Alliance for Cancer Drug Discovery, Development & Education
BCM (DLDCCC)-UHCOP

Baylor College of Medicine

DAN L. DUNCAN
COMPREHENSIVE
CANCER CENTER

Diana Monsivais, PhD
Assistant Professor
Baylor College of Medicine
Houston, TX
PACHE Conference
ESI Investigators and Postdoc Breakout Session
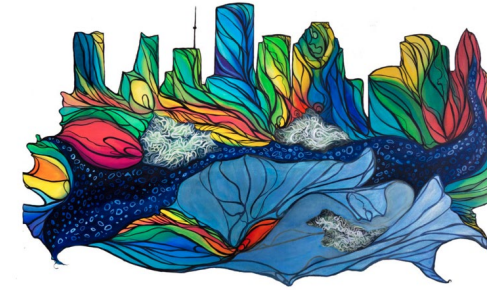9/21/21

University of Houston
College of Pharmacy

Overall Goals of BCM-UH NIH P20 grant

UHCOP-DLDCCC alliance:
Cancer drug discovery/development and education

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To **enlarge the pipeline for underrepresented (UR) trainees** to establish careers in cancer research and to generate data for subsequent NCI funding that further supports UR training.

We will accomplish this by **increasing the student opportunities** to conduct high-quality, innovative cancer drug discovery/development research at the University of Houston College of Pharmacy (UHCOP) and the Dan L. Duncan Comprehensive Cancer Center (DLDCCC) at Baylor College of Medicine (BCM), and through the **implementation of newly developed curricula and lectures** designed to educate trainees and the community about cancer research and cancer health disparities.
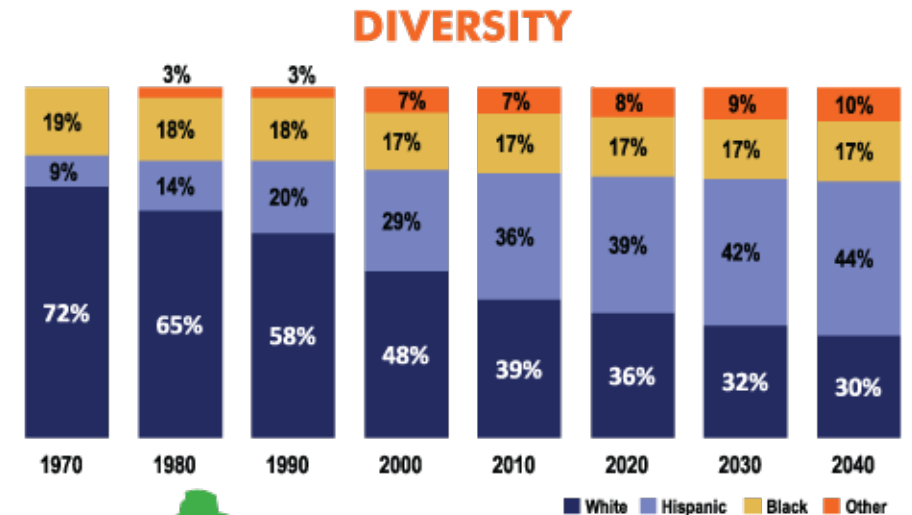
Population served by the BCM-UH NIH P20 grant

DIVERSITY

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HOUSTON, TX

- 4th largest city in the US

- Population of ~2.3M

  -22% African American

  -45% Hispanic/Latino

  -24.4% White/not Hispanic/Latino

  -6.8% Asian

  -<1% Native American, Alaskan, Hawaiian or Pacific Islander

Source: US Census and Houston-Galveston Area Council

Population served by the BCM-UH NIH P20 grant

UHCOP-DLDCCC alliance:
Cancer drug discovery/development and education

University of Houston

- ~46,000 students
    - ~28,000 UG, ~5,300 Grad
- Demographics
    - 10.6% African American
    - 33.6% Hispanic/Latino
    - 21.7% White/not Hispanic/Latino
    - 23.6% Asian
    - <10% Native American, Alaskan, Hawaiian or Pacific Islander or other

Baylor College of Medicine

- Ranked 1st in Texas in NIH funding (20th in the nation)
- Ranked 1st in Texas Medical Schools
- 753 medical students
- 578 graduate students
- 261 health professions students
- 1,085 clinical residents and 489 clinical fellors
- 464 postdoctoral fellows

