

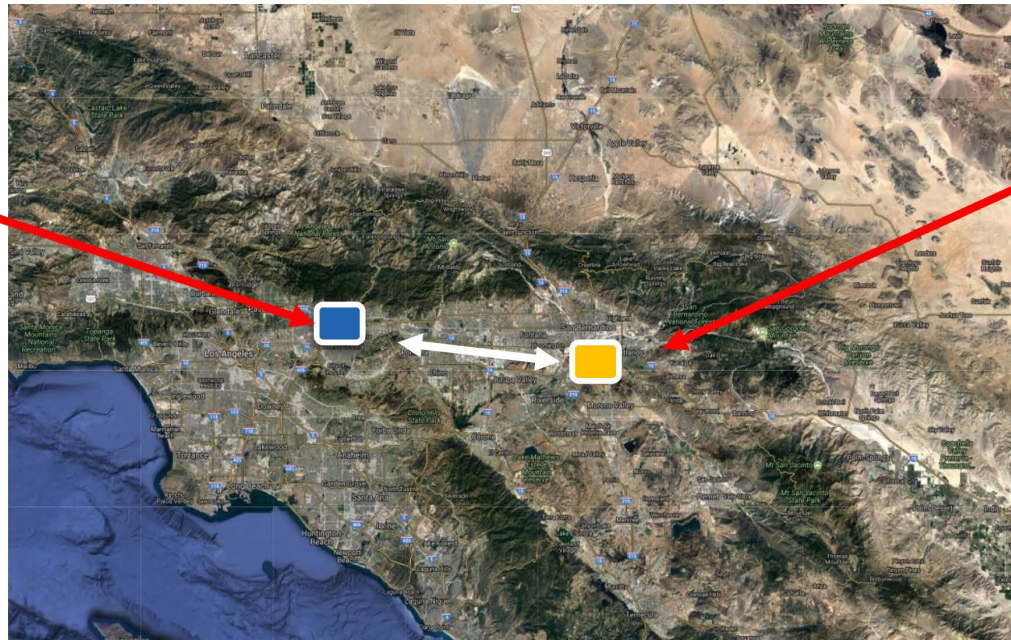
University of California at Riverside - City of Hope Comprehensive Cancer Center P20 Partnership in Drug Discovery and Translation

Ernest Martinez, PhD – University of California at Riverside

Victoria Seewaldt, MD – City of Hope



- 26-year free standing CCC
- 143 investigators
- Focus on drug development translation, clinical research



- Newest UC Med School
- No. 1 in U.S. social mobility. (US News 2020)
- No. 3 in Hispanic STEM graduates. (NSF)
- No. 12 overall in the U.S. (Money Mag 2019)
- Strong Engineering, Bio/Life Sciences
- >25,000 students
- U54 (SOM; IE environment/health disparities)

- 39 miles
- 35 minutes (fastest)
- 3 hours (maximum traffic)

**Thank you to NCI and CRCHD
P20CA24619**

Catchment – UCR-CoHCC

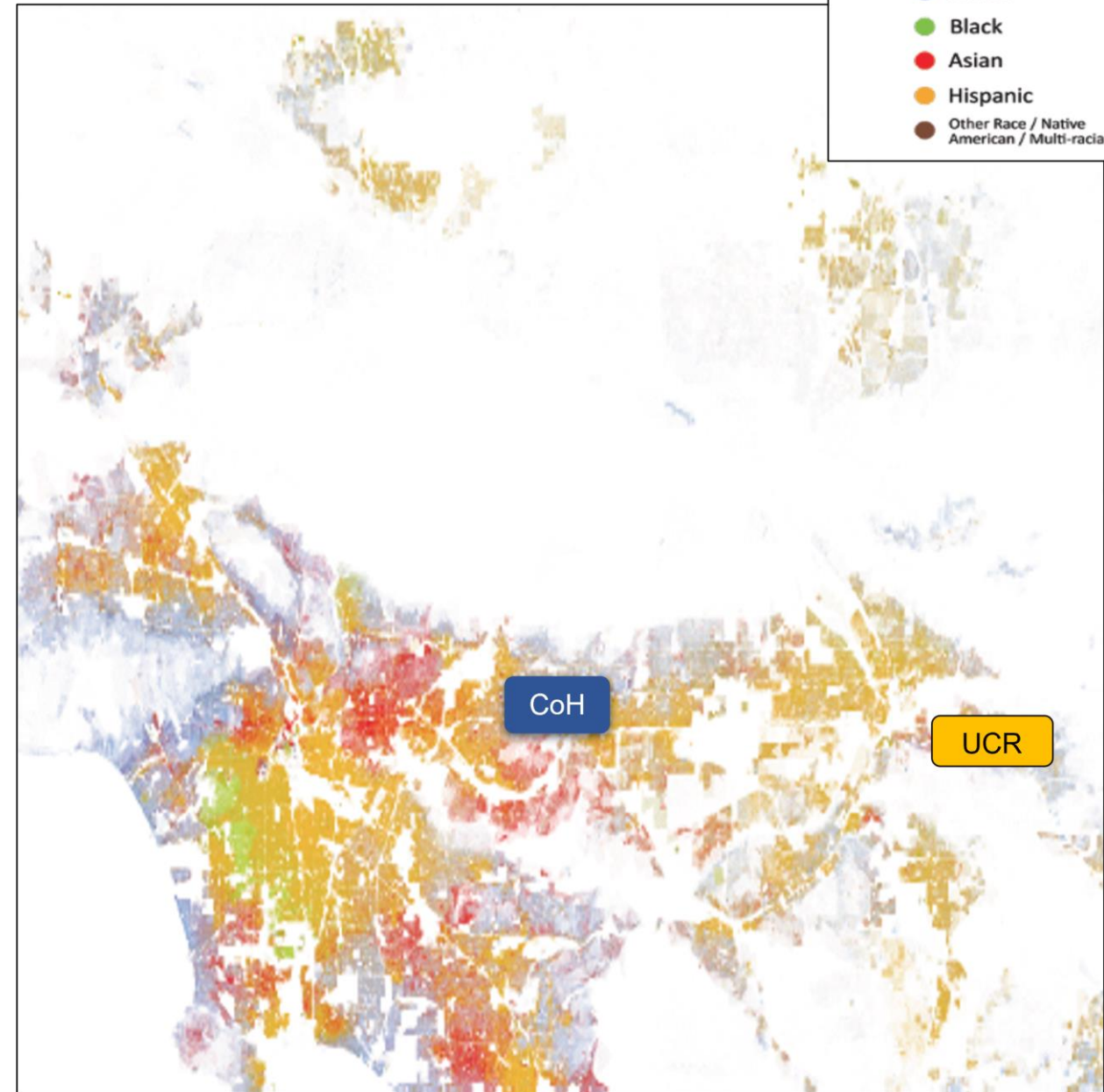
Densely Populated:

