

**BIOGRAPHICAL SKETCH**

NAME: Flores-Rozas, Hernan A.

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

POSITION TITLE: Associate Professor

**EDUCATION/TRAINING**

INSTITUTION AND LOCATION	DEGREE	Completion Date MM/YYYY	FIELD OF STUDY
University of Concepcion, Concepcion, Chile	B.S.	12/1987	Biochemistry
University of Concepcion, Concepcion, Chile	M.S.	08/1989	Biochemistry
Cornell University Medical College, New York, NY	Ph.D.	08/1996	Molecular Biology
Harvard Medical School, Boston, MA	Postdoc	07/1997	Molecular Genetics
Ludwig Institute for Cancer Research, San Diego, CA	Postdoc	03/2002	Molecular Genetics

**A. Personal Statement**

I am an Associate Professor of Basic Pharmaceutical Sciences at Florida A&M University (FAMU) College of Pharmacy and Pharmaceutical Sciences (COPPS). I received my Ph. D. from Cornell University Medical College, where I carried out my research work with Dr. Jerard Hurwitz, at the Sloan-Kettering Cancer Center, investigating the mechanism of DNA replication. I then joined Dr. Richard Kolodner's lab as a postdoctoral fellow at the Dana-Farber Cancer Institute-Harvard Medical School and then at the Ludwig Institute for Cancer Research-UCSD, where I was funded by an exclusive fellowship from the Jane-Coffin Childs Memorial Fund for Medical Research to study the role of DNA repair in the prevention of hereditary colon cancer. I moved to the Medical College of Georgia to start my independent research as an Assistant Professor at the Institute for Molecular Medicine and Genetics during which time he was a Distinguished Cancer Scholar of the Georgia Cancer Coalition. During this period my laboratory was supported by extramural funds from different agencies, including the National Institute of Health. My current research is aimed at understanding the mechanisms that allow cancer cells to survive chemotherapy, particularly the type that involve drugs that damage DNA. I have been involved in the field of DNA replication and repair for over 20 years and have contributed with seminal studies that have been published in top journals, such as the Proceedings of the National Academy of Sciences and Nature Genetics. I have trained undergraduate and graduate students, as well as postdoctoral fellows and currently I have 3 PhD students in my laboratory. I have been invited to present his work at numerous international and national meetings and have served in grant review panels as well as a reviewer for several scientific journals. I currently serve as the Shared Resources Core Leader at FAMU on the NCI U54. My expertise in molecular biology and genetics has resulted in published work, some of which is described below.

**B. Positions and Honors****Positions and Employment**

1987-1989 Graduate Student in Biochemistry, Catholic University, Chile  
 1989-1995 Graduate Student in Molecular Biology. Cornell University Medical College  
 1995-1997 Research Fellow in Enzymology/Molecular Biology, Dana-Farber Cancer Institute  
 1997-2002 Research Fellow in Enzymology/Molecular Biology, Ludwig Institute for Cancer Research, San Diego  
 2002- 2010 Assistant Professor. Department of Medicine. Medical College of Georgia.

2010- present Associate Professor, Division of Basic Science, College of Pharmacy, Florida A&M University.

### **Other Experience and Professional Memberships**

1984-1989	Chilean Society of Biochemistry Students. Member.
1987	Clinical Laboratory Assistant, Valparaiso Teaching Hospital, Valparaiso-Chile.
1989	Graduate Research Assistant. Catholic University of Chile.
1999-2000	New York Academy of Sciences. Member.
1997-2002	American Association for the Advancement of Science. Member.
2002-2010	American Society for Biochemistry and Molecular Biology. Regular member.
2010- present	American Association for Cancer Research

### **Honors**

1989	Honors received in Biochemistry Thesis Defense. Universidad de Concepcion, Chile
1994	Julian R. Rachele Prize at Cornell University Medical College
1996 - 1999	Jane Coffin Childs Memorial Fund for Medical Research. Postdoctoral Fellowship
2002 - 2003	Fraternal Order of Eagles Award.
2002 - 2007	Distinguished Cancer Scientist, Georgia Cancer Coalition.
2011	AACR Minority-Serving Institution Faculty Scholar Award.
2015-2016	Florida A&M University Faculty Research Award, FRAP.
2020 – present	Sigma Xi. The Scientific Research Honor Society. Full Member

