OMB No. 0925-0001 and 0925-0002 (Rev. 10/2021 Approved Through 01/31/2026)

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.  
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: **Cristel V. Camacho**

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

POSITION TITLE: **Assistant Professor, Cecil H. and Ida Green Center for Reproductive Biology Sciences**

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 |
| --- | --- | --- | --- |
| Hardin-Simmons University, Abilene, TX | B.S. | 05/2005 | Biology/Biochemistry |
| University of Cambridge, UK |  |  | Biology |
| University of Texas Southwestern Medical Center, Dallas | Ph.D. | 05/2012 | Cancer Biology |
| University of Texas Southwestern Medical Center, Dallas | Postdoc | 08/2012 | Cancer Biology |
| St. Jude Children’s Research Hospital, Memphis, TN | Postdoc | 01/2017 | Cancer Biology |

**A. Personal Statement**

I am a trained cancer biologist with an expertise in animal modeling. The overarching theme of my research studies has focused on understanding key genetic events that lead to cancer in an effort to identify novel targets that will help improve current therapies. During my graduate studies, I exploited the use of animal models to study the role of stochastic radiation-induced DNA damage and its ability to cooperate with existing sensitizing mutations in driving brain cancer initiation. Similarly, my postdoctoral studies employed various animal models of DNA repair deficiency to elucidate the role of DNA ligases in the development of brain cancer. Currently, my research focuses on characterizing the molecular basis of breast cancer phenotypes with an emphasis on PARP biology.

• Ongoing and recently completed projects that I would like to highlight include:

**RP220325- Kraus (PI)** Period: 3/2022 through 2/2025 (3 years)

Cancer Prevention and Research Institute of Texas

“Loss of Site-Specific ADP-ribosylation of Oncohistones in Cancers”

Role: Collaborator

**ACS-IRG-21-142-16 - Camacho (PI)** Period: 4/2023 through 3/2024 (1 year)

Harold C. Simmons Comprehensive Cancer Center

American Cancer Society - “The Role of PARP1-mediated FoxA1 ADP-Ribosylation in Breast Cancer Biology”

**Role: PI**

**B. Positions, Scientific Appointments, and Honors**

**Positions and Employment:**

12/20 to Present Assistant Professor, Cecil H. and Ida Green Center for Reproductive Biology Sciences, University of Texas Southwestern Medical Center, Dallas.

09/19 to 12/20 Senior Research Scientist, Cecil H. and Ida Green Center for Reproductive Biology Sciences, University of Texas Southwestern Medical Center, Dallas (with Dr. W. Lee Kraus).

09/17 to 08/19 Research Scientist, Cecil H. and Ida Green Center for Reproductive Biology Sciences, University of Texas Southwestern Medical Center, Dallas (with Dr. W. Lee Kraus).

01/17 to 08/17 Senior Research Associate, Cecil H. and Ida Green Center for Reproductive Biology Sciences, University of Texas Southwestern Medical Center, Dallas (with Dr. W. Lee Kraus).

09/12 to 01/17 Postdoctoral Research Associate, Department of Genetics, St. Jude Children’s Research Hospital, Memphis, TN (with Dr. Peter J. McKinnon).

05/12 to 08/12 Postdoctoral Research Fellow, Department of Radiation Oncology, University of Texas Southwestern Medical Center, Dallas (with Dr. Sandeep Burma).

**Awards and Honors:**

2016 Hardin-Simmons University, Outstanding Young Alumni Award.

2013 Brookhaven National Laboratory, First Place RHIC & AGS Thesis Award.

2012 St. Jude Children’s Research Hospital, selected to attend National Graduate Student Symposium.

2011 NASA Space Radiation Investigator’s Workshop, First Place Graduate Student Poster Presentation Award.

2011 National Institutes of Health, selected to attend National Graduate Student Research Conference.

2009 International Workshop on Space Radiation Research, Young Scientist Oral Presentation Award.

2009 International Workshop on Space Radiation Research, Student Travel Award.

2008 NASA Space Radiation Investigator’s Workshop, Third Place Graduate Student Poster Presentation Award.

2008 NASA Space Radiation Investigator’s Workshop, Student Travel Award.

2007-2009 University of Texas Southwestern Medical Center, T32 Cancer Biology Program

Training Grant, Ruth L. Kirschstein National Research Service Award.

**C. Contributions to Science**

My research over the past 17 years has contributed to our understanding of key genetic and regulatory events in the initiation, promotion and progression of cancer. Each of my studies has a clear translational aspect, revealing exciting new clinical applications to be explored.

