BIOGRAPHICAL SKETCH

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NAME: Renato J. Aguilera

eRA COMMONS USER NAME (credential, e.g., agency login): raguilera

POSITION TITLE: Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Texas at El Paso	B.S.	1981	Microbiology
University of Texas at El Paso	M. S.	1982	Biology
University of California at Berkeley	Ph.D.	1982-1987	Immunology
University of California at Berkeley	Postdoctoral	1987-1989	Immunology

A. Personal Statement: Dr. Aguilera has extensive experience in immunology, cancer research, molecular and cell biology, and drug screening. Dr. Aguilera is the current Program Director of the Border Biomedical Research Center and Director of the Cytometry, Screening and Imaging (CSI) Core facility. In the next iteration of the BBRC, Dr. Aguilera will continue on as the Research Deputy Director and the Director of the Research Infrastructure Core facility and will oversee the management of the proposed research projects and the core facility. As director of the CSI unit within the Research Infrastructure Core, he manages three staff that maintain the core, service instruments, develop assays, and train new staff and students on equipment use and data analysis. Since the inception of the CSI facility, the unit staff have screened drugs from investigators at several RCMI institutions. Rigorous data analysis has and will continue to be performed by the faculty and staff of our RCMI-funded Bioinformatics/Biostatistics Unit. As and a BBRC member, he and his staff have developed assays for screening of chemical libraries on a variety of human cancer cells. The simultaneous screening of compounds of various human cancer cell lines resulted in the detection of novel lead compounds with anti-cancer activity. A recent screen of >9,000 compounds has resulted in the identification of several compounds with anticancer activities that induce apoptosis. This work is expected to lead to translational research with health care implications. Over the past 29 years, Dr. Aguilera has been continuously funded by federal and foundation research grants and generated over 55 peer-reviewed publications. The following are recent publications that have included core staff and members of his laboratory:

(1) Santiago-Vazquez,Y., Das, U., Varela-Ramirez, A., Baca, S.T., Ayala-Marin, Y., Lema, C., Das, S., Baryyan, A., Dimmock J.R. and Aguilera, R.J. (2016). Tumor-selective cytotoxicity of a novel pentadiene analogue on human leukemia/lymphoma cells. Clin. Cancer Drugs 3(2)138-146. PMC5110259

(2) Nunes LM, Robles-Escajeda E, Santiago-Vazquez Y, Ortega NM, Lema C, Muro A, Almodovar G, Das U, Das S, Dimmock JR, Aguilera* RJ, Varela-Ramirez A. The gender of cell lines matters when screening for novel anti-cancer drugs. The AAPS journal. 2014; 16(4):872-4. PMC4070257. *Co-contributing author

(3) Villanueva, P., Martinez, A., Baca, S.T., DeJesus, R.E., Larragoity, M., Contreras, L., Gutierrez, D.A., Varela-Ramirez, A., Aguilera, R.J. (2018). Pyronaridine exerts potent cytotoxicity on human breast and hematological cancer cells through induction of apoptosis. PLoS ONE Nov. 5; 13(11):e0206467. https://doi.org/10.1371/journal.pone.0206467. PMID: 30395606

(4) Montoya, A., Amaya, C.N., Belmont, A., Diab, N., Trevino, R., Villanueva, G., Rains, S., Sanchez, LA, Badri, N, Otoukesh, S, Khammanivong, A, Liss, D, Baca, S.T., Aguilera, R.J., Dickerson, E.B., Torabi, A., Dwivedi, A.K., Abbas, A., Chambers, K., Bryan, B.A., Nahleh Z. Use of non-selective beta-blockers is

associated with decreased tumor proliferative indices in early stage breast cancer. Oncotarget 2017; (8) 6446-6460. PMC5351644

B. Positions and Honors

Positions:

