Professional Advancement Virtual Engagement Series (PAVES)

NCI Center to Reduce Cancer Health Disparities

NIH NATIONAL CANCER INSTITUTE

November 29, 2023

ANNOUNCEMENTS

Apply by DECEMBER 1!

Early Investigator Advancement Program (EIAP)

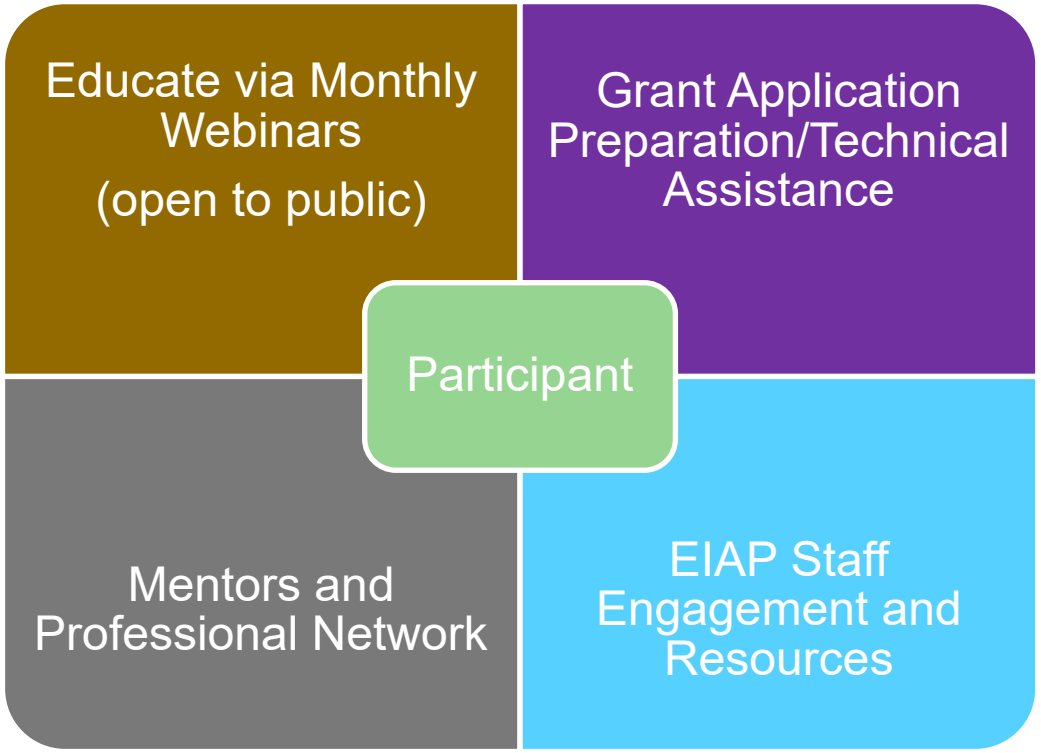
Early Investigator Advancement Program (EIAP) aims to promote the transition of early career investigators from diverse backgrounds to become established investigators

Contact

JoBeth McCarthy (C), MPH, CPH
jobeth.mccarthy-jean@nih.gov

Dr. Jay Revilleza
mariajamela.revilleza@nih.gov

MENTORED GRANTSMANSHIP PROGRAM COMPONENTS



- **1 cohort per year**
- **20-25 participants per cohort**
- **FY2024 cohort application period: due November 1, 2023**

Outcomes for Each Participant

- **Complete and submit an R01 grant proposal by October 5, 2024**
- Become part of a group of peers with similar career goals
- Engage with mentors who are established investigators
- Become familiar with job and funding opportunities
- Develop professional and management skills critical to growing a research group

Intramural Continuing Umbrella of Research Experiences Program

- Supports mentored research experiences (**2-3 years depending on training level**) for students and scientists from diverse backgrounds on **NCI campuses** in Bethesda, Rockville and Frederick, Maryland
- Centralized review and program-facilitated matches for scholars to NCI PIs; **applicants do not need to pre-identify a PI to apply**
- **NCI values diversity** and particularly encourages applications from individuals from diverse backgrounds, including those from groups underrepresented in the cancer research workforce, for example those from groups noted in the Notice of NIH's Interest Diversity (NOT-OD-20-031).