Full publications list: <https://www.ncbi.nlm.nih.gov/myncbi/1b9Kt-s8txbQDF/bibliography/public/>

**1) *Gene Expression Regulation Mediated by Estrogen Receptor ***

In my current research I am interested in understanding the molecular mechanisms that drive ER-regulated transcriptional responses, in both normal physiology and cancer. We have recently shown that the transcriptional coregulator BRD3 is recruited to and controls the activity of a subset of ERtranscriptional enhancers, regulating gene expression and breast cancer cell growth. Our recent studies also provide evidence that PARP1 can regulate estrogen-dependent ER and FoxA1 binding and gene expression. High PARP1 correlates with poor survival and its inhibition can attenuate the estrogen-dependent growth of ER-positive breast cancer cells. These studies shed insight into the molecular basis of clinical cancer phenotypes and suggest novel therapeutic opportunities to target ER-positive breast cancer in the clinic. Further, we have explored the molecular and genomic mechanisms that underlie the functional interplay between estrogen and relaxin in the myometrium. Our studies have identified a pathway that integrates estrogen and relaxin signaling, resulting in a convergence of membrane and nuclear signaling pathways to control genomic and biological outcomes.

Murakami, S., R. Li, A. Nagari, M. Chae, **C. V. Camacho** and W. L. Kraus (2019) Distinct Roles for BET Family Members in Estrogen Receptor alpha Enhancer Function and Gene Regulation in Breast Cancer Cells. *Mol Cancer Res.* 17(12): 2356-2368. PMCID: PMC6891197

\*Gadad, S.S., \***C.V. Camacho**, V. Malladi, C.R. Hutti, A. Nagari, and W.L. Kraus (2021) PARP-1 Regulates Estrogen-Dependent Gene Expression in Estrogen Receptor α-Positive Breast Cancer Cells. *Mol Cancer Res*. 19(10): 1688-1698. PMCID: PMC8492518

\*Kim D.S., \***C.V. Camacho**, R. Setlem, K.Kim , S. Malladi, T.Y. Hou, T. Nandu, S.S. Gadad, W.L. Kraus (2022). Functional Characterization of lncRNA152 as an Angiogenesis-Inhibiting Tumor Suppressor in Triple-Negative Breast Cancers. *Mol Cancer Res*. 20(11): 1623-1635. PMCID: PMC9633386

Tripathy S., Nagari A., Chiu S-P., Nandu T., **Camacho C.V.**, Mahendroo M., Kraus W.L. (2024) Relaxin modulates the genomic actions and biological effects of estrogen in the myometrium by reducing estrogen receptor alpha phosphorylation. *bioRxiv.* Apr 16:2024.04.15.589654. doi:10.1101/2024.04.15.589654. PMCID: PMC11042280

**\*equal contributing authors**

**2) *PARPs: Biological Roles of ADP-ribosylation and Cancer***

Historically, the study of PARPs focused heavily on their roles in DNA damage repair and genome maintenance. However, thousands of substrates of nuclear PARPs have been identified beyond proteins involved in these processes, suggesting alternative roles for PARP1. In my current research, I have participated in studies that have outlined key roles for nuclear ADP-ribosylation by PARP1 in fundamental physiological processes. In one such study, we showed that PARP1 can promote enhanced ribosome biogenesis and cell proliferation through modulation of DDX21. This research presents an exciting new mechanism of PARP1 action that could broaden the utility of PARP inhibitors in the clinic. Further, we showed that PARP1 mediated ADP-ribosylation of H2B modulates gene expression outcomes in breast cancer. ADP-ribosylation of histones is thus an important signaling modification that plays an important role in gene regulation. Finally, we show that PARP16 mediated mono-ADP-ribosylation of ribosomes can inhibit translation and maintain protein proteostasis in ovarian cancer, which sheds light on a new potential therapeutic target.

Kim, D. S., **C. V. Camacho**, A. Nagari, V. S. Malladi, S. Challa and W. L. Kraus (2019) Activation of PARP-1 by snoRNAs Controls Ribosome Biogenesis and Cell Growth via the RNA Helicase DDX21. *Mol Cell*. 75(6): 1270-1285 e1214. PMCID: PMC6754283

Challa, S., B.R. Khulpateea, T. Nandu, **C.V. Camacho**, K.W. Ryu, H. Chen, Y. Peng, J.S. Lea, and W. L. Kraus (2021) Ribosome ADP-ribosylation inhibits translation and maintains proteostasis in cancers. *Cell*. 184(17):4531-4546. PMCID: PMC8380725

Huang, D., **C. V. Camacho**, S. Martire, A. Nagari, R. Setlem, X. Gong, A. D. Edwards, S.P. Chiu, L. A. Banaszynski, and W. L. Kraus (2022) Oncohistone Mutations Occur at Functional Sites of Regulatory ADP-ribosylation. *Cancer Res*. 82(13): 2361-2377. PMCID: PMC9256803

Aljardali, M.W., K.M. Kremer, J.E. Parker, E. Fleming, H. Chen, J.S. Lea, W.L. Kraus, **C.V. Camacho** (2024) Nucleolar Localization of the RNA Helicase DDX21 Predicts Survival Outcomes in Gynecological Cancers. *Cancer Res Comm*. 4(6): 1495-1504. PMCID: PMC11172406