### **C. Contribution to Science**

1. My early studies involved the characterization of nucleic acids metabolizing enzymes in human cells. I isolated and characterized of a novel RNA helicase (RNA Helicase II), which displayed an ATP-dependent 5' to 3' polarity for the unwinding of dsRNA. The enzyme was also unique in its ability to refold RNA when bound to non-hydrolyzable NTPs (distinct from ATP or dATP). RNA Helicase II was later cloned as an auto-antibody in the auto-immune disease known as "watermelon stomach disease" and determined to be a member of the ATP-dependent RNA helicases superfamily with the signature motif DEVD, involved in rRNA processing. This work was performed when significant findings in the field of RNA processing (particularly RNA splicing) revealed a crucial role for these enzymes in RNA metabolism.
  - a. Flores-Rozas, H. and Hurwitz, J. Characterization of a New RNA Helicase from Nuclear Extracts of HeLa Cells that Translocates in the 5' to 3' Direction. *J. Biol. Chem.* **268**, 21372 – 21383, 1993.
  - b. Valdez, B.C., Henning, D., Busch, R.K., Woods, K., Flores-Rozas, H., Hurwitz, J., Perlaky, L. and Busch, H. A Nucleolar RNA Helicase Recognized by Autoimmune Antibodies from a Patient with Watermelon Stomach Disease. *Nucleic Acids Res.* **7**, 1220-1224, 1996.
2. I also contributed to the work aimed at understanding the role of DNA polymerase accessory factors. Most of the focus was on the clamp, PCNA, and the clamp loader, RFC. Within this work I demonstrated that the binding of the p53-induced cyclin kinase inhibitor p21 inhibited DNA synthesis, providing a regulatory mechanism for cells with DNA damage during DNA synthesis. This is a highly cited paper (over 500 citation, this far).
  - a. Flores-Rozas, H., Kellman, Z., Dean F., Pan, Z.-Q., Harper, J.W., Elledge, S., O'Donnell, M., and Hurwitz, J. Cdk-Interacting protein 1 directly binds with proliferating cell nuclear antigen and inhibits DNA replication catalyzed by the DNA polymerase delta holoenzyme. *Proc. Natl. Acad. Sci. USA*, **91**, 8655-8659, 1994. PMID: 7915843.
  - b. Pan, Z-Q., Reardon, J., Lei L., Flores-Rozas, H., Legerski, R, Zancar, A. and Hurwitz, J. Inhibition of Nucleotide Excision Repair by the Cyclin-Dependent Kinase inhibitor p21. *J. Biol. Chem.* **270**, 22008-22016, 1995.
  - c. Uhlmann, F., Cai, J., Flores-Rozas, H., Dean, F. B., Finkelstein, J., O'Donnell, M. and Hurwitz, J. *In vitro* reconstitution of human replication factor C from its five subunits. *Proc. Natl. Acad. Sci. USA.* **93**, 6521-6526, 1996. PMCID: PMC39056
  - d. Cai, J., Uhlmann, F., Gibbs, E., Flores-Rozas, H., Lee, C.-G., Phillips, B., Finkelstein, J., Yao, N., O'Donnell, M. and Hurwitz, J. Reconstitution of human replication factor C from its five subunits in baculovirus-infected insect cells. *Proc. Natl. Acad. Sci. USA.* **93**, 12896-12901, 1996.

3. We continued to work on DNA metabolic pathways and made significant contributions in the area of DNA Mismatch repair. Using biochemical and molecular genetic approaches, we identified a new MutL homolog in yeast and demonstrated its role in the repair pathway. We described a link between DNA replication and Mismatch Repair, by describing the interaction between the clamp PCNA and mismatch repair recognition factor MSH6 and MSH3. These findings were published in Nature Genetics and are highly cited.
  - a. Flores-Rozas, H. and Kolodner R. D. The *Saccharomyces cerevisiae* *MLH3* gene functions in MSH3-dependent suppression of frameshift mutations. *Proc. Natl. Acad. Sci. USA.* **95**, 12404-12409, 1998. PMID: 9770499. PMCID: PMC22844
  - b. Flores-Rozas, H., Clark, D.D. and Kolodner R.D. Proliferating cell nuclear antigen and MSH2p-MSH6p interact to form an active mismatch recognition complex. *Nature Genetics.* **26**, 375-378, 2000. PMID: 11062484
  - c. Banerjee, S., and Flores-Rozas, H. Cadmium inhibits mismatch repair by blocking the ATPase activity of the MSH2–MSH6 complex. *Nucleic Acids Res.* **33**, 1410-1419, 2005. PMID: 15746000. PMCID: PMC552968
  - d. Labazi, M., Jaafar, L., and Flores-Rozas, H. Modulation of the DNA binding activity of *S. cerevisiae* MSH2-MSH6 complex by the high-mobility-group protein NHP6A in vitro. *Nucleic Acids Res.* **37**:7581-7589, 2009. PMCID: PMC2794155
  