1978-1980	MBRS Undergraduate Trainee Department of Biological Sciences, University of Texas at El Paso.
1980-1982	MBRS MS Graduate Fellow, Department of Biological Sciences, University of Texas at El Paso.
1982-1985	NSF-Predoctoral Fellow, Department of Immunology, University of California at Berkeley
1984-1987	Ford Foundation Dissertation Fellow, University of California at Berkeley.
1987-1989	University of California President's Postdoctoral Fellow, Department of Molecular and Cellular Biology, Division of Immunology, University of California at Berkeley.
1989-2002	Assistant/Associate Professor, Department of Molecular, Cell and Developmental Biology, University of California at Los Angeles
1998-2002	Director of the Minority Access to Research Careers Program (MARC U*STAR) at UCLA.
2002-	Professor, Department of Biological Sciences, The University of Texas at El Paso.
2002-2005	Deputy Director of the Border Biomedical Research Center (RCMI) at UTEP.
2004-2008	Board of Scientific Counselors of the National Institute of Environmental Health Sciences (NIEHS).
2005-2011	Director of the SCORE Institutional Program at UTEP.
2010-2015	Chair of Minority Affairs Committee (MAC) of the American Society of Cell Biology.
2002-	Professor, Department of Biological Sciences, The University of Texas at El Paso.
2002-	Director of Graduate Program in Biology, The University of Texas at El Paso.
2004-	Director of the Research Initiative for Scientific Enhancement (RISE) Program at UTEP
2007-	Director of the Cytometry, Screening and Imaging Core Facility, Border Biomed. Res. Ctr.

Honors:

1995	Departmental Distinguished Teaching Award, UCLA
2007	College of Science (UTEP) Distinguished Teaching Award
2010	American Society for Microbiology, William A. Hinton Research Training Award
2013	Triumphant Hispanic (Hispanos Triunfadores) Award
2013	SACNAS Distinguished Research Mentor Award
2017	Selected as a Lifetime Fellow of the American Society for Cell Biology

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C. Contribution to Science

1. The work initiated during my Ph.D. research involved the characterization of factors involved in normal and abnormal immunoglobulin (Ig) gene recombination in murine lymphomas. During this period a lymphocyte-specific DNA binding factor was characterized that interacted with the Ig recombination signals (1). This work resulted in the first description of DNA binding proteins with specificity for the Ig signals and led to the subsequent cloning of the gene by another group. In addition to this work, I co-authored work describing the identification of a nuclease activity that cleaved at the Ig recombination signals (2). In related work, my group cloned and characterized the transcriptional regulatory regions of the Recombinase Activating Genes 1 and 2 (*rag-1* and *rag-2*). This work resulted in the identification of key tissue-specific and non-specific transcription factors that regulate *rag* gene expression (3-4). These diverse projects provided me with the training and confidence to pursue research in a variety of areas from basic cell and molecular biology to biochemistry in various model systems.

(1) Aguilera, R.J., Akira, S., Okazaki, K., and Sakano, H. (1987). A pre-B nuclear protein which specifically interacts with the immunoglobulin V-J recombination sequences. Cell 51, 909-917.

(2) Hope, T.J., Aguilera, R.J., Minie, M., Sakano, H. (1986). Endonucleolytic activity that cleaves immunoglobulin recombination sequences. Science 231, 1141-1145.

(3) Miranda, G. A., Villalvazo, M., Galic, Z., Alva, J., Abrines, R., Yates, Y., Evans, C.J. and Aguilera, R.J. (2002). Combinatorial regulation of the murine RAG-2 Promoter by Sp1 and distinct lymphocyte-specific transcription factors. Molecular Immunology 38:1151-1159.