- 17.1 million individuals
- Greater than population of
- individual 46 states
- Urban and Rural

Race:	58%	White
	22%	Other (multi-race, Middle East, N. Africa)
	13%	Asian/Pacific Islander (Chinese, Korean, Japanese, Vietnamese)
	7%	Black/AA (West Africa, Afro-Caribbean, East African)
	2%	Native American

Ethnicity: 46% Latino/Hispanic
(Mexico, El Salvador, Guatemala)

Other: 33% Catchment population foreign born
51% Speak language home not English



Aims of UCR-CoH Partnership

Aim 1: Strengthen UCR's cancer research capacity and develop the resources to increase UCR/CoH's ability to jointly develop therapeutic agents optimized for Latino/Hispanic- and African-Americans.

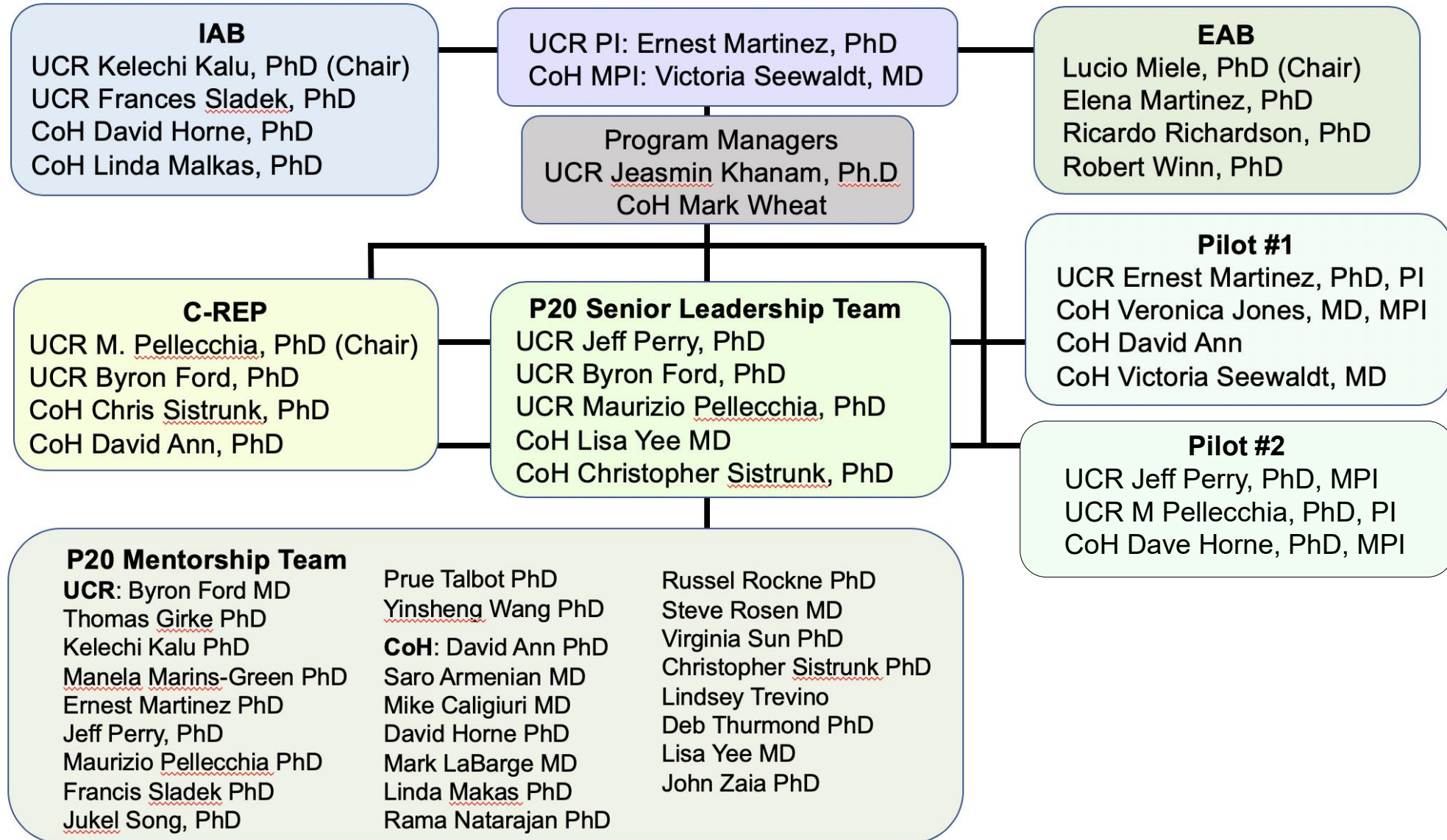
Aim 2: Increase the capacity of UCR and CoH-CCC to jointly develop drugs that target disparities in survival affecting individuals of color in our SoCal community.

Aim 3: Provide the training, opportunity, and mentorship to ensure that the next generation of therapeutic scientists and clinicians that reflect the diversity of our SoCal community.

