BIOGRAPHICAL SKETCH

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NAME: Cox, Marc B.

eRA COMMONS USER NAME (credential, e.g., agency login): mbc678

POSITION TITLE: Associate 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 Missouri, Columbia	B.S.	12/1997	Biology
Tulane University School of Public Health and Tropical Medicine	M.S.P.H.	05/1999	Environmental Health Sciences
Tulane University	Ph.D.	05/2003	Molecular and Cellular Biology
Mayo Clinic Arizona	Postdoctoral	05/2007	Biochemistry and Molecular Biology

A. Personal Statement

Over the last nineteen years I have worked in the areas of steroid hormone receptor function, environmental endocrine disruption, and chaperone biology. During that time, I acquired a vast amount of experience in both the molecular chaperone field and the steroid hormone receptor field. I have published extensively on the cochaperone regulation of receptor function, most recently focused on the FKBP immunophilin proteins. This work has led to established collaborations with some of the leading laboratories in the field, a number of high profile publications, both U.S. and International patent applications, and possible licensing opportunities. I have become a recognized leader in the cochaperone regulation of steroid hormone receptor function, and in the development of novel strategies for treating prostate cancer. Given my expertise in the molecular chaperone-mediated stress response, I also maintain a wealth of reagents relevant for research in any system and/or disease involving chaperones and the stress response including a wide variety of cancers, neurodegenerative diseases and toxicant-induced cellular stress. As a result, I collaborate on a number of projects that are outside of my major research foci. In addition to environmental monitoring and prostate cancer therapeutics, I have published with collaborators in areas as diverse as Alzheimer's Disease, stress, depression, and chronic pain. In conjunction with these research efforts I have trained a large number of undergraduate and graduate students in my laboratory. In addition to my contributions to research and science education, I have served in a number of faculty leadership roles at UTEP and within the University of Texas System, and as Deputy Director of the BUILDing SCHOLARS Center where I have participated in the administration of both pilot project and seed funding grant programs and formal mentoring programs for students, faculty, and post-doctoral fellows. I currently serve as UTEP's founding Director of the Center for Faculty Leadership and Development, which focuses on a broad set of faculty development initiatives that strive for excellence in teaching and learning, scholarship and mentoring, entrepreneurship and innovation, and leadership and engagement. Given my strong background in cancer research, and my experience in leading and developing faculty researchers at UTEP, I am uniquely suited to lead the Investigator Development Core of the BBRC.

B. Positions and Honors

Positions and Employment

2007-2012 Assistant Professor, Dept. of Biological Sciences, University of Texas at El Paso

2008- Faculty Member, Environmental Science and Engineering PhD Program, University of Texas at El Paso
2010- Co-Director, Toxicology and Cancer Cluster, Border Biomedical Research Center, University of Texas at El Paso
2012- Associate Professor, Dept. of Biological Sciences, University of Texas at El Paso
2015- Deputy Director, BUILDing SCHOlARS Center, University of Texas at El Paso
2016- Director, Center for Faculty Leadership and Development, University of Texas at El Paso

Other Experience and Professional Memberships

2002- Member, Endocrine Society
2012- Member, Society for Basic Urologic Research

Honors

2004-2007 Individual NRSA Postdoctoral Fellowship (NIH-NIDDK)
2010 Outstanding Performance Award, Office of Research and Sponsored Projects, UTEP
2012 Outstanding Performance Award, Office of Research and Sponsored Projects, UTEP
2016 Texas Inventor of the Year, Intellectual Property Law Section, Texas State Bar
2017 Outstanding Performance Award, Office of Research and Sponsored Projects, UTEP

C. Contribution to Science

1. My primary research interests include the identification and characterization of chaperone and cochaperone proteins that bind to and regulate the steroid hormone receptors. At least twelve chaperone and cochaperone proteins are required for normal receptor function, including Hsp70 and Hsp90. All of these factors offer the potential opportunity for therapeutic intervention. My lab is interested in understanding the manner in which these factors influence receptor folding, hormone binding, nuclear translocation, dimerization, and DNA binding with the ultimate goal of therapeutically targeting these factors for the treatment of hormone-dependent diseases. We have focused largely on the steroid hormone receptor-associated FKBP proteins, as these are the only factors that display specificity for small subsets of Hsp90-dependent client proteins and represent attractive targets. My early work as a student significantly contributed to understanding the manner by which the p23 cochaperone regulates receptor function. The more recent work that I have directed in this area, starting with my postdoctoral studies, has contributed significantly to the understanding of FKBP biology and has firmly established FKBP52 as an emerging target for the treatment of prostate cancer. More recently we have contributed to the understanding of steroid hormone receptor regulation by the SGTA cochaperone, another protein that has emerged as an important factor in prostate cancer.