**3) *Glioblastoma in the Clinic: Novel Implications for Therapy***

Glioblastoma is highly resistant to IR and chemotherapy, making it one of the deadliest types of cancer. During my graduate work I participated in studies aimed at elucidating the genetic basis of this radioresistance. Our results showed that a key glioma-specific mutant EGFRvIII receptor confers radioresistance through its modulation of the DNA repair enzyme DNA-PKcs, accelerating the rate of DNA double-strand break (DSB) repair. Further studies showed that NVP-BEZ235, a potent dual PI3K/mTOR inhibitor, could also inhibit DNA-PKcs. Using mouse xenografts, we showed that NVP-BEZ235 could significantly attenuate DSB repair *in vivo*, conferring an extreme degree of radiosensitization. We also uncovered a novel potential use of PARP inhibitors by showing that PTEN-null astrocytes are deficient in homologous recombination, rendering cells sensitive to PARP inhibition due to synthetic lethality. These studies presented important implications for the informed and rational design of much needed clinical trials using drugs that target DNA-repair pathways exploited by this highly resistant tumor type.

Mukherjee, B., B. McEllin, **C. V. Camacho**, N. Tomimatsu, S. Sirasanagandala, S. Nannepaga, K. J. Hatanpaa, B. Mickey, C. Madden, E. Maher, D. A. Boothman, F. Furnari, W. K. Cavenee, R. M. Bachoo and S. Burma (2009) EGFRvIII and DNA double-strand break repair: a molecular mechanism for radioresistance in glioblastoma. *Cancer Res*. 69(10): 4252-4259. PMCID: PMC2694953

McEllin, B., **C. V. Camacho**, B. Mukherjee, B. Hahm, N. Tomimatsu, R. M. Bachoo and S. Burma (2010) PTEN loss compromises homologous recombination repair in astrocytes: implications for glioblastoma therapy with temozolomide or poly(ADP-ribose) polymerase inhibitors. *Cancer Res*. 70(13): 5457-5464. PMCID: PMC2896430

Mukherjee, B., N. Tomimatsu, K. Amancherla, **C. V. Camacho**, N. Pichamoorthy and S. Burma (2012) The dual PI3K/mTOR inhibitor NVP-BEZ235 is a potent inhibitor of ATM- and DNA-PKCs-mediated DNA damage responses. *Neoplasia*. 14(1): 34-43. PMCID: PMC3281940

Tomimatsu, N., B. Mukherjee, M. Catherine Hardebeck, M. Ilcheva, **C. V. Camacho**, J. Louise Harris, M. Porteus, B. Llorente, K. K. Khanna and S. Burma (2014) Phosphorylation of EXO1 by CDKs 1 and 2 regulates DNA end resection and repair pathway choice. *Nature Comm*. 5: 3561. PMCID: PMC4041212

**4) *Genetic Events Underlying Radiation-Induced Gliomagenesis***

My graduate research focused on understanding the possible carcinogenic consequences of prolonged exposure to ionizing radiation (IR). In this NASA funded work, using a combination of cell-based systems and mouse models, I was able to systematically show that heavy particles found in space, similar to those currently being used in the clinic for targeted cancer therapy, pose a significant cancer risk to astronauts. My studies showed that persistent DNA damage caused by heavy particles induce high levels of senescence by upregulation of the tumor suppressor p16/Ink4a. Abrogating this fail-safe mechanism using mouse models, I showed that cells are rapidly transformed in response to IR, resulting in the formation of *de novo* brain tumors. While radiation-induced DNA damage is stochastic, common recurrent mutational events were discovered that have important implications for IR-induced gliomagenesis and for the development of therapy-resistant recurrent tumors.

Mukherjee, B., **C. V. Camacho**, N. Tomimatsu, J. Miller and S. Burma (2008) Modulation of the DNA-damage response to HZE particles by shielding. *DNA Repair (Amst)*. 7(10): 1717-1730. PMID: 18672098

**Camacho, C. V.**, B. Mukherjee, B. McEllin, L. H. Ding, B. Hu, A. A. Habib, X. J. Xie, C. S. Nirodi, D. Saha, M. D. Story, A. S. Balajee, R. M. Bachoo, D. A. Boothman and S. Burma (2010) Loss of p15/Ink4b accompanies tumorigenesis triggered by complex DNA double-strand breaks. *Carcinogenesis*. 31(10): 1889-1896. PMCID: PMC2950935

**Camacho, C. V.**, P. K. Todorova, M. C. Hardebeck, N. Tomimatsu, C. R. Gil del Alcazar, M. Ilcheva, B. Mukherjee, B. McEllin, V. Vemireddy, K. Hatanpaa, M. D. Story, A. A. Habib, V. V. Murty, R. Bachoo and S. Burma (2015) DNA double-strand breaks cooperate with loss of Ink4 and Arf tumor suppressors to generate glioblastomas with frequent Met amplification. *Oncogene*. 34(8): 1064-1072. PMCID: PMC4167163