We are now accepting applications for research experiences beginning Fall 2024. Check out the website for all the details including the slides and recording from the pre-application webinar.

Contact
Dr. Gregory Adams, Jr.
Dr. Jessica Calzola
iCURE@nih.gov

Supplements Within the CURE:
Diversity and Re-Entry and Re-Integration (PA-21-071)

- Provide additional funding to currently active NIH grants to support research experiences of trainees → **bridge** toward next career level
- Parent grant must have **at least 2 years** of active status left at the time of supplement application
- NCI does not accept P30 as parent grants for these supplements
- R01 or equivalent – 2 supplements at the same time; R21 or equivalent – 1 supplement at a time to support grad student or more junior

Receipt Cycle	Application Receipt Date
1	Oct 1- Dec 1
2	Feb 1- Mar 31

Contact
Dr. Belem López
Dr. Jason Liu
Fulera Salami, MPH
Dr. Chantel Fuqua
CUREsupplements@nih.gov

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Center to Reduce Cancer Health Disparities

Administrative Supplements to Support Cancer Disparity Collaborative Research

The purpose of the Collaborative is to promote cancer disparities research among NCI-funded non-disparity researchers and encourage collaboration with cancer disparities-focused researchers.

Contact

Dr. Jay Revilleza

mariajamela.revilleza@nih.gov

Due Date: January 23, 2024

LEARN MORE: https://www.cancer.gov/about-nci/organization/crchd

Best Practices for Success after Receiving Your R01

Harold Saavedra, Ph.D.
Professor, Department of Basic Sciences
Pharmacology Department
Ponce Health Sciences University
Collaborating Member, Cancer Biology & Evolution Program, Moffitt Cancer Center
Administration Core, Ponce Health Sciences University-Moffit Cancer Center U54
Co-leader, Planning and Evaluation Core, Ponce Health Sciences University-Moffit Cancer Center U54
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Talk to the PAVES Program of the NCI on November 29, 2023

Learning Objective

LO1: Learn best practices for managing the R01 post-award

LO2: Identify strategies for ensuring compliance

LO3: Understand how to sustain your research agenda

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L01: Learn Best Practices for Managing the R01 post-award

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E2F3: a suppressor of centrosome amplification

Grant #: 7K01CA104079-05

Emory University School of Medicine

Start Date: 05.01.2004 **– End Date:** 04.30.2010

Institutional Training and Education Study Section (F)[NCI-F]

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Administration

- Administrators at Emory (Department-Centered):
- Ms. Diane Cassels-Rad Onc Chief Department Administrator
- Ms. Sheryl Bowie –Pre-Award Specialist
- Ms. Lashundra Kirkland-Pre-Award Specialist
- Patrice Moua-HR
- Central Grant Administration

Nek2 and NPM in Centrosome Amplification

Grant #: 1R01CA151521-01

Emory University School of Medicine

Start Date: 07.01.2010 **– End Date:** 04.30.2016 (NCE)

Molecular Oncogenesis Study Section

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- Specific aim 1: To distinguish between a classical and an alternative pathway to centrosome amplification.

Specific aim 2: To assess how the alternative pathway impinges on centrosome amplification.

Specific aim 3: To address how interfering with the classical pathway in vivo prevents centrosome amplification in pre-malignancy and suppresses mammary tumorigenesis.

Lab Members

- Arsene Adon, Ph.D., 2005-2010. Current Position: Assistant Professor, Institute Pasteur, Ivory Coast.
- Xiangbin Zeng, M.D., Ph.D., 2006-2011. Current position: Biologist, Product Assurance and Characterization Testing, Center for Cellular Engineering, National Institutes of Health.
- Mi-Young Lee, Ph.D., Post-doctoral Fellow, Emory University, 2011-2015. Current Position: Instructor of Pediatrics, Aflac Cancer & Blood Disorders Center, Emory University School of Medicine
- Mihaela Marina, Ph.D., Post-doctoral Fellow, Emory University, 2011-2015. Current Position: Associate Scientific Director at Ashfield MedComms
- Mary K. Harrison, Ph.D., Graduate Program of Genetics and Molecular Biology, 2008-2013. Current position: Senior Medical Science Liaison at Seattle Genetics.
- Jamie King, Ph.D. Student, Graduate Program of Cancer Biology, 2013-2015. Because I joined the faculty at PHSU as an associate professor she then transferred to Dr. Jin-Tang Dong's laboratory at Emory University, where she completed her Ph.D. in 2018. However, I remained a committee member until her graduation. Current position: Senior Medical Writer at CiTRUS Health Group