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Specific Aim 1: Oversee the P20 pilot projects, promote scientific interactions between CREP and pilot projects, manage finances and oversight meetings, and develop future cancer drug platforms, all focused on promoting UR training and awareness in cancer health disparities. (**Administrative Core**)

Specific Aim 2: Provide high quality, comprehensive cancer research experiences and develop new cancer-specific curricula and educational outreach designed to encourage and prepare UR trainees and others to enter careers in cancer research. (**C-REP**)

Specific Aim 3: (a) Develop novel compounds to reverse global methylation patterns in hepat ocellular carcinoma, which not only exhibits incidence disparity but will be germane and important for UR trainees whose ethnic groups may suffer from such disparity. (**Pilot Project 1**, 2018-2020);

(b) Identifying novel kinases and phosphatases for drug discovery in endometrial cancer (**Pilot Project 3**, 2021-2022)

Specific Aim 4: (a) Discover small molecule inhibitors of FOXA1, implicated in endocrine therapy–resistance in breast cancer, which shows prognostic disparity for African-Americans. (Pilot Project 2, 2018-2020);

(b) Validation of cell surface plectin as a new drug-target for cancer stem cells (CSCs) and a specific peptoid-PCS2 as a drug-lead (**Pilot Project 4**, 2021-2022)

Specific Aim 5: Begin to develop the platform at the UHCOP for future pharmaceutical development of potential cancer drug candidates based on lead compounds identified in the discovery phase.

Accomplishments Worth Mentioning (2020-2021)

A. **BCM-UH graduate course** of Technologies for

   Cancer Drug Discovery and Development, **GS-CC-6401**, offered the first time in Spring 2021

B. Graduate students received **awards at national meetings**

   1. **AACR Scholar-in-Training,** 2020, Lorita Agu & Victor Lincha

   2. **ASPET** (Cancer Pharmacology), 2021, Noor Abdelkarim

C. **Research Pilot Projects 1 & 2** completed in 2021, resulted in publication in Scientific Reports, R01 submission, CPRIT funding granted

D. **Research Pilot Projects 3 & 4,** on going, delivered milestones. Resulted in publication and Pilot Project Award from DLDCCC.

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Benefits from my participation in the BCM-UH P20 Program

1. Awarded a P20 Pilot Award: 2-year collaborative program with a Co-PI at UH (Dr. Greg Cuny)

"Identifying novel kinases and phosphatases for drug discovery in endometrial cancer"

* Provides funds for pilot experiments related to health disparities in endometrial cancer: DLDCCC Pilot Project Recipient in Dec. 2020

* Interaction with Dr. Greg Cuny and expertise in medicinal chemistry

* Expanded network of scientists inside and outside my home institution

* Crucial opportunities to build preliminary studies in preparation for NIH R01 applications

2. Opportunities to network with undergraduate students at the University of Houston (Hispanic serving institution)

* *"Lunch with Cancer Researcher"* seminar series (before COVID19 restrictions)
* Great interaction with undergraduate students

Cancer Research Education Program(C-REP)

