. Jurnak, Dan Mercola, Bang H. Hoang and Xiaolin Zi, 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, *Molecular Cancer Therapeutics*, 2009 Feb;8(2):458-68. Epub 2009 Jan 27. PMCID 2768341; PMID 19174556.

124. Saynur Vardar-Sengul, Shilpi Arora, Haluk Baylas, and Dan Mercola. Expression profile of human gingival fibroblasts induced by interleukin-1 β reveals central role of NF- κ B in stabilizing human gingival fibroblasts during inflammation. *J. Periodontal Res.* 2009;80(5):833-49. PMID 19405838, PMCID 4150685.

125. 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.

Reprinted as 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 in C. Pizzuti, M.D. Ritchie, and M. Giacobini (Eds.): *EvoBIO 2009*, LNCS 5483, pp. 1–12, 2009. Springer-Verlag, Berlin Heidelberg 2009. This is a reprint Publication 125 owing to oral presentation by invitation at a meeting.

127. Jianfei Qi, Koh Nakayama, Robert D. Cardiff, Alexander D. Borowsky, Karen Kaul, Roy Williams, Stan Krajewski, Dan Mercola, Philip M. Carpenter, David Bowtell, and Ze'ev A. Ronai. Siah2-Dependent Concerted Activity of HIF and FoxA2 Regulates Formation of Neuroendocrine Phenotype and Neuroendocrine Prostate Tumors. *Cancer Cell*, 2010; 18: 1–16, July 13. PMID: 20609350. PMCID: PMC29193332 <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3786411/>; <http://www.benthamscience.com/cmca/MSandI.htm>.

128. Wang Y, Xia XQ, Jia Z, Sawyers A, Yao H, Wang-Rodriquez J, Mercola D, McClelland M. In silico estimates of tissue components in surgical samples based on expression profiling data. *Cancer Res.* 2010 Aug 15; 70 (16):6448-55. Epub 2010, Jul 27. PubMed PMID: 20663908.

129. 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, Joseph Monforte, Michael McClelland* and Dan Mercola. Diagnosis of Prostate Cancer Using Differentially Expressed Genes in Stroma. *Cancer Research*, 2011;71(7):2476-2487. PMID: 21459804. PMCID: PCM3071046. *Contributed equally. <http://cancerres.aacrjournals.org/content/71/7/2476.full.pdf+html>.

130. 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). PMCID: PCM3044730. (e17382. doi:10.1371/journal.pone.0017382).