Lab Members (RadOnc Residents)

1. Sandra Zaky, M.D., M.S., 2009-2010. Current Position: Clinical Associate Professor of Radiation Oncology and Radiation Therapy, Stanford University Hospital and Clinics, California
2. Shannon Kahn, M.D., 2009-2010. Current position: Associate Professor, Department of Radiation Oncology Emory University School of Medicine, Medical Director of Radiation Oncology Emory Saint Joseph's Hospital
3. Svetlana Kats, M.D., M.PH. 2010-2011. Current position: Radiation Oncologist, Carteret Health Care Medical Center and Carolina East Medical Center, North Carolina

Management

- Meeting with the postdocs individually.
- Lab meeting every Friday.
- A larger group means that a lot of time is dedicated to managing data and conflicts between lab members.
  - Performance Management (most were outstanding performers).
  - An Excel sheet and e-mail were maintained for poor performers. HR was regularly informed of this record of poor performance. If there was no improvement, the legal department was involved, and a decision on the employment status of the individual was made.

Output-R01 (12 Publications)

Journal (Link to PubMed abstract)	Authors	Publication Year	Similar Publications	CitedBy	ICite RCR
The Nek2 centrosome-mitotic kinase contributes to the mesenchymal state, cell invasion, and migration of triple-negative breast cancer cells.					
Scientific reports2021 04 27; 11 (1) 9016	Rivera-Rivera, Yainyrette; Marina, Mihaela; Jusino, Shirley; Lee, Miyoung; Velázquez, Jaleisha View All ón-Colón, Camille;	2021			2.03
TTK promotes mesenchymal signaling via multiple mechanisms in triple negative breast cancer.					
Oncogenesis2018 Sep 12; 7 (9) 69	King, Jamie L; Zhang, Baotong; Li, Yixiang; Li, Kathy P; Ni, Jianping J; Saavedra, Harold I; Dong, Jin-Tang	2018			2.35
Silencing of E2F3 suppresses tumor growth of Her2+ breast cancer cells by restricting mitosis.					
Oncotarget2015 Nov 10; 6 (35) 37316-34	Lee, Miyoung; Oprea-Ilies, Gabriela; Saavedra, Harold I	2015			0.97
Nek2 and Plk4: prognostic markers, drivers of breast tumorigenesis and drug resistance.					
Frontiers in bioscience (Landmark edition)2014 Jan 01; 19 352-65	Marina, Mihaela; Saavedra, Harold I	2014			2.59
E2F activators signal and maintain centrosome amplification in breast cancer cells.					
Molecular and cellular biology2014 Jul; 34 (14) 2581-99	Lee, Mi-Young; Moreno, Carlos S; Saavedra, Harold I	2014			1.26
Differential expression of centrosome regulators in Her2+ breast cancer cells versus non-tumorigenic MCF10A cells.					
Cell division2014; 9 3	Lee, Mi-Young; Marina, Mihaela; King, Jamie L; Saavedra, Harold I	2014			0.37
Poldip2 knockout results in perinatal lethality, reduced cellular growth and increased autophagy of mouse embryonic fibroblasts.					
PloS one2014; 9 (5) e96657	Brown, David I; Lassègue, Bernard; Lee, Minyoung; Zafari, Rostam; Long, James S; Saavedra, Harold I; Griendling, Kathy K	2014			1.08
Cdk4 and nek2 signal binucleation and centrosome amplification in a her2+ breast cancer model.					
PloS one2013; 8 (6) e65971	Harrison Pitner, Mary Kathryn; Saavedra, Harold I	2013			0.77
Silencing CDK4 radiosensitizes breast cancer cells by promoting apoptosis.					
Cell division2013 Jul 25; 8 (1) 10	Hagen, Katie R; Zeng, Xiangbin; Lee, Mi-Young; Tucker Kahn, Shannon; Harrison Pitner, Mary View All , Sandra S; Liu,	2013			0.90
The G1 phase Cdks regulate the centrosome cycle and mediate oncogene-dependent centrosome amplification.					
Cell division2011 Jan 27; 6 2	Harrison, Mary K; Adon, Arsene M; Saavedra, Harold I	2011			0.51
Cdk2 and Cdk4 regulate the centrosome cycle and are critical mediators of centrosome amplification in p53-null cells.					
Molecular and cellular biology2010 Feb; 30 (3) 694-710	Adon, Arsene M; Zeng, Xiangbin; Harrison, Mary K; Sannem, Stacy; Kiyokawa, Hiroaki; Kaldis, Philipp; Saavedra, Harold I	2010			1.50
The Ras oncogene signals centrosome amplification in mammary epithelial cells through cyclin D1/Cdk4 and Nek2.					
Oncogene2010 Sep 09; 29 (36) 5103-12	Zeng, X; Shaikh, F Y; Harrison, M K; Adon, A M; Trimboli, A J; Carroll, K A; Sharma, N; Timmers, C; Chodosh, L A; Leone, G; Saavedra, H I	2010			1.35