(4) Brown, S. T., Miranda, G., Galic, Z., Hartman, I.Z. Lyon, C. and Aguilera, R.J. (1997). Regulation of the RAG-1 promoter by the NF-Y transcription factor. J. Immunology 158: 5071-5074

2. During our search for enzymes involved in antibody gene recombination, we detected a nuclease activity in plasmacytoma extracts that cleaved precisely at the G-rich antibody switch region that are commonly involved in normal and abnormal gene rearrangements. This nuclease activity was further characterized by my group and the gene was cloned (1) resulting in one patent (US Patent # 6,455,250). The cloning and further characterization of this gene resulted in the realization that the gene encoded DNase II, an enzyme involved in phagocyte-mediated DNA degradation. Mutation of this gene in *Drosophila melanogaster* was subsequently found to result in the inability of flies to fend of bacterial infection (2). Subsequent genome-wide gene expression microarray analyses of DNase II mutant flies resulted in the discovery of a novel nuclease that we named Stress Induced DNase (SID) that was found to be induced by bacterial infection and oxidative stress (3). The structure of DNase II was finally solved during the past year and resulted in the novel discovery that the enzyme behaves a dimmer with a unique structure not previously reported for a nuclease (4).

(1) Lyon, C.J., Evans, C.J., Bill, B.R., Otsuka, A.J. and Aguilera, R.J. (2000). The C. elegans apoptotic nuclease Nuc-1 is related in sequence and activity to mammalian DNase II. Gene 252:147–154.

(2) Seong, C., Varela-Ramirez, A., and Aguilera, R.J. (2006). DNase II deficiency impairs innate immune function in Drosophila. Cellular Immunology, 240:5-13. PMC2430755

(3) Seong, C., Varela-Ramirez, A., Tang, X., Anchondo, B., Magallanes D. and Aguilera, R.J. (2014). Cloning and Characterization of a Novel Drosophila Stress Induced DNase. PLoS One 9(8):e103564; PMC411890055.

(4) Varela-Ramirez, A., Abendroth,J., Mejia, A.A., Phan, I.Q., Lorimer, D.D., Edwards,T.E., Aguilera, R.J. (2017). Structure of acid deoxyribonuclease. Nucleic Acids Research 45(10):6217-6227. PMC5449587

3. Our prior work with lymphomas resulted in a logical move to discover novel therapeutics against these malignancies. In collaboration with various synthetic chemists, we were able to develop a robust high-content screening assay to detect and characterize novel anti-cancer compounds (1). Using the same high–content screening assays, we recently identified several potent anti-lymphoma compounds in a small library of compounds (n=145; 1-2). Most recently, we determined that these compounds elicit cell death via proteasome inhibition (3). In addition, a small subset of the anti-lymphoma compounds induced cell death via apoptosis on triple-negative breast cancer cell lines after increasing exposure to the compounds to 72 h (4).

(1) Santiago-Vazquez,Y., Das, S., Das, U., Robles-Escajeda, E., Ortega, N. M., Lema, C., Varela-Ramirez, A., Aguilera, R.J., Balzarini, J., De Clercq, E., Dimmock, S.G., Gorecki, D.K.J., and Dimmock, J. (2014). Novel 3,5-bis(arylidene)-4-oxo-1-piperidinyl dimers: structure-activity relationships and potent antileukemic and antilymphoma cytotoxicity. Eur. J. Med. Chem. 77:315-322. PMC421594550

(2) Nunes, L.M., Hossain, M., Varela-Ramirez, A. Das, U., Dimmock, J. R., and Aguilera, R. J. (2016). A novel class of piperidones exhibit potent, selective and pro-apoptotic anti-leukemia properties. Oncology Letters 11(6) 3842-3848. (3) Nunes, L.M., Hossain, M., Varela-Ramirez, A. Das, U., Dimmock, J. R., and Aguilera, R. J. (2016). A novel class of piperidones exhibit potent, selective and pro-apoptotic anti-leukemia properties. Oncology Letters 11(6) 3842-3848. PMC4888252

(3) Contreras, L., Calderon, R.I., Varela-Ramirez, A., Zhang, H.Y., Quan, Y., Das, U., Dimmock, J.R, Skouta, R., Aguilera, R.J. (2018). Induction of apoptosis via proteasome inhibition in leukemia/ lymphoma cells by two potent piperidones. Cellular Oncology 2018; Aug 7. doi: 10.1007/s13402-018-0397-1 PMID: 30088262