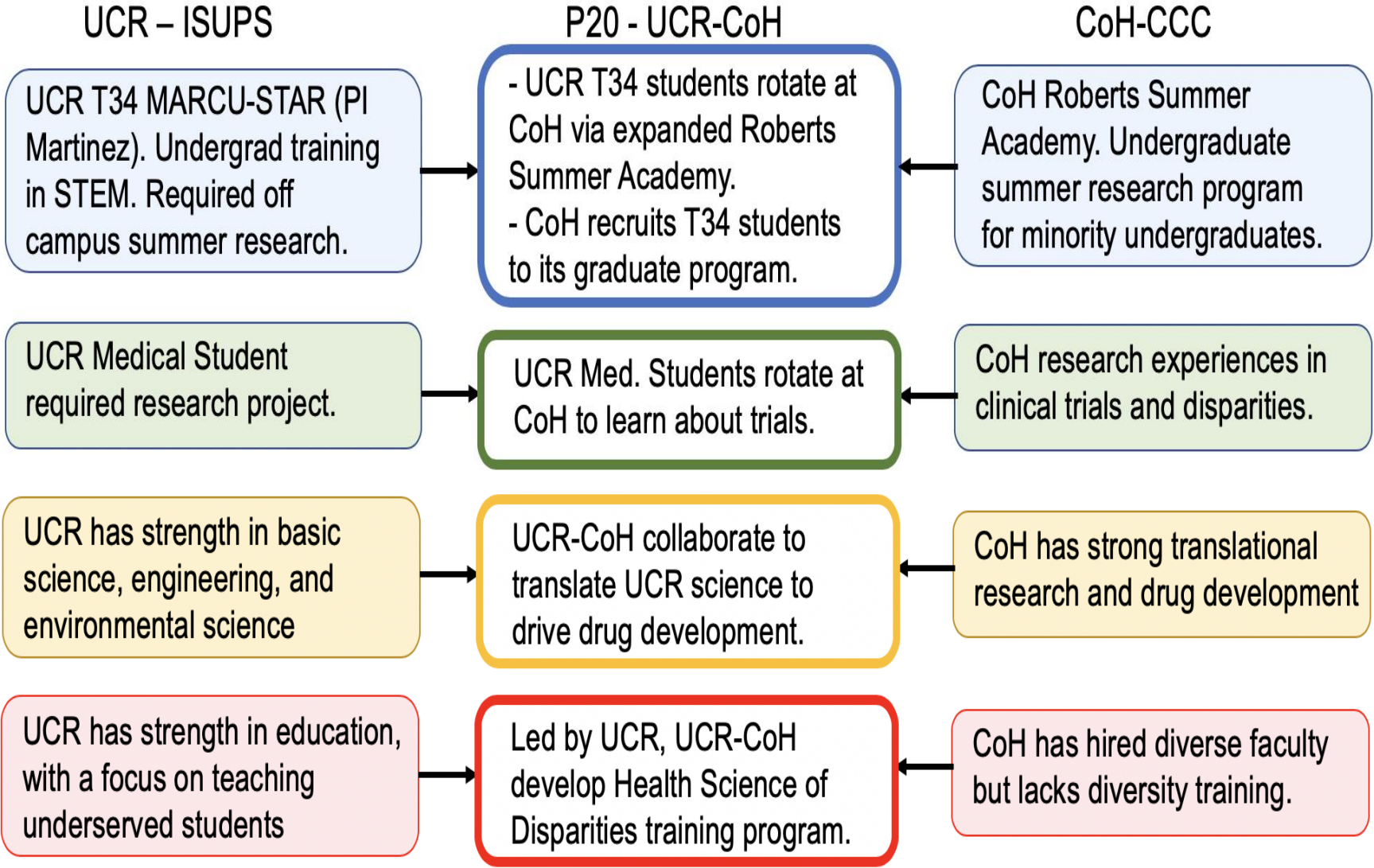
community → education → research → translation → training → clinical trials → community



Research Team - UCR-CoH Partnership



Mutual Benefit - Synergy between UCR and CoH



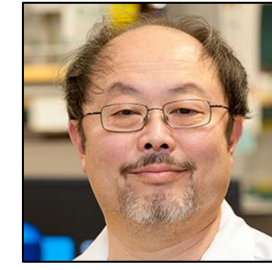
Pilot 1: Improving Survival in Latinas and AA women with Luminal B BrCA



Ernest Martinez, Ph.D.
UCR – Professor of Biochemistry;
Director MARC U-STAR Program



Veronica Jones, M.D.
CoH – Assistant Professor
Department of Surgery



David Ann PhD
CoH – Professor
Diabetes Metabolism



Victoria Seewaldt MD
CoH – Professor & Chair PopSci
AD CoH CCSG PopSci

Aim 1: Chromatin acetylation and/or acetylation of MYC predict poor prognosis in SoCal Latinas with luminal B breast cancer?

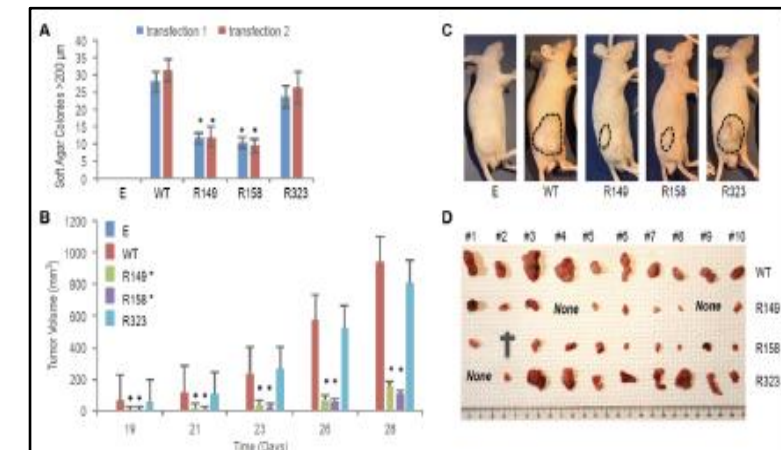
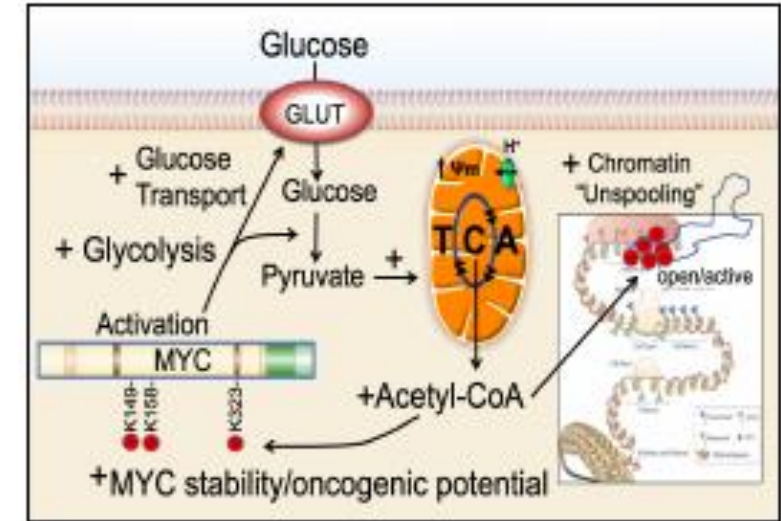
1.1 Retrospective study of Latinas vs. Non-Hispanic women with luminal B breast cancer.