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Targeting Centrosome-Mitotic Kinases as a Novel Therapeutic Approach Against Breast Cancer in Hispanic/Latinas

Grant #: R01CA266046

Start Date: 09.15.2022 – **End Date:** 08.31.2027

Harold Saavedra, Ph.D.
Professor, Department of Basic Sciences
Pharmacology Department
Ponce Health Sciences University
Collaborating Member, Cancer Biology & Evolution Program, Moffitt Cancer Center
Administration Core, Ponce Health Sciences University-Moffit Cancer Center U54
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SPECIFIC AIMS

- **Aim 1:** Investigating signaling pathways linking mitotic kinases to early metastasis and poor prognosis of non-Hispanic black (NHB), Caribbean Hispanic/Latino (C-H/L), and Hispanic/Latino (H/L) women with breast cancer.

- **Aim 2:** To address how co-inactivation of mitotic kinases suppresses the mesenchymal state, metastasis, and restores Palbociclib responses in TNBC cells.

Collaborators

Dr. Doug Cress, Co-PI, and Co-Director of the PACHE U54 Puerto Rico Biobank (Moffitt Cancer Center)

Julie Dutil, Ph.D., Co-Investigator (PHSU and Puerto Rico Cancer Center)- Ancestral Genetics

Steven Eschrich, Ph.D.(Moffitt Cancer Center) - Bioinformatics and Ancestral Genetics

Qianxing Mo, Ph.D. – Bioinformatics and Biostatistics

Marilin Rosa, M.D. (Pathologist)

Roberto Díaz, M.D., Ph.D. (Radiation Oncologist)

Zuleika Díaz, M.D., Breast Cancer Surgeon (PHSU)

Idhaliz Flores, Ph.D., Director of the PACHE U54 Puerto Rico Biobank (PHSU)

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What happens immediately after receiving the NOA

- If a multiple PI grant the institution of the contact PI commences budget negotiations with the collaborating institution through a subaward.

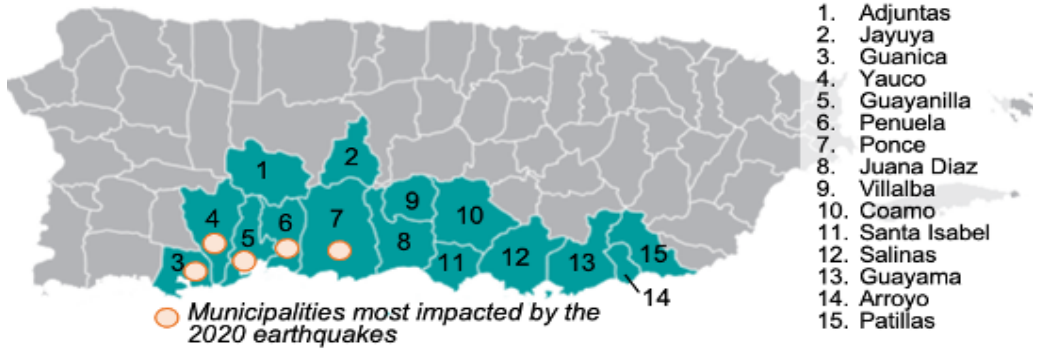
- The Offices of Research Development (ORDs) from Moffitt Cancer Center and of PHSU discuss the details (e.g. negotiated indirect costs per institution).