(4) Robles-Escajeda, E., Das,U., Ortega N.M., Parra, K., Francia, G., Y., Dimmock, J. R., Varela-Ramirez, A., and Aguilera, R. J. (2016). A novel curcumin-like dienone induces apoptosis in triple-negative breast cancer cells. Cell Oncol. 39(3):265-277. PMC4899127

4. In work recently completed by our group, we have also ventured into the analysis of natural plant products that have therapeutic potential as in the case of Green Barley that for years has been ascribed to have anticancer activity with little if any scientific proof. Our group revealed that indeed Green Barley does contain compounds that induce apoptosis and arrest the cell cycle in human leukemias/lymphomas (1). During the course of our anti-cancer screening analyses, we also noticed that certain compounds were more active against cancers derived from male patients; thus corroborating the long held belief that distinct compounds could have gender-dependent differences in their mode of action or activity (2). In addition, a recent analysis of Ruthenium-based compounds, we determined that two compounds induced apoptosis in lymphoma lines and were also cytotoxic to androgen receptor positive prostate cancer cell lines (3).

Arsenic contamination of well water in the Southwest region of the US has the potential to lead to significant health problems in the foreseeable future and for this reason, we collaborated with other investigators to determine the effects of arsenic on human keratinocytes (4). Our results revealed that several microRNAs that have been implicated in the genesis of melanoma were differentially expressed after arsenic exposure (4).

(1) Robles-Escajeda, E., Lerma, D., Nyakeriga, A.M., Ross, J., Kirken, R.A., Aguilera, R.J., and Varela-Ramirez, A. (2013). Searching in Mother Nature for anti-cancer activity: mechanism of antiproliferative and proapoptotic effect elicited by green barley on leukemia/lymphoma cells. PLOS One 8:9 e7350-8. PMC3767772

(2) Nunes, L.M., Robles-Escajeda, E., Santiago-Vazquez, Y., Ortega N.M., Lema, C., Muro, A., Almodovar, G., Das, U., Das,S., Dimmock, J. R., Aguilera, R. J., and Varela-Ramirez, A. (2014). The gender of cell lines matters when screening for novel anti-cancer drugs. Amer. Assoc. Pharm. Sci. May 30. PMC407025751)

(3) Robles-Escajeda, E., Martínez, A., Varela-Ramirez, A., Sánchez-Delgado, R. A. Aguilera, R.J. (2013). Analysis of the cytotoxic effects of ruthenium-ketoconazole and ruthenium-clotrimazole complexes on cancer cells. Cell Biol.and Tox. 29(6):431-43. PMC4207122

(4) Gonzalez, H., Lema, C., Kirken, R.A., Maldonado, R.A., Varela-Ramirez, A., and Aguilera, R.J. (2015). Arsenic-exposed keratinocytes exhibit differential microRNAs expression profile; potential implication of miR-21, miR-200a and miR-141 in melanoma pathway. Clinical Cancer Drugs 2:138-147. PMC4819983

Complete List of Published Work in My Bibliography:

http://www.ncbi.nlm.nih.gov/myncbi/browse/collection/47273512/?sort=date&direction=descending

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

2G12MD007592 (PI: R. Kirken) 7/01/14-6/30/19
Border Biomedical Research Center
PD and Director of Cell Culture Core Facility
Roles: Program Director and Core Director

UT Star Award (PI: R. Aguilera) 9/01/06-8/30/21
Award for Supplies and Equipment
Role: Principle Investigator

1R25 GM069621-13 (Aguilera) 4/01/17-5/31/22
NIGMS
Title: RISE Scholars Program at UTEP
The RISE training grant assists minority students to transition to graduate/ academic careers.
Role: Program Director

Completed Research Support

1SC3GM103713-03
NIGMS SCORE SC3 (Aguilera) 7/01/13-1/31/18
Title: Characterization of novel anti-lymphoma compounds with selective toxicity.
The goal of this project is to characterize several anti-lymphoma compounds detected by drug screening
Role: Principal Investigator