1.2 Prospective study of fresh tissue from Latina/Hispanic women with luminal B breast cancer.

Aim 2: Targeting acetylation/metabolic signaling in MYC+ luminal B breast cancers from LA Latina women.

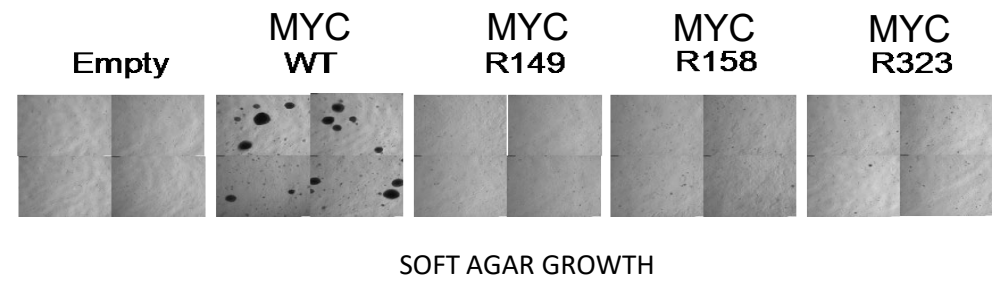
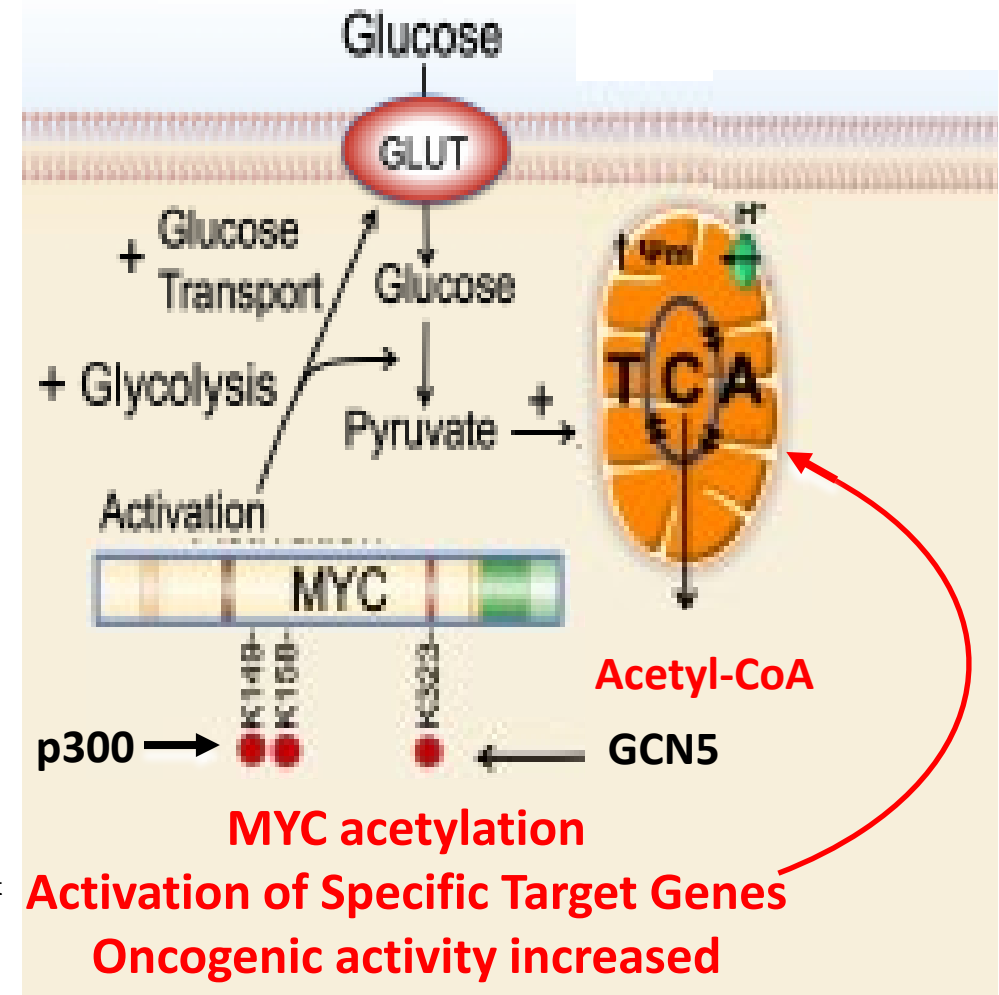
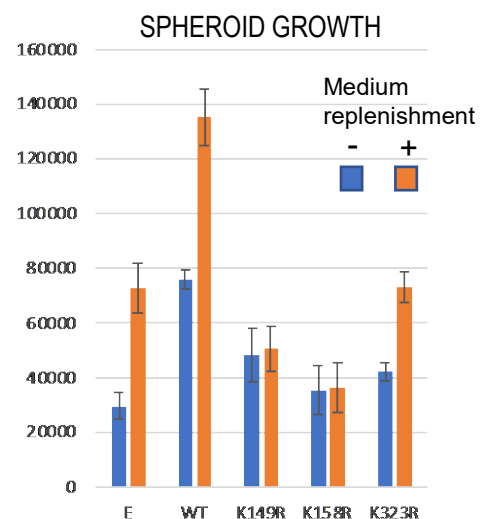
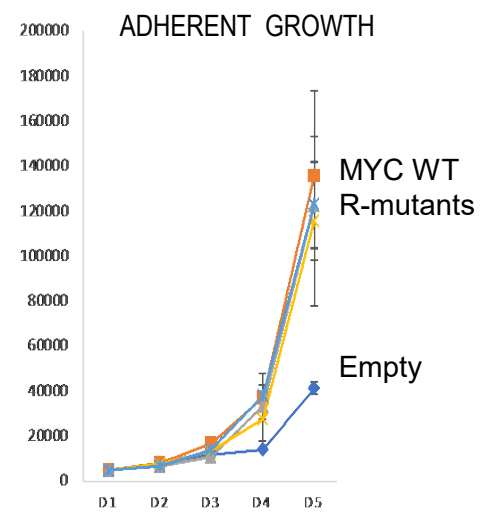
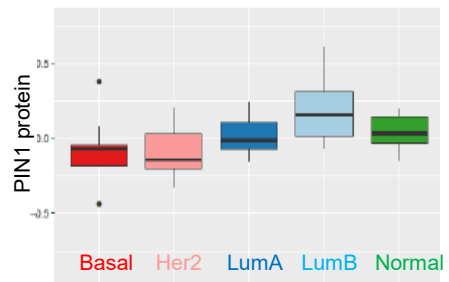
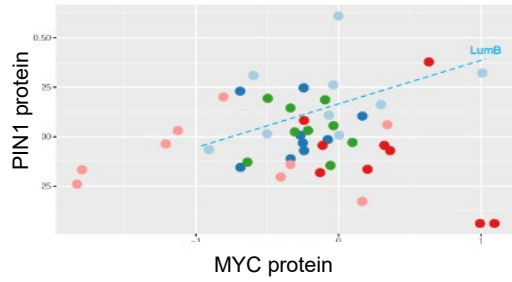
2.1 Retrospective and Prospective analysis of signaling pathways