Hiring for a new grant

- Once the budget is approved by ORD and the President of the Institute (Dr. Kenira Thompson), position request for every level (Principal investigators, co-Investigators, Research Associate) are placed through Human Resources.
- While PIs and co-PIs were previously selected, postdoc fellows, students and research associates are not.
- Human resources announces the position trough The University website. Several candidates are interviewed, and one with the appropriate level of experienced is hired.

The greater Ponce area.

The greater Ponce area is a rural area with a medium household income of ~18K; great for studying disparities because it has the highest cancer rate in Puerto Rico.



1. Adjuntas
2. Jayuya
3. Guanica
4. Yauco
5. Guayanilla
6. Penuela
7. Ponce
8. Juana Diaz
9. Villalba
10. Coamo
11. Santa Isabel
12. Salinas
13. Guayama
14. Arroyo
15. Patillas

Catchment area Characteristics

- 15 municipalities
- 474,243 residents
- 14.4% of PR population

Population Characteristics

- >98.8 % Hispanic
- 52.0 % below poverty level
- 19.9 % Elderly (Ages 65+)

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Difficulties of hiring postdoctoral fellows in a minority-serving institution.

- We were unsuccessful in getting postdocs to apply for the position through USA websites.
- The founder of Ciencia En Tus Manos, Dr. Marcos Ramos, an association of minority students, put me in contact with one minority candidate who wrote a postdoctoral supplement, but decided to go to Moffitt.
- My strategy was to approach Ph.D. students from Puerto Rico (UPR Río Piedras and PHSU) that were in their last year of their Ph.D.
- I got two applicants interested and hired Dr. Alexandra Aquino (PHSU).

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Advantages of Having a Ph.D. Training Program in your Institution

- Dr. Caroline Appleyard is the PI of 5T32GM144896-02 (G-RISE).
- This and the Biomedical Sciences Program accepts between 2 and 6 students per year. Students usually come from smaller UPR campuses in South and Western Puerto Rico.
- Since there are 2-3 cancer research labs with enough funding to accept the students, this allows us to have excellent Ph.D. students in the labs.
- This program is the major source of postdoc fellows in PHSU.

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Additional obstacles

- The co-PI of the grant retired, so a new co-MPI had to be identified.
- The whole process of getting the new co-MPI (Dr. W. Doug Cress) took a few months.
- The PO (Dr. Grace Ault) and the Grants Manager (Ms. Jennifer Meininger) had to be contacted by the ORD in PHSU to start the change of PI process.
- A new NOA is received and the sister institution, Moffitt Cancer Center had to approve the modified subaward.

LO2: Identify strategies for ensuring compliance

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Compliance

- The Office of Research Development (ORD) manages my grant proposal pre- and post-award.
- The Program announcement of the grant has all the restrictions and salary caps.
- The Office of Research Development ORD director (e.g. Claris Vega at PHSU) receives the NOA.
- PHSU has policies of what items can be paid for in addition to the policies of the NCI.
- Compliance also involves maintaining IRB and IACUC certificates and protocols active during the granting period.

What happens immediately after receiving the NOA

- After receiving the NOA the ORD director of your institution contacts you.
- Preparation of the modified budget after a 17% budget cut.
- The President of the University, as well as the budget and accounting office must sign off on any item ordered in the R01.

Compliance

- The NIH grant manager and the PO of the grant must be kept informed of changes to the grant proposal, including applications for administrative supplements for students and postdocs.
- At the end of the fiscal year (mine are in July) we must submit a progress report to the NIH, where I must indicate if the specific aims have been modified and why.