a. Cheung-Flynn, J., Prapapanich, V., **Cox, M.B.**, Riggs, D.L., Suarez-Quian, C., and Smith, D.F. (2005) Physiological role for the cochaperone FKBP52 in androgen receptor signaling. *Molecular Endocrinology*. **19**(6): 1654-1666.
b. Cox, M.B., Riggs, D.L., Hessling, M., Buchner, J., and Smith, D.F. (2007) FK506-binding protein phosphorylation: a potential mechanism for regulating steroid hormone receptor activity. *Molecular Endocrinology*. **21**: 2956-2967.
c. Paul, A., Garcia, Y., Zeirer, B., Patwardhan, C., Gutierrez, O., Hildenbrand, Z., Harris, D.C., Balsiger, H.A., Johnson, J.L., Buchner, J., Chadli, A., and Cox, M.B. (2014) The cochaperone SGTA (small glutamine-rich tetratricopeptide repeat-containing protein alpha) demonstrates regulatory specificity for the androgen, glucocorticoid and progesterone receptors. *Journal of Biological Chemistry*. **289** (22): 15297-308. PMCID: PMC4140887
d. Storer Samaniego, C., Suh, J.H., Chattopadhyay, A., Olivares, K., Guy, N., Sivils, J.C., Dey, P., Yumoto, F., Fletterick, R., Strom, A., Gustafsson, J-A., Webb, P., and **Cox, M.B.** (2015) The FKBP52 cochaperone acts in synergy with β-catenin to potentiate androgen receptor signaling. *PLoS One*. **10**(7): e0134015. PMCID: PMC4514735

2. Using the knowledge gleaned from our studies of steroid hormone receptor-associated cochaperones I have worked to improve prostate cancer outcomes through the development of new therapeutic approaches. Since androgens (i.e. testosterone and derivatives) control growth and survival of early stage metastatic prostate cancer, the current therapeutic strategies include combinations of androgen deprivation therapy (ADT) and

anti-androgens. Unfortunately, this approach only delays disease progression and within a few years the tumors recur in a form that no longer responds to these treatments. Thus, the current treatment options, while effective in early stage prostate cancer, are largely ineffective in late stage disease. The studies that I have directed have led to the development of a new class of prostate cancer drugs that show promise in targeting both early and late stage prostate cancer, which hopefully will greatly decrease the mortality rate associated with prostate cancer. This class of drugs is the first to target an androgen receptor-associated cochaperone for the treatment of prostate cancer. Through targeting the androgen receptor BF3 surface, MJC13 specifically inhibits FKBP52-regulated receptor activity leading to impressive effects on prostate cancer cell proliferation and tumor growth in a prostate cancer xenograft model. We currently have one allowed patent on MJC13 and a pending patent on MJC13 soluble formulations suitable for in vivo administration. The proof-of-principle data that we generated is being used to push the commercial development of MJC13 forward.