131. Xin Chen, 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, in "Pattern Recognition in Bioinformatics", M. Loog et al. (Eds.): PRIB 2011, LNBI 7036, pp. 63–74, 2011. Springer-Verlag Berlin, 2011.
132. 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. Bentham Science Publishers. *Anti-Cancer Agents in Medicinal Chemistry*. 2012;13:203-211. Epublication, August 24, 2012. PMID: 22934703; PMCID: PMC3786411 .<http://www.ncbi.nlm.nih.gov/pubmed/22934703>.
133. Zhenyu Jia, Farahnaz Rahmatpanah, Xin Chen, Waldemar Lernhardt, Yipeng Wang, Xiao-Qin Xia, Anne Sawyers, Michael McClelland, and Dan Mercola. Expression changes in the stroma of prostate cancer predict subsequent relapse. *PloS ONE* 2012;7: Epublication 8/3/12. PMID: 22870216. PMCID:3411675. <http://www.ncbi.nlm.nih.gov/pubmed/22870216>.
134. Chen X, Xu S, McClelland M, Rahmatpanah F, Sawyers A, Jia Z, Mercola D. An accurate prostate cancer prognosticator using a seven-gene signature plus Gleason score and taking cell type heterogeneity into account. *PLoS ONE* 2012;7(9):e45178. doi: 10.1371/journal.pone.0045178. Epub 2012 Sep 28. PMCID 3460949; PMID 3460942. http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=2302883
135. Khan S, Jutzy JM, Valenzuela MM, Turay D, Aspe JR, Ashok A, Mirshahidi S, Mercola D, Lilly MB, Wall NR. Plasma-derived exosomal survivin, a plausible biomarker for early detection of prostate cancer. *PLoS ONE*. 2012;7(10):e46737. doi: 10.1371/journal.pone.0046737. Epub 2012 Oct 16. PubMed PMID: 23091600; PMCID: PMC3473028. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3473028/>
136. Lee C, Zhang Q, Zi X, Dash A, Soares MB, Rahmatpanah F, Jia Z, McClelland M, Mercola D. TGF- β Mediated DNA methylation in prostate cancer. *Translational Andrology and Urology* 2012;1(2):78-88.DOI: 0.3978/j.issn.2223-4683.2012.05.06. PMCID: 4131550. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4131550/>.
137. Rahmatpanah F, Jia Z, Chen X, Jones FE, McClelland M, Mercola D. Expression of HER2 in Breast Cancer Promotes a Massive Reorganization of Gene Activity and Suggests a Role for Epigenetic Regulation. *J Data Mining Genomics Proteomics*. 2012;3: pii: e102. doi: 10.4172/2153-0602.1000e102. PMID: 24009986; PubMed Central PMCID: PMC3760961.September 3, 2012. JDMGP an open access journal <http://www.omicsonline.org/2153-0602/2153-0602-3-e102.php?aid=10410>.
138. Rebecca Pio, Zhenyu Jia, Veronique T. Baron, and Dan Mercola. Early Growth Response Gene 3 (Egr3) is highly over-expressed in non-relapsing prostate cancer but not in relapsing prostate cancer. *PloS ONE*, 2013; 8: January 14, 2013. PMCID: PMC3544741; DOI 10.1371. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3544741/> <http://dx.plos.org/10.1371/journal.pone.0054096>.
139. Matthew A. Kinseth, Zhenyu Jia, Farahnaz Rahmatpanah, Anne Sawyers, Manuel Sutton, Jessica Wang-Rodriguez, Kathleen L. McGuire*, and Dan Mercola*. Expression differences between African American and Caucasian prostate cancer tissue reveals that stroma is the site of aggressive changes. *Int. J. Cancer*, 2013;134 : 81-91.PMID:23754304; PMCID: PMC3800217. Online June 10, 2013, DOI: 0.1002/ijc.28326. *Contributed equally. <http://onlinelibrary.wiley.com/doi/10.1002/ijc.28326/pdf>. notice in MDLinx.com: http://www.mdlinx.com/oncology/news-article.cfm/4669757.*+Cpmytoniyrf.
140. Chung Lee; Qiang Zhang, James Kozlowski, Charles Brendler, Marcelo B. Soares, Atreya Dash, Michael McClelland, and Dan Mercola, Natural products and transforming growth factor-beta (TGF- β) signaling in cancer development and progression. *Current Cancer Drug Targets*. 2013; 13(5): 500-505. PMID:23597196. ISSN (Print): 1568-0096, ISSN (Online): 1873-5576, DOI: 10.2174/15680096113139990034. <http://www.ncbi.nlm.nih.gov/pubmed/23597196?dopt=Citation>.
141. Xuejiao Tian, Saiyang Zhang, Hong-Min Liu, Yan-Bing Zhang, Christopher A Blair, Dan Mercola, Paolo Sassone-Corsi and Xiaolin Zi. Histone Lysine-Specific Methyltransferases and Demethylases, in *Carcinogenesis: New Targets for Cancer Therapy and Prevention*. *Current Cancer Drug Targets*. 2013;13:558-579.PMID: 23713993; PMCID: PMC3703250 <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3703250/> <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3703250/>.