LO3: Sustaining your research agenda

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Strategies for Getting the R01

- Get as many pilot projects and state funding as you can to generate preliminary data.

  2016 Puerto Rico Clinical and Translational Research Consortium pilot grant (2U54MD007587)

  2017 Puerto Rico Science Trust and Technology Small Grant

  2018 Research Centers in Minority Institutions (5U54MD007579-37) pilot grant

  2019-2022 Advanced Project, Puerto Rico Science Trust

The Partnerships to Advance Health Care Disparities (PACHE) Program (5U54CA163071-11 and 5U54CA165068-11)

- This partnership from Moffitt Cancer Center in Tampa, Florida and Ponce Health Science University (Southern Puerto Rico) allowed me a Full Project (**Understanding how mitotic kinases drive EMT in breast cancers)**
- Moffitt co-I was Dr. Srikumar Chellappan, an expert on cell cycle regulation and metastasis in cancer.
- This allowed the generation of substantial preliminary data for the R01.

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Be persistent!!!

- I tried to get this R01 since 2016 with one resubmission per year.
- Another R01, dealing with how the E2F transcription factors drive metastasis, never scored.

Previous Lab Members (PHSU)

- Yainyrette Rivera, Ph.D. Postdoctoral Research Associate 2015-2020. Current Position: Pharma industry, Barcelona, Spain.

- Shirley Jusino, Ph.D. 2016-2021. Current Position: Second-year MD student at PHSU.

Lab Members

- Alexandra Aquino, Ph.D. (postdoc)
- Melanie Cruz, BSc (research assistant)
- Joel Orengo, MSc (Ph.D. student)
- Gretchen Albarrán, (Ph.D. student)
- Stephanie Colón, MD student

Managing the lab team

- The lab has a Microsoft Teams (MS Teams) page and a common e-mail address (Saavedra lab) where new data, fellowships, and papers that are must-reads are placed.
- A postdoc of the lab (Dr. Aquino) and the lab manager (Ms. Cruz) have a schedule within MS Teams of daily experiments and common lab tasks.
- Meet the lab manager every day to address lab issues (how trainees are working, broken freezers, etc.).

Managing the lab team

- I have a set daily meeting with the Ph.D. students (on Thursdays), or as needed.
- The postdoc fellow meets me on a need basis.
- I ask every other day every member of the lab about data progress.
- Everyone in the lab presents their original data in lab meeting (Fridays at 3 PM).

Managing the MPIs and PIs

- The R01 team from MCC and PHSU has a monthly Zoom meeting with an agenda.
- Discuss issues regarding rigor and reproducibility, where original data is shown to the whole group, generally by the postdoc fellow, or the PI.

Managing the MPIs and PIs

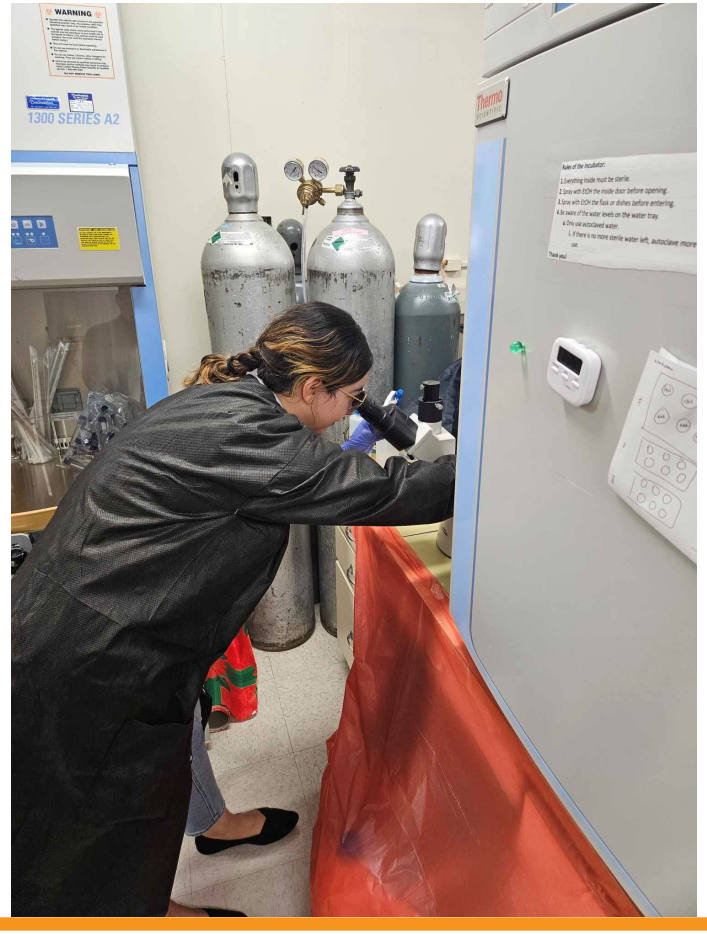
- Usually given 2 days in advance through e-mail.
- The typical agenda is:
  - Discussion of Aim 1.1 findings regarding bioinformatic analyses of breast cancer patient gene expression and ancestry data from the Oncology Research Information Exchange Network (Drs. J. Dutil and Eschrich).
  - The biostatistician, Dr. Qianxing Mo, is always present to discuss potential statistical approaches.
  - Discussion of Aim 1.2., specifically MCC and PHSU cohort of breast cancer patients for which RNA seq and DNA seq and a breast tissue microarray have been done.