a. Tonos De Leon, J., Iwai, I., Feau, C., Garcia, Y., Balsiger, H.A., Storer, C., Suro, R.M., Lee, S., Kim, Y.S., Chen, Y., Ning, Y.M., Garza, K.M., Riggs, D.L., Trepel, J., Guy, R.K., Fletterick, R.J., Neckers, L.M., and **Cox, M.B.** (2011) Targeting the regulation of androgen receptor signaling by the heat shock protein 90 cochaperone FKBP52 in prostate cancer cells. *Proceedings of the National Academy of Sciences USA.* **108**(29): 11878-11883**.** PMCID: PMC3141981
b. Liang, S., Bian, X., Liang, D., Sivils, J., Neckers, L.M., **Cox, M.B.**, and Xie, H. Solution formulation development and efficacy of MJC13 in a preclinical model of castration-resistant prostate cancer. *Pharmaceutical Development and Technology*. **7**: 1-6. PMCID: IN PROCESS
c. Suh, J.H., Chattopadhyay, A., Sieglaff, D.H., Storer Samaniego, C.L., **Cox, M.B.**, and Webb, P. (2015) Similarities and distinctions in actions of surface-directed and classic androgen receptor antagonists. *PLoS One*. 10(9):e0137103. PMCID: IN PROCESS
d. Cox, Marc B., Neckers, Leonard M., Neckers, Jane B., Kim, Yeong Sang, Iwai, Aki, Ning, Yangmin, Meneses De Leon, Johanny, Balsiger, Heather A., Fletterick, Robert. “Pharmaceutical compositions which inhibit FKBP52-mediated regulation of androgen receptor function and methods of using same”; Claims Priority to U.S. Provisional Patent Application No. 61/242,541, Priority Date: September 15, 2009; Application No: US 13/395,976; Publication Date: November 8, 2012; International Patent Application No. PCT/US10/48705, filed September 14, 2010; Publication numbers WO2011034834A2, CA2774327A1, EP2477700A2, US20120283215A1, WO2011034834A3, Australia Patent # 2010295806

3. My established expertise in FKBP biology has led to many collaborative projects aimed at characterizing a role for the FKBP proteins in neurodegenerative diseases, depressive disorders, and chronic pain. The FKBP proteins have been shown to regulate microtubule assembly and Tau aggregation. As a result, I have collaborated with Chad Dickey at the University of South Florida on a project to characterize the role of various chaperone proteins in tauopathies (the aggregation of tau protein in Alzheimer’s disease). In addition, given the role of the glucocorticoid receptor in stress and depression, I have established collaborations to understand the role of FKBP52 in these processes. I have served as a co-investigator in these studies offering my expertise in FKBP52 protein structure and function, and offering help with various biochemical and cellular assays.

a. Jinwal, U.K., Koren III, J., Borysov, S.I., Schmid, A., Abisambra, J.F., Blair, L.J., Johnson, A.G., Jones, J.R., Shults, C., O’Leary, J., Jin, Y., Buchner, J., **Cox, M.B.**, and Dickey, C.A. (2010) The Hsp90 cochaperone, FKBP51, increases Tau stability and polymerizes microtubules. *Journal of Neuroscience*. **30**(2): 591-599. PMCID: PMC2830818
b. Touma, C., Gassen, N.C., Herrman, L., Cheung-Flynn, J., Bull, D.R., Ionescu, I.A., Heinzmann, J.M., Knapman, A., Siebertz, A., Depping, A.M., Hartmann, J., Hausch, F., Schmidt, M.V., Holsboer, F., Ising, M., **Cox, M.B.**, Schmidt, U., and Rein, T. (2011) FKBP5 shapes stress responsiveness: Modulation of neuroendocrine reactivity and coping behavior. *Journal of Biological Psychiatry*. **70**: 928-936. PMCID: IN PROCESS
c. Hartmann, J., Wagner, K.V., Liebl, C., Scharf, S.H., Wang, X., Wolf, M., Hausch, F., Rein, T., Schmidt, U., Touma, C., Cheung-Flynn, J., **Cox, M.B.**, Smith, D.F., Holsboer, F., Muller, M.B., and Schmidt, M.V. (2012) The Involvement of the FK506-binding protein 51 (FKBP51) in the behavioral and neuroendocrine effects of chronic social defeat. *Neuropharmacology.* **62**: 332-339. PMCID: IN PROCESS
d. Maiarù, M., Tochiki, K.K., **Cox, M.B.**, Anand, L., Bell, C.G., Feng, X., Hausch, F., and Géranton, S.M. (2016) Deletion of the stress regulator FKBP51 promotes resistance to the development of chronic pain. *Science Translational Medicine*. **8**(325): 325ra19. PMCID: IN PROCESS

4. In addition to having expertise in the study of human receptor signaling pathways in yeast, I also have a background in toxicology and endocrine disruption. As a result, I have interests in the application of the yeast-based steroid hormone receptor signaling assays to the monitoring of environmental samples for endocrine disrupting chemicals. The studies that I served as PI on led to the development of a significantly improved yeast-based assay for the assessment of estrogenic activity in environmental samples. Importantly we have achieved a 4-hour assay time that allows for the detection of estrogenic activity directly in wastewater without the need for sample extraction, concentration and sterilization. As a result of this work, we have established a number of collaborations to screen environmental samples.