2.2 Pilot: Leverage CoH-CCC – Jackson Labs partnership to develop PDX models of Latina chemo-resistant luminal B breast cancer.



MYC acetylation enhances malignant mammary cell transformation

- MYC is acetylated in aggressive TN Breast cancer cells (MDA-MB-231)
- MYC acetyl-lysine (AcK) residues stimulate MYC oncogenic activity and malignant transformation of mammary epithelial cells (MCF10A).
- MYC AcK residues regulate only select target genes.
- MYC AcK-dependent genes include metabolic enzymes that regulate Acetyl-CoA production and oxidative phosphorylation.
- MYC cofactor PIN1 correlates with MYC in Luminal B breast cancer

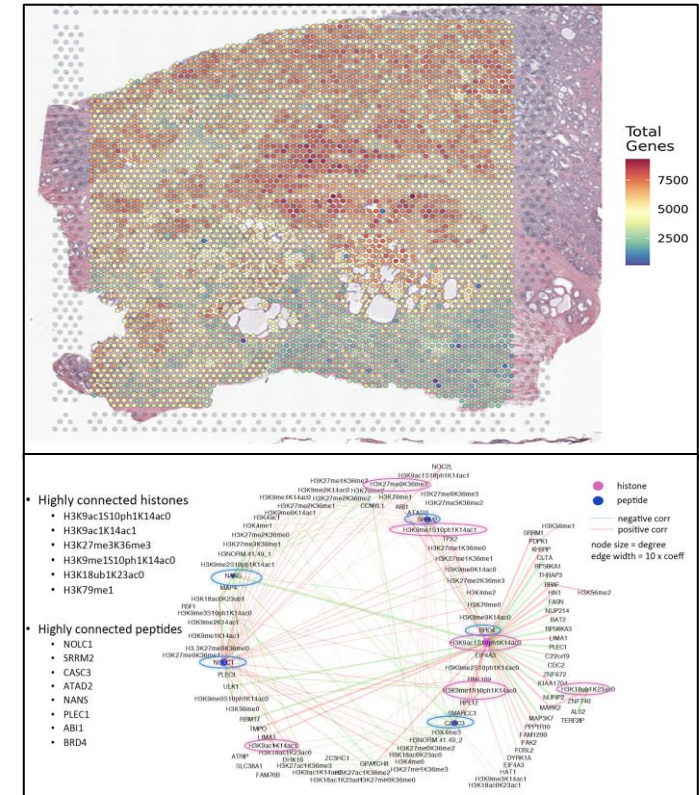
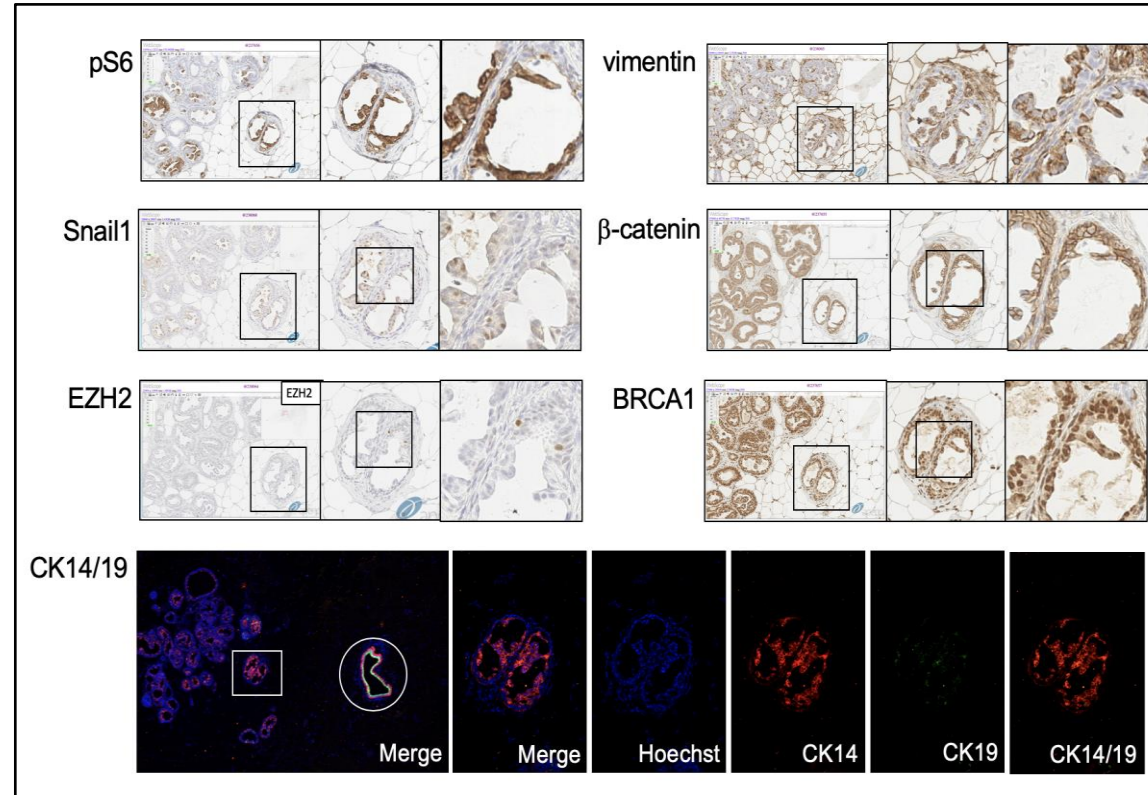
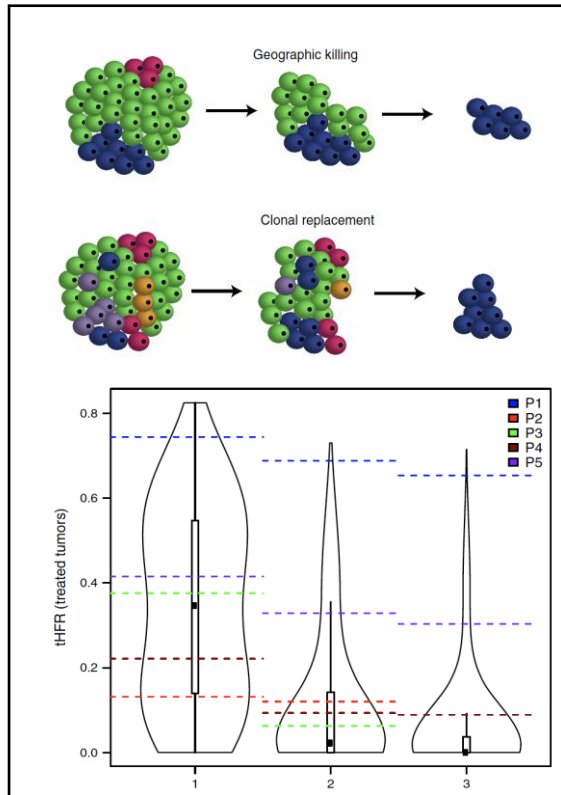