Meeting agenda

Aim 2. Discussed by Dr. Saavedra's lab

- All raw data is presented to the group.
  - This allows for compliance with rigor and reproducibility. All experiments are quantified and presented to the group.
  - If an experiment does not work (for example, insufficient knockdown of a gene, or appearance of bands outside the right molecular range), it is also presented, so the team suggests alternative approaches.
  - Presenting raw data also helps in the presentation of figures for journals.

Alexandra Aquino is the current postdoc in the lab.



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Stress Hormones are Associated with Inflammatory Cytokines and Attenuation of T-cell Function in the Ascites from High-Grade Serous Ovarian Cancer

Alexandra N. Aquino-Acevedo
5th-year PhD Candidate
Thesis Dissertation Defense
Armaiz Lab
March 30, 2023

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Know the students because they may become your postdocs

- I was Alexandra's RISE graduate advisor
- Was in her dissertation committee
- We both knew our research programs, and our strengths and limitations.

Career Development Plan for Postdoc Fellows

- Be flexible and let them develop their career.
  - In a minority-serving institutions they can do some limited proctoring (Biochemistry and Pharmacology).
- Currently writing a postdoctoral supplement to the R01 (development of writing skills)
- Presentation in national meetings (AACR, AACR Diversity Meetings).
- In our institute some postdoc fellows have transitioned to Assistant Professors.

RESEARCH PLAN		REQUESTED FUNDING PERIOD YEAR 1	YEAR 2	YEAR 3
Activity	**Milestone**			
Sub Aim 1.1	Identification of pathways synergistically regulated by TTK and Nek2 that results in mesenchymal phenotype			
Sub Aim 1.2	Identification of downstream signaling effector phosphorylated proteins regulated by TTK and Nek2			
Publications	1st First author manuscript preparation and submission on Sub Aim 1.1			
	2nd First author manuscript preparation and submission on Sub Aim 1.2			
	Review paper			
CAREER DEVELOPMENT PLAN		**YEAR 1**	**YEAR 2**	**YEAR 3**
Meetings and Conference	AACR Annual Meeting AACR in Health Disparities Puerto Rico Cancer Meeting Florida and PR Oncology Meeting PHSU-PRI Scientific Conference			
Grant Writing and Submission	K01, American Cancer Society transition grants			
			FRECUENCY	
Teaching Experience	Class Group Discussions	Four sessions per semester		
	Biochemistry and Molecular Genetics	Ten sessions per year		
	Advanced Topics in Biomedical Sciences	Once per year		
	Cellular and Molecular Basis of Cancer	Every two years		

Plans for New R01s

- A possibility is one to explore how increasing/suppressing chromosome instability by suppressing the activity of mitotic kinases modulate the immune system and inflammation in breast cancers –Dr. Guillermo Armaiz, Alexandra Aquino's Ph.D. advisor.
- Be prolific in publishing to be able to renew the existing R01.

Questions?