a. Balsiger, H.A., and **Cox, M.B.** (2009) Yeast-based reporter assays for the functional characterization of cochaperone interactions with steroid hormone receptors. In *Methods in Molecular Biology: The Nuclear Receptor Superfamily*, vol. 505. Edited by I.J. McEwan. The Humana Press, Totowa, New Jersey.
b. Balsiger, H.A., **de la Torre, R., Lee, W., and **Cox, M.B**. (2010) A four-hour yeast bioassay for the direct measure of estrogenic activity in wastewater without sample extraction, concentration, and sterilization. *Science of the Total Environment*. **408**: 1422-1429. PMCID: PMC2839367
c. Sellin Jeffries, M.K., Conoan, N.H., **Cox, M.B**., Sangster, J.L., Balsiger, H.A., *Bridges, A.A., Cowman, T., Knight, L.A., Bartlet-Hunt, S.L., and Kolok, A.S. (2011) The anti-estrogenic activity of sediments from agriculturally-intense watersheds: Assessment using in vivo and in vitro assays. *Aquatic Toxicology*. 105: 189-198. PMCID: IN PROCESS
d. Sangster, J.L., Zhang, Y., *Hernandez, R., **Garcia, Y.A., ***Sivils, J.C., **Cox, M.B.**, Snow, D.D., Kolok, A.S., and Bartlet-Hunt, S.L. (2014) Bioavailability and fate of sediment-associated trenbolone and estradiol in aquatic systems. *Science of the Total Environment*. 496: 576-584. PMCID: IN PROCESS

Complete List of Published Work in MyBibliography:
https://www.ncbi.nlm.nih.gov/sites/myncbi/1Fe1im6HWqdQw/bibliography/47213198/public/?sort=date&direction=ascending

D. Research Support

Ongoing Research Support

Lizanell and Colbert Coldwell Foundation Cox (PI) 6/1/2018-- 5/31/2019
A Novel Approach to Treating Castration Resistant Prostate Cancer
The overall goal of this project is to further our understanding of the mechanisms by which FKBP52 and beta-catenin regulate unique androgen-regulated transcriptional programs and define how GMC1 affect those transcriptional programs.
Role: PI

W81XWH-17-1-0435 (DOD PCRP) Cox (PI) 8/1/2017-- 7/30/20
Direct Targeting of the FKBP52 Cochaperone for the Treatment of Castration Resistant Prostate Cancer
The studies detailed in the proposal aim to perform hit-to-lead optimization of a first-in-class direct FKBP52 targeting drug (GMC1), and lead characterization in both cellular and animal models of prostate cancer.
Role: Initiating PI submitted in conjunction with J. Chaudhary and A. Cherkasov as Partnering PIs

1UL1MD009598-01 (NIH U54) Multi-PI 9/26/14-- 6/30/19
Building Infrastructure Leading to Diversity: Southwest Consortium of Health-Oriented Education Leaders and Research Scholars (BUILDing SCHOLARS)
BUILDing SCHOLARS is a center of excellence established at The University of Texas at El Paso with support from the National Institutes of Health - Common Fund. Our goal is to implement a suite of programs and activities that will positively transform the training of the next generation of biomedical researches from U.S. Southwest through a multi-institution consortium in Texas, New Mexico and Arizona, as well as three extraregional sites.
Role: Multi-PI team including Stephen Aley, Thomas Boland, Marc B. Cox, Timothy Collins, Sara Grineski, Lourdes Echegoyen, Osvaldo Morera, and Homer Nazeran

Completed Research Support

RP110444-P2 (CPRIT) Cox (PI) 7/1/2011-- 12/31/2016
Roles of chaperone/β-catenin interactions in prostate cancer
The studies detailed in the proposal aim to characterize FKBP52/β-catenin/AR interactions, elucidate the mechanism(s) by which those interactions promote AR function, and to use this knowledge to develop targeting strategies and candidate small molecule drugs for the treatment of prostate cancer.
Role: PI

TX Office of Governor Cox (PI) 1/1/2015-- 6/31/2015
Pharmaceutical Compositions Directly Targeting FKBP52 for the Treatment of Prostate Cancer
Studies aimed at generating early proof-of-concept data needed to move GMC1 closer to commercialization.
Role: PI