- Opportunities for student training/mentoring:
  - Faith Joseph, (TBMM Graduate program at BCM) Fall 2020
  - Sydney Parks, (CCB Graduate program at BCM) Winter 2021
  - Kersten Pierre, (SMART undergraduate student, Spellman U) Summer 2021
  - Bradly Ramirez, (SMART undergraduate student, UH Victoria) Summer 2020
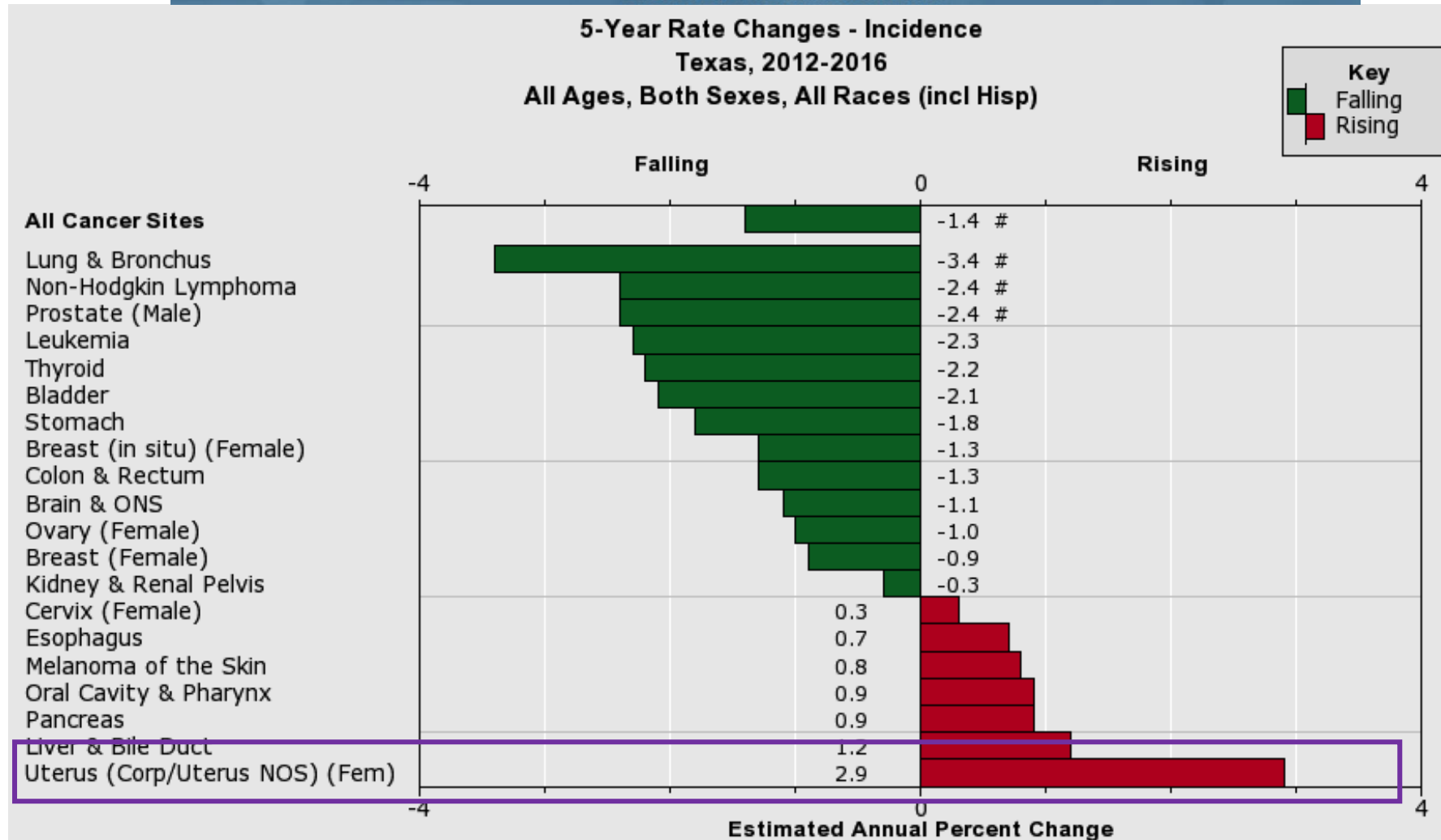 - Stella Shumblon, (NY state high school student, virtual) AY 2020-21

- Presentations at national meetings:
  - 3 UG students attended ABRCMS or SACNAS
  - Travel award to SACNAS
  - 2 graduate students –working in pharmaceutical companies;
  - 2 UG students – medical school;
  - 1 UG student- in MS program with plan to pursue PhD

# Endometrial Cancer is one the most rapidly rising cancer types

STATE CANCER PROFILES
Dynamic views of cancer statistics for prioritizing
cancer control efforts across the nation

5-Year Rate Changes - Incidence
Texas, 2012-2016
All Ages, Both Sexes, All Races (incl Hisp)

Key
Falling
Rising

Cancer Site	Falling	Rising
	Falling	Rising
	-4	0	4
All Cancer Sites	-1.4 #	
Lung & Bronchus	-3.4 #	
Non-Hodgkin Lymphoma	-2.4 #	
Prostate (Male)	-2.4 #	
Leukemia	-2.3	
Thyroid	-2.2	
Bladder	-2.1	
Stomach	-1.8	
Breast (in situ) (Female)	-1.3	
Colon & Rectum	-1.3	
Brain & ONS	-1.1	
Ovary (Female)	-1.0	
Breast (Female)	-0.9	
Kidney & Renal Pelvis	-0.3	
Cervix (Female)		0.3
Esophagus		0.7
Melanoma of the Skin		0.8
Oral Cavity & Pharynx		0.9
Pancreas		0.9
Liver & Bile Duct		1.2
Uterus (Corp/Uterus NOS) (Fem)		2.9