4. Our current interest is more translational. We have investigated the genes and pathways which provide protection to cells exposed to cytotoxic chemotherapeutic agents. We mainly focus on anthracyclines and cisplatin, which are well known DNA damaging agents. Our efforts are aimed at understanding the underlying mechanisms that allow cells to survive these drugs and are investigating critical pathways, such as the heat-shock response, metabolic intermediates such as aldehydes, etc. Targeting these pathways in cancer cells may provide more effective therapeutic alternatives.
  - a. Xia, L., Jaafar, L., Cashikar, A., and Flores-Rozas, H. Identification of Genes Required for the Protection from Doxorubicin by a Genome-Wide Screen in *Saccharomyces cerevisiae*. *Cancer Research* **67**, 11411-11418, 2007. PMID: 18056469. PMCID: PMC3635107
  - b. Miles D. Freeman, Tryphon Mazu, Jana S. Miles, Selinda Darling-Reed and Hernan Flores-Rozas. Inactivation of Chromatin Remodeling Factors Sensitizes Cells to Selective Cytotoxic Stress. *Biologics: Targets and Therapy.* 2014 **8**:269-280. PMID: 25484574
  - c. Jana S. Miles, Samantha J. Sojourner, Lahcen Jaafar, Aurellia Whitmore, Selina Darling-Reed and Hernan Flores-Rozas. The Role of Protein Chaperones in the Survival From Anthracycline-Induced Oxidative Stress in *Saccharomyces cerevisiae*. *Int. J. of Adv. Res.* 2018. **6** (3):144-152. PMID: 29657945
  - d. Samantha J. Sojourner, Willie M. Graham, Aurellia M. Whitmore, Jana S. Miles, Devon Freeny and Hernan Flores-Rozas. The Role of HSP40 Conserved Motifs in the Response to Cytotoxic Stress. *Journal of Nature and Science (JNSCI).* 2018. **4**(4):e500, 1-7. PMID: 29682607
  - e. Jana S. Miles, Samantha J. Sojourner, Aurellia M. Whitmore, Devon Freeny, Selina Darling-Reed and Hernan Flores-Rozas. Synergistic Effect of Endogenous and Exogenous Aldehydes on Doxorubicin Toxicity in Yeast. 2018. *BioMed Research International.* 2018:4938189. doi: 10.1155/2018/4938189. PMID: 30003101
  - f. Aurellia Whitmore, Devon Freeny, Samantha Sojourner, Jana Miles, Willie Graham, and Hernan A Flores-Rozas. Evaluation of the Role of Human DNAJAs in the Response to Cytotoxic Chemotherapeutic Agents in a Yeast Model System. *BioMed Research International.* 2020: 9097638. Doi: 10.1155/2020/9097638

**Complete List of Published Work in MyBibliography:**

<https://www.ncbi.nlm.nih.gov/myncbi/1fqhueoed0SQH/bibliography/public/>

Ongoing Research Support

1U54CA233396-01

Reams (MPI)

09/19/2018 – 08/31/2023

**Project Title:** 1/3 Florida-California Cancer Research, Education and Engagement (CaRE2) Health Equity Center.

The long term goals of the CaRE2 center are to reduce cancer disparities in Blacks and Latinos, to train and increase the pool of underrepresented Black and Latino scientists conducting health disparity research, to

increase research capacity at an ISUPS (FAMU), and to increase cancer disparity research at UF and USC-NCCC. The proposed two full projects and pilot project include investigators from the three institutions and will leverage on specimens collected across the partnership from Blacks and Latinos, representing a wide range of subpopulations within these minority groups. Thus, our studies will reveal unprecedented findings about these two understudied minority populations.

**Role: Leader of the Shared Resources Core**

**Completed Research Support**

2G12MD007582 Soliman (PI) 08/06/2013-03/31/2018 (No cost extension)

RCMI (NIH/NIMHD) - **Pharmaceutical Research Center – Molecular Genetics**

The goal of this project is to determine the involvement of DNAJAs in the protection of cells exposed to anthracyclines and cisplatinated compounds which are commonly used in cancer chemotherapy.

**Role: Faculty Development Investigator**

1 P20 MD006738-01 Soliman (PI) 06/16/12-01/31/18

NIH-NCMHD Exploratory COE (P20)

Title: *Center of Excellence for Cancer Research, Training and Community Service.*

The goal of this research is to elucidate metabolic pathways involved in ATP production in tumor cells exposed to hypoxia, identify molecular targets and screen natural therapeutic compounds to modify these targets in order to develop effective treatments for end stage aggressive cancers.

**Role: Flores-Rozas Co-Investigator**