Retrospective cased matched recurrence vs. no-recurrence Prospective analysis of chemotherapy resistance

Veronica Jones MD – MPI Pilot 1



- Luminal B: Retrospective (Jones) 194 matched – 5 yr. recurrence vs. no recurrence
 - Pathway analysis, IHC validation – EMT and Cell Cycle pathways – recurrence
- Luminal B: Prospective (Jones) neoadjuvant chemotherapy – 51 women
 - Single Cell and Spatial Transcriptomics – is resistance present at diagnosis vs. acquired?



Pilot 2: Targeting the PIN1/Notch axis in breast and lung cancer for therapeutic development



Jeff Perry, Ph.D.
UCR – Assistant Professor of
Biochemistry;



Maurizio Pellecchia PhD
UCR – Professor of
Biomedical Sciences



David Horne PhD
CoH – Professor
Director CoH Therapeutics Program

Aim 1: Identify novel, fragment-based inhibitors of Pin1 to target the Notch1 and/or MYC pathway

Aim 2: Identify novel peptide-based inhibitors of Pin1 to target the Notch1 and/or MYC pathway

Pin1 has an active site pocket region that has ‘druggable’ characteristics, indicating that covalent fragment-based or covalent peptide-based compounds could inhibit its cancer-essential catalytic activities. We will develop such inhibitors through three sub-aims that form an iterative research cycle:

- a) Rapid screening assays, to identify peptide and fragment-based binders.
- b) Biophysical analyses, including structural approaches and methods to measure Kds and IC50s.
- c) In vitro and in cellulo analyses, to generate and confirm biologically relevant Ki measurements.

Accomplishment – Mentorship – Year 2

Courses

Introduction Translational Drug Development

UCR BMSC 252 (Byron Ford)

UCR BMSC 254 (Byron Ford) Faculty, PDF, Med/grad students, and UCR T34-MARC.

Science of Health Disparities

CoH BIOSCI 675 (Rick Kittles)

Programs for Mentorship:

- **Roberts Academy:** CoH Undergraduate student summer research experience
- **T34-MARCU:** UCR URM undergraduate student training in Basic/Translational Research.
- **Eat Move Live:** Community Clinic translation to basic science.
- **Grant Writing Workshop** at CoH

UCR-CoH Synergistic Training and Career Development

UCR T34 students/Summer Roberts entered CoH Graduate School of Biological Sciences PhD program

- Fall 2019: Hector Ruvalcaba (Latino)
- Fall 2020: Jonathan Calero (Latino)
- Fall 2021: Cathrine Elix (Latina)