Estimated Annual Percent Change

www.statecancerprofiles.cancer.gov

Health disparities in EC : higher incidence rates and decreased 5-year survival in African American women

Non-endometrioid EC

5-year survival rates in non-endometrioid EC
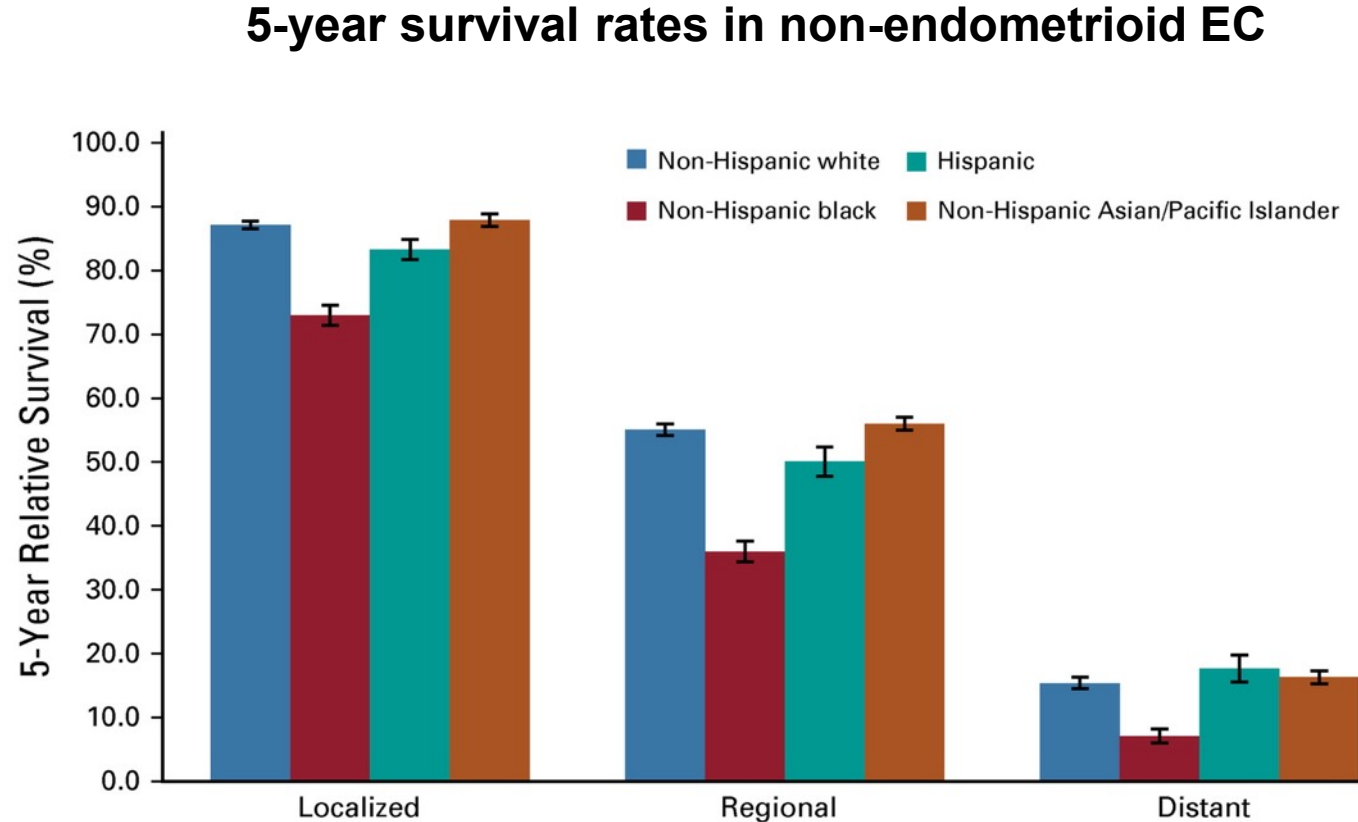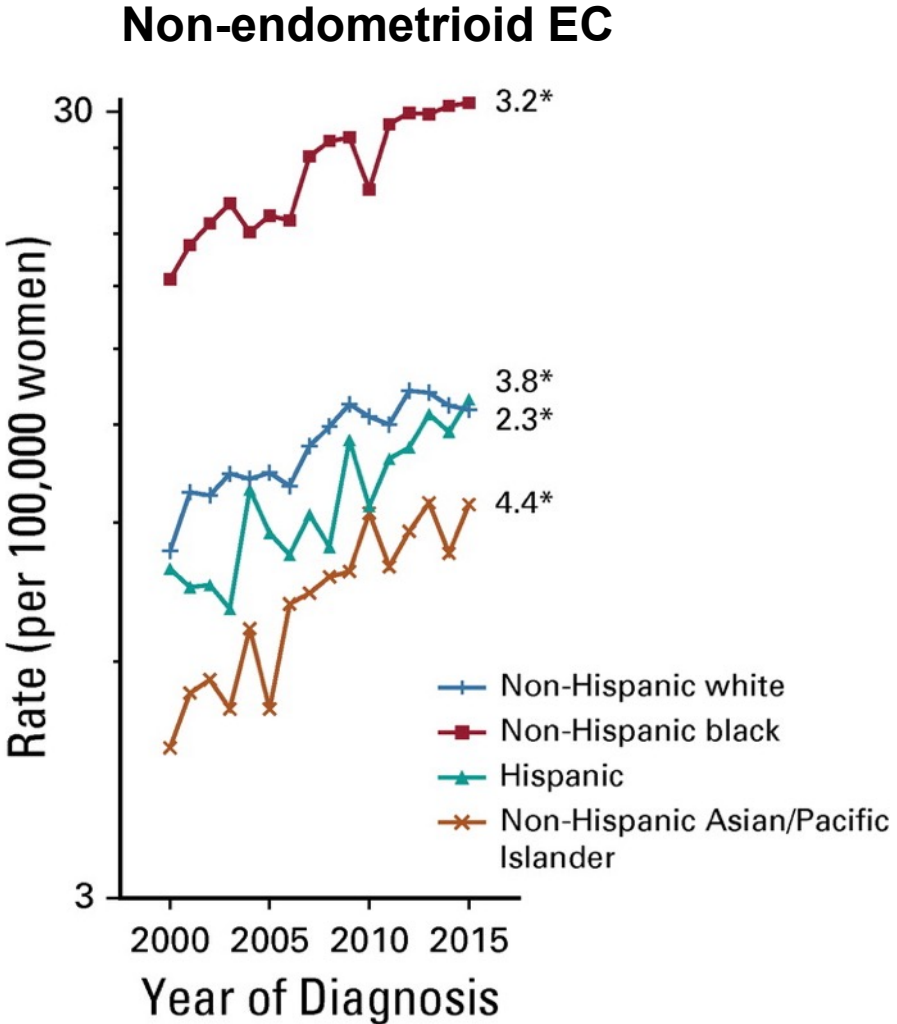
Clarke M et al., (2019) Journal of Clinical Oncology