142. Yifei Chen, Zhenyu Jia, Dan Mercola and Xiaohui Xie, A gradient boosting algorithm for survival analysis via direct optimization of concordance index. *Computational and Mathematical Methods in Medicine*. Volume 2013, Article ID 873595, 8 pages, Hindawi Publishing Corp., Epub 1/2013. PMCID: 2434876; PMID: 24348746. <http://dx.doi.org/10.1155/2013/873595>.
143. Zhenyu Jia, Michael Lilly, James A. Koziol, Xin Chen, Xiao-Qin Xia, Yipeng Wang, Douglas, Skarecky, Manuel Sutton, Anne Sawyers, Herb Ruckle, Philip Carpenter, Jessica-Wang Rodriguez, J. Jiang, Thomas Ahlering, Michael Kattan, and Dan Mercola. A method for generation of virtual controls for single arm prostate cancer adjuvant trials with application to a high risk cohort. *PloS ONE*, 9(1): e85010. doi:10.1371/journal.pone.0085010 Epublication January 21, 2014. PMCID: 3897405; PMID: 24465467. <http://www.plosone.org/article/fetchObject.action?uri=info%3Adoi%2F10.1371%2Fjournal.pone.0085010&representation=PDF>.
144. Yokoyama NN, Shao S, Hoang BH, Mercola D (CPP), Zi X (CPP): Wnt signaling in castration-resistant prostate cancer: implications for therapy. *Am J Clin Exp Urol* 2014 2(1): 27-44. PMCID: 4135057; PMID 25143959. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4135057/pdf/nihms588426>.
145. Ponti, D., Bellenchi, G. C., Puca, R., Bastianelli, D., Maroder, M., Ragona, G., Roussel, P., Thiry, M., Mercola, D. and Calogero. "The Transcription Factor EGR1 Localizes to the Nucleolus and Is Linked to Suppression of Ribosomal Precursor Synthesis" *Plos ONE*, 2014; Epublication. PMCID: 4006901; PMID: 24787739. <http://www.ncbi.nlm.nih.gov/pubmed/24787739>. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4006901/pdf/pone.0096037.pdf>.
147. Chung Lee, Zhenyu Jia, Farahnaz Rahmatpanah, Qiang Zhang, Xiaolin Zi, Michael McClelland, and Dan Mercola. Role of the Adjacent Stroma Cells in Prostate Cancer Development and Progression: Synergy between TGF- β and IGF Signaling. *BioMed Research International*. 2014; volume 2014: Epub, 8 pages, Article ID 502093 (review article). PMCID: PMC4095744. <http://dx.doi.org/10.1155/2014/502093> <http://www.hindawi.com/journals/bmri/2014/502093/>.
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150. Heifand, B. T., et al. Associations of prostate cancer risk variants with disease aggressiveness: results of the NCI-SPORE Genetics Working Group analysis of 18,343 cases. *Human genetics* 2015;134: 439-450; PMCID: PMC25715684. <http://www.ncbi.nlm.nih.gov/pubmed/25715684>.
151. Rahmatpanah, F. B., Jia, Z., Chen, X., Char, J. E., Men, B., Franke, A. C., Jones, F. E., McClelland, M., and Mercola, D. A class of genes in the HER2 regulon that is poised for transcription in breast cancer cell lines and expressed in human breast tumors. *Oncotarget* 2015;6:1286-130; PMCID: PMC25428913. <http://www.ncbi.nlm.nih.gov/pubmed/25428913>.
152. Tian, Y., Choi, C. H., Li, Q. K., Rahmatpanah, F. B., Chen, X., Kim, S. R., Veltri, R., Chia, D., Zhang, Z., Mercola, D., and Zhang, H. Overexpression of periostin in stroma positively associated with aggressive prostate cancer. *PLoS One* 2015; 10: e0121502. PMCID: PMC25781169. <http://www.ncbi.nlm.nih.gov/pubmed/26043260>.
153. Zhu, Jianguo, Cong Pan, Jun Jiang, Mingsen Deng, Hengjun Gao, Bozhao Men, Michael McClelland, Dan Mercola, Wei-De Zhong and Zhenyu Jia. Six stroma-based RNA markers diagnostic for prostate cancer in European-Americans validated at the RNA and protein levels in patients in China. *Oncotarget* 2015;6:16757-65. Epub. PMCID 4599350. <http://www.impactjournals.com/oncotarget/index.php?journal=oncotarget&page=article&op=view&path%5B%5D=4430&path%5B%5D=10106>.
157. Li, X., Yokoyama, N. N., Zhang, S., Ding, L., Liu, H. M., Lilly, M. B., Mercola, D., and Zi, X. (2015) Flavokawain A induces deNEDDylation and Skp2 degradation leading to inhibition of tumorigenesis and cancer progression in the TRAMP transgenic mouse model. *Oncotarget* 6, 41809-41824, PMID 26497688, <http://www.ncbi.nlm.nih.gov/pubmed/26497688>.

158. vanDraanen, J. M., Davidson, H. Bour-Jordan, L. Bowman-Carpio¹, D. Boyle³, S. Dubinett¹, B. Gardner, J. Gardner, C. McFall, D. Mercola, T. Nakazono, S. Soares, H. Stoppler, M. Tempero, S. Vandenberg, Y.Y. Wan, S. Dry Assessing Researcher Needs for a Virtual Biobank. *Biopreservation and Biobanking*. 2016, DOI. 10.1089/bio.2016.0009; as print 2017;15:203-210.
159. Jia A, Lee C, McClelland M, Mercola D. Tumor Microenvironment: Prospects for Diagnosis and Prognosis of Prostate Cancer Based on Changes in Tumor-Adjacent Stroma. In: Mosquera. BDRaJM, editor. *Molecular Pathology of Prostate Cancer*. New York.: Springer International Publishing.; 2017 (in press).