Accomplishment – Mentorship – Year 2

Level	Mentee	Race/Ethnicity	Mentor	Institution/Program (grant application)	
Undergraduates	Ryan Gates	Hispanic	Martinez	UCR/T34	
	Emily Villalpando	Hispanic	Martinez	UCR/T34	
	Abel Vargas	Hispanic	Borkovich/Seewaldt	UCR/T34-CoH/Roberts	
	Paul Stolarov	NH-White	Perry	UCR	
	Kai Littlejohn	Black	Sistrunk/Seewaldt	CoH – now grad. school engineering	
	Cristal Resto	Hispanic	Seewaldt	CoH/Roberts/EML	
	Angela Sanchez	Hispanic	Seewaldt	CoH/EML – now medical school	
	Myriam Robles	Hispanic	Seewaldt	CoH/Roberts/EML	
	Jasmine Robinson	Black	Yee	CoH/Roberts	
	Rosa Robles	Hispanic	Yee	CoH/Roberts/EML	
	Alan Nuñez	Hispanic	Seewaldt	CoH – now Graduate School	
	Graduate Students	Jasma Tapia	Black	Ann/Seewaldt	CoH
		Christina Vidal	Latina	Ann/Seewaldt	CoH
Jeffrey Pino		Hispanic	Martinez	UCR	
Yifan Zhao		Asian	Martinez	UCR	
Kay Jang		Asian	Martinez	UCR	
Dan-Linh Le		Asian	Martinez	UCR	
Jingyi (Jenna) Xu		Asian	Perry	UCR	
Sarah Rodriguez		Hispanic	Perry	UCR	
Myra Serano		Hispanic	Seewaldt	CoH/EML – now graduate school	
Postdoctoral Fellow	Nikita Wright	Black	Seewaldt	CoH/GWW (K99/R00)	
	Danielle Thompson	Black	Yee	CoH/EML	
Assistant Prof.	Veronica Jones	Black	Seewaldt	CoH/GWW (R01)	
	Lindsay Traviño	Hispanic	Seewaldt	CoH/GWW(R01)	
	Loretta Erhunmwunsee	Black	Seewaldt	CoH/GWW (R01 pending)	
	Jeff Perry	Caucasian	Pelleccchia	UCR-CoH/GWW(R01)	

Accomplishment – Grants, Models and Resources

● Major Grants – Funded and Pending

- ➔ **Welcome Trust - Delta Tissue** – single cell and spatial transcriptomics - funded
- ➔ **R01CA220693-S COVID19** - Community based research in cancer prevention – contactless trial in Riverside and San Bernardino FAR zip codes - funded
 - **CoHCCC Supplement** – Cancer risk in Middle Eastern Women – not funded
- ➔ **CoH CCC Supplement** FAR interventions in underserved women with pre-diabetes
 - **R25** Training in Translational Research – resubmission
 - **R01** MPI Martinez (UCR), Seewaldt (CoH), Ann (CoH) – pending
- ➔ **R25 Training Genetic Counseling** - funded
- ➔ **Diversity Supplement – Veronica Jones, MD** - funded
 - **Diversity Supplement - Christine Vidal, PhD** - pending

● Models and Resources

- Partnership JAX Labs Luminal B PDX models for Women of Color – Black/AA women and Latinas
- Cell Strains – 227 HMEC with matched ASC, fibroblasts –annotated
27 Latina, 8 Asian, 21 Black/African American

Impact/Outcomes - UCR and CoH Partnership

UCR Student Jonathan Calero-Lando (Latino)

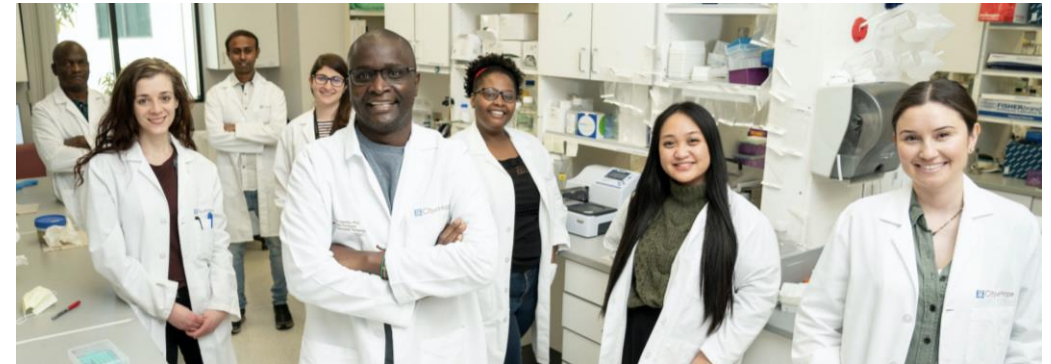
2017-2020 T34-MARC Undergraduate (Martinez)
Summer 2019 CoH Roberts Summer Academy - Ann, Sistrunk, Seewaldt)
Fall 2020 CoH Biomedical Graduate School PhD
Fall 2021 Joined lab of Gordon Obengo (Seewaldt mentee)



UCR T34 MARC U-Star
Ernest Martinez



CoH Roberts Academy
Summer 2019



Graduate School CoH - 2020
Laboratory Dr. Gordon Obengo - 2021

Impact/Outcomes – Unique Approaches

- **Postbac training for future medical and graduate students**

Identify pre-med students from UCR and ISUPs – “Student that broke your heart”

Hire and train as clinical research associate - \$65K per year in LA

Year 1: training – EMR, rigor reproducibility samples, ethics, inclusion, publish, MCAT

Year 2: Summer - Attend UNC MED Postbac-Premed – some immediate admission UNC

Year 2: Summer/Fall - Apply to medical school; assist with essays

Year 2 Fall/Winter – Assist with interview preparation

- **Since 2010 - 27 URM to medical school – all passed Boards Part 1&2 first time – all graduated in upper 1/3 of class - half remained in research**