National Cancer Institute's Clinical Proteomic Tumor Analysis Consortium (CPTAC) performed "multi-omic" characterization of 95 uterine tumors to identify new potential therapeutic targets
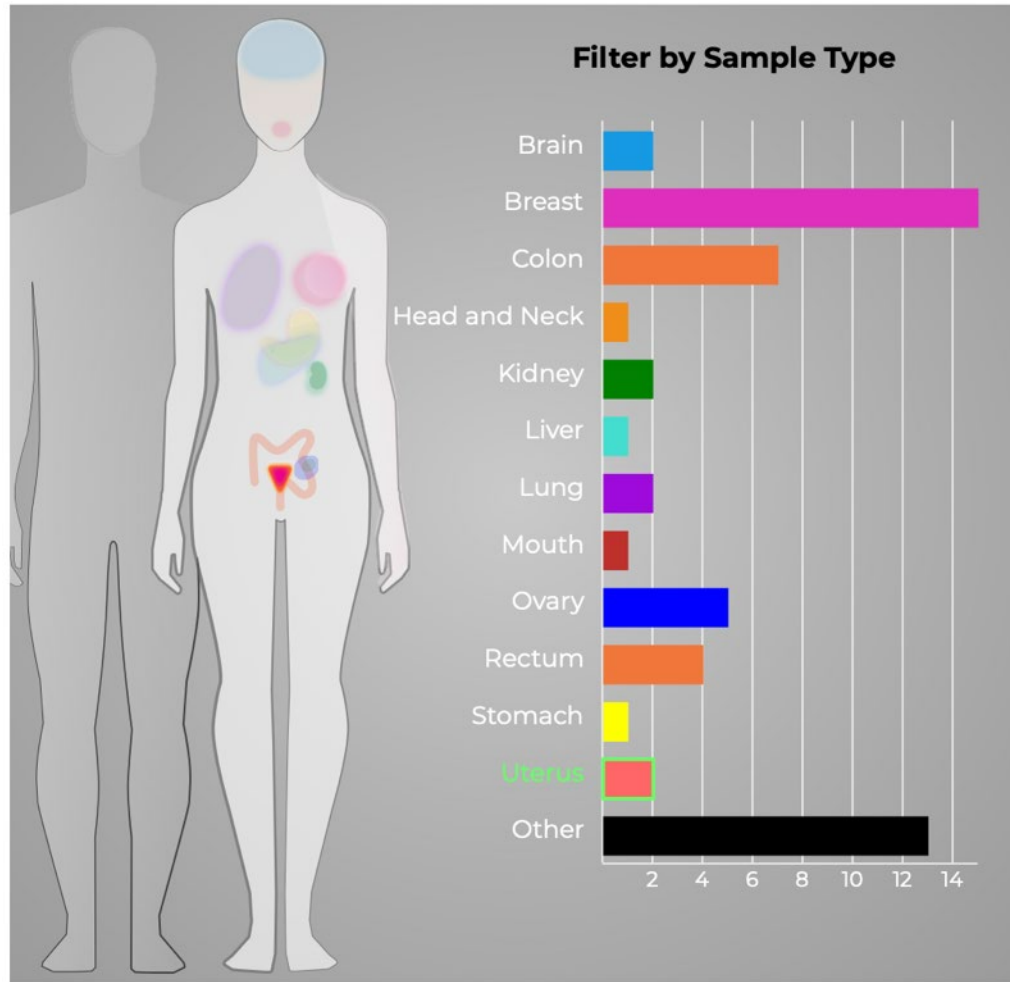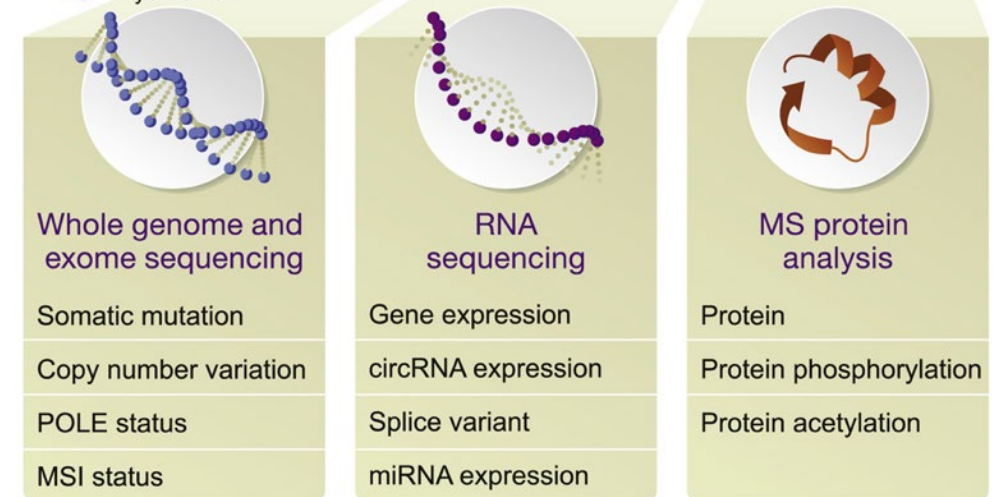

Dou Y., et al., Cell, Feb 2020

Experimental approach to validate, screen, and test novel endometrial cancer therapeutics

Endometrial cancer cell lines

| Cell Line	Type	Grade
Ishikawa	I	Grade 1
HEC-1-A	I or II, likely II	Grade 2
KLE	I or II, likely II	Grade 3
AN3CA	I	Grade 3
SK-UT-1B		Grade3, Sarcoma
MFE-319	I	
HEC-1-B	I or II, likely II	
ETN1	I	Metastatic skin nodule
EN1	I or II, likely II	low
EI	I or II, likely II	

siRNA-mediated knockdown of targets

Cell Viability

Cell Migration

DNA Encoded Library selections

Medicinal Chemistry for further validation
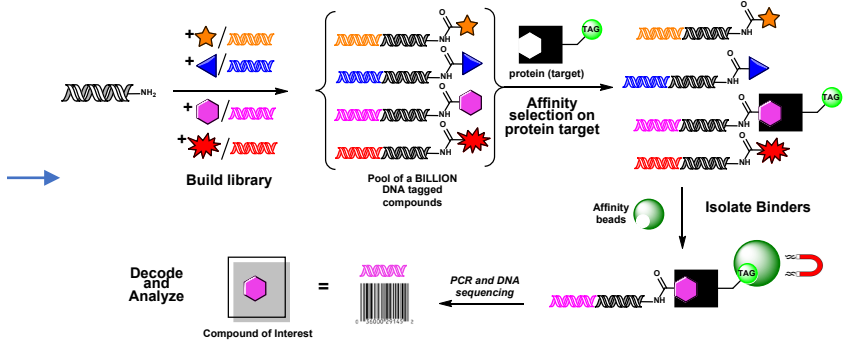
1) Off-DNA synthesis
2) *In vitro* validation
3) Cell-based assays

EC CPTAC data were analyzed according to tumor grade and stage to identify most highly overexpressed kinases and phosphatases