2019-2021 Graduates

Angela Sanchez – Western DO

Alen Nuñez – NC State - PhD

Angela Wong – UNC - MD

Christine Tsai – UNC MD

Obeni Idassi – Meharry - MD

Adrian Ambrose – ECU – MD

Kendall Kennedy – Morehouse - MD

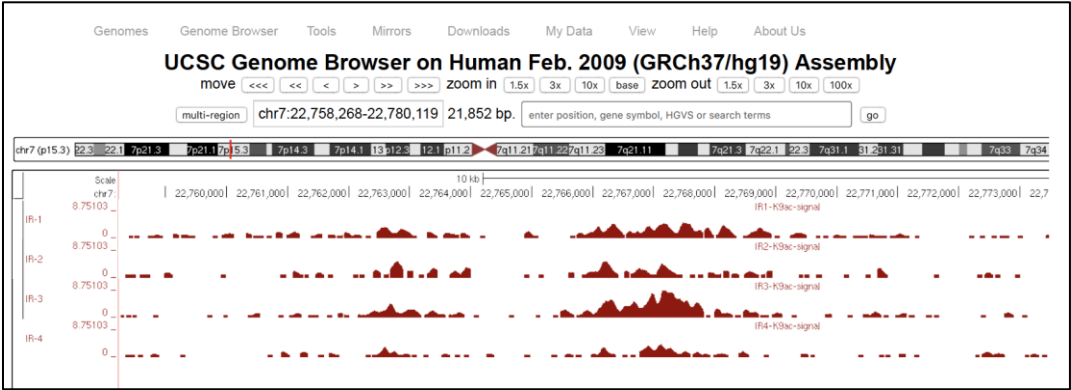


Impact/Outcomes – Eat Move Live

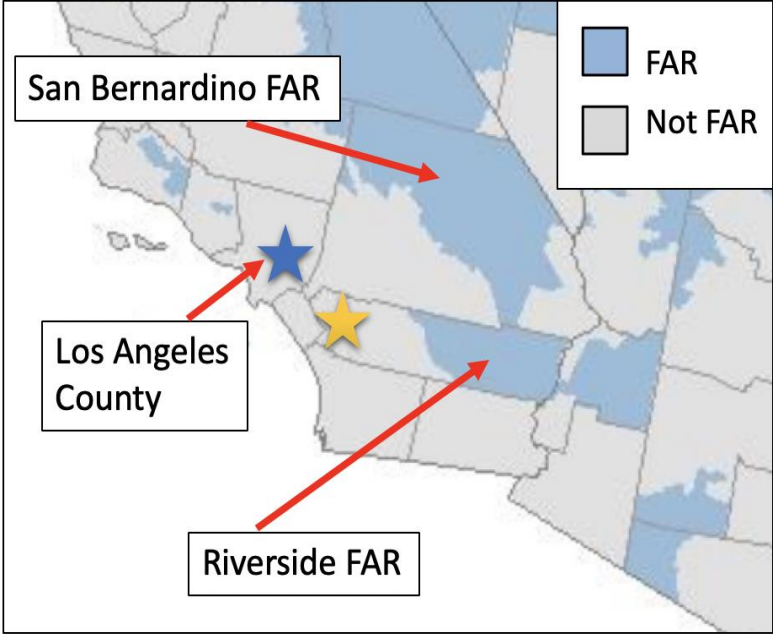
Eat Move Live - Latina community-based exercise program

Frontier & Rural (FAR) Zip code – synergize UCR U54 (Lo)

- Model of how basic science can impact community health
- Community-based research, diabetes prevention, epigenetics



Food desert zip codes associated with increased insulin resistance
Insulin resistance – ChIP-seq - chromatin acetylation H3K9Ac
Top hits - IL6, TNFalpha, IL12, IL1beta
Question: Is epigenetic damage reversible



Sustainability – UCR and CoH Partnership

Grant Funding

- R25CA233431 YES2Success – 3rd grade into HS
- R25GM119975 Riverside Bridges to the Baccalaureate Training Grant - HS to undergraduate
- T34GM061146 MARC UCR Training Grant - undergraduate
- T32CA221709 Training Grant URM – Metabolism & Cancer - PDF
- R25 Training in Genetics
- P20CA252717 Disparity SPORE in Lung Cancer
- U54 – UCR – Center in Disparities

Investment in Training

- CoH CCC Tissue Bank – will hire 8 CRA per year – use PostBac URM training model
- Roberts Academy – 100 students per year – 20 guaranteed slots for URM

Unique Resources – UCR – CoH Partnership

- CoH BIOSCI 675 – The Science of Cancer Disparities
- CoH PhD in Drug Discovery
- CoH Biomarkers Core – Genetic Admixture – Rick Kittles, PhD.
- CoH Population Science – Majority Minority and Majority Women

Collaborations - UCR and CoH Partnership

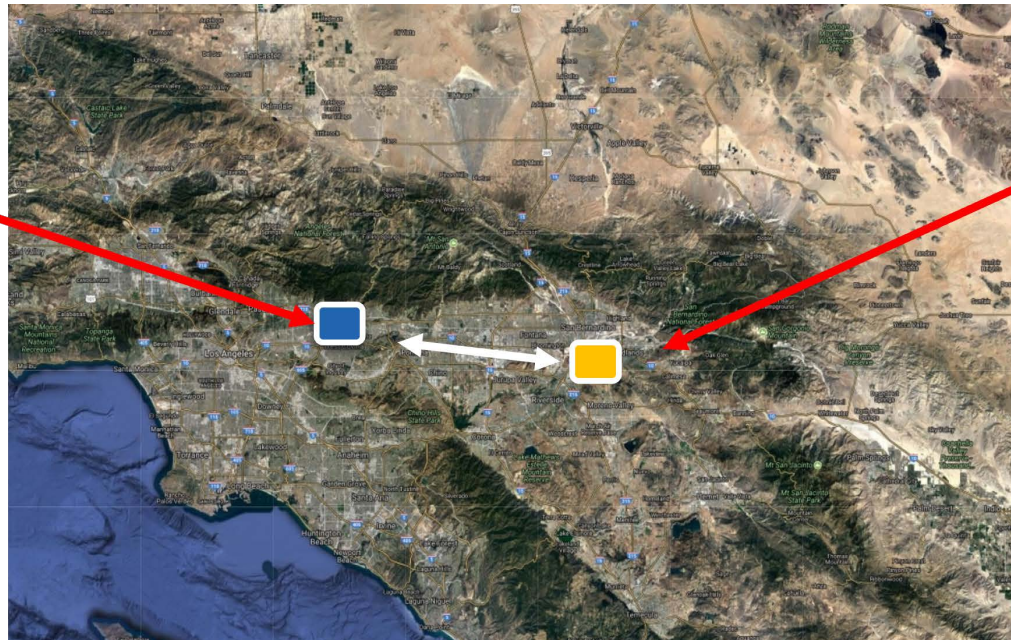
- P20CA233374 Disparities SPORE LSU – Lucio Miele and Augusto Ochoa – Luminal B breast cancer in Latina/Hispanic Women
- P20CA252717 Disparities SPORE in Lung Cancer – Rob Winn, Chanita Hughes Halbert, Victoria Seewaldt – Lung cancer disparities in Black/African American Men.
- Welcome Trust – TNBC disparities in high-risk women – UCSD, CoH, LSU, UCR focus on Black/African American women and Latinas. Single cell and spatial transcriptomics

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