Monsivais D. et al., *Oncogene* (2021)
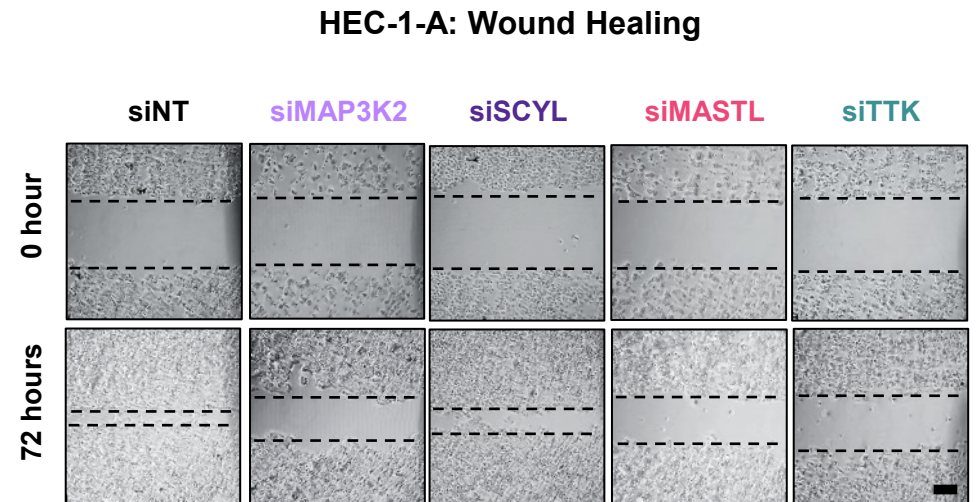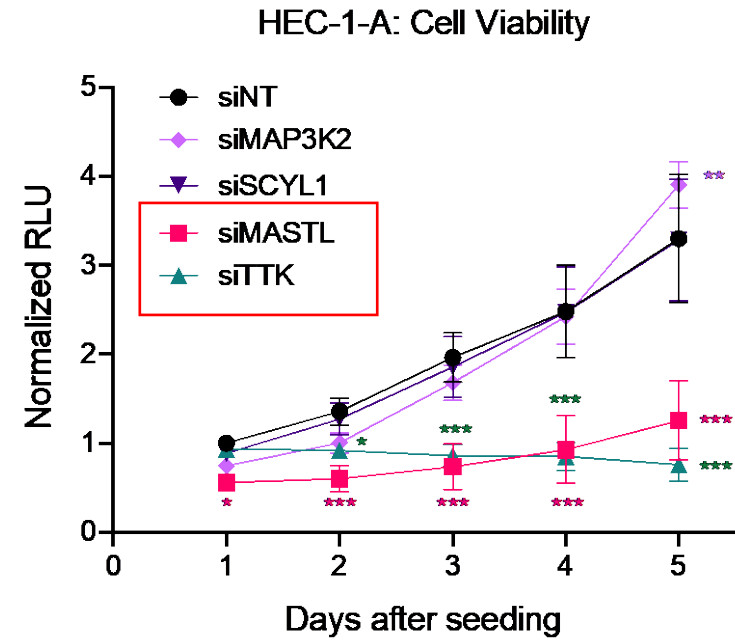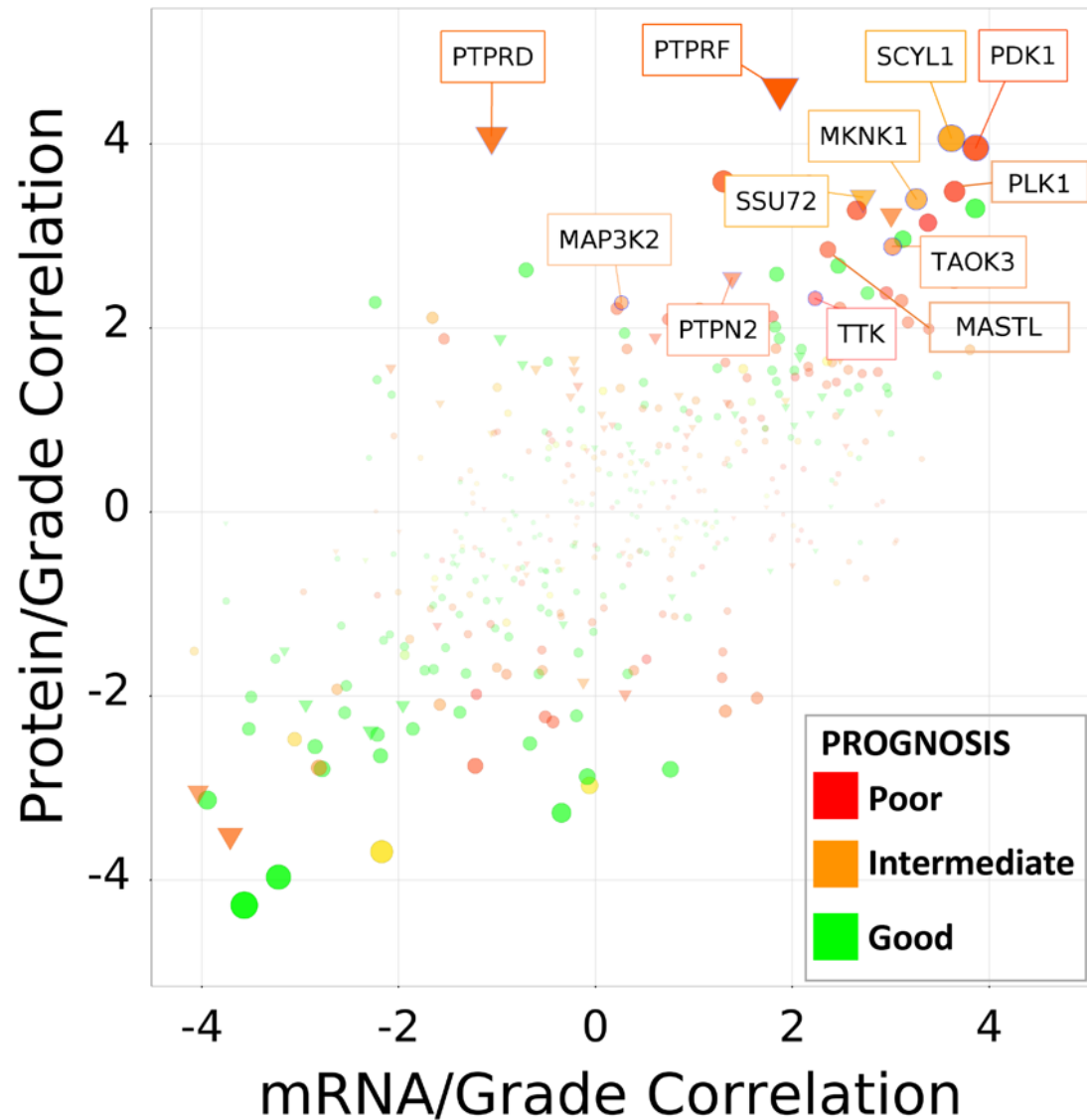
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STUDENTS INVOLVED

- Faith Joseph, (TBMM Graduate program at BCM) Fall 2020
- Sydney Parks, (CCB Graduate program at BCM) Winter 2021
- Kersten Pierre, (SMART undergraduate student, Spellman U) Summer 2021
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