Interrogating the molecular profile of solid tumors in Puerto Rican Hispanics:

Defining *actionable mutations* and *drivers of carcinogenesis*

Marcia Cruz-Correa, MD, PhD

Professor of Medicine and Biochemistry UPR Medical Sciences Campus

UPR Comprehensive Cancer Center

CENTRO COMPRENSIVO DE CANCER UNIVERSIDAD DE PUERTO RICO

ESCUELA DE MEDICINA UNIVERSIDAD DE PUERTO RICO 1950

CARISPOA PRECISION ONCOLOGY ALLIANCE

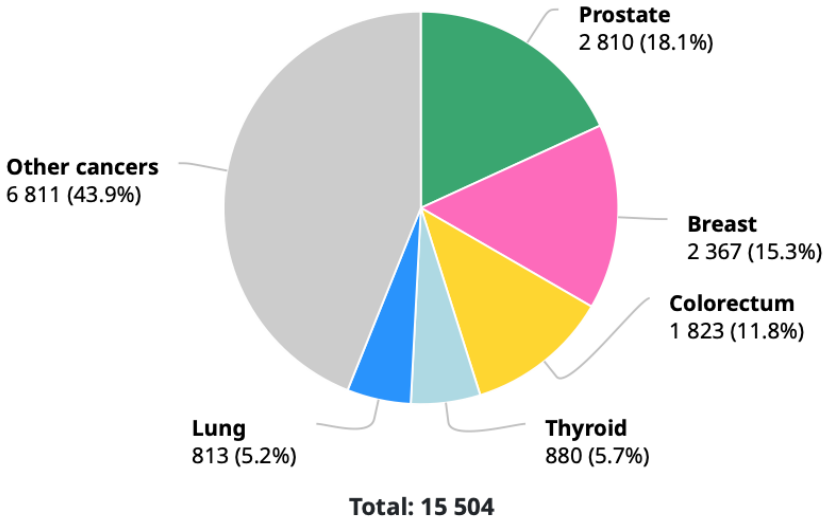
Background & Significance

International Agency for Research on Cancer
World Health Organization

Since 2014, **cancer** is the leading cause of morbidity and mortality in Puerto Rico

WHO International Agency for Research on Cancer 2018:

- Incidence: 15,504
- Prevalence in a 5-year period:
- Most common cancer types
  - **Prostate**
  - **Breast**
  - **Colorectum**

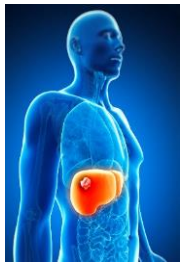


Cancer Related Death in Puerto Rico 2018

Cancer death in Puerto Rico: **5,502**

Cancer types with highest mortality rates in PR in 2018	**Cancer types with highest mortality rates globally in 2018**
Colorectal Cancer (12.3%)	Breast cancer (12.9%)
Lung/Bronchus (11.3%)	Prostate Cancer (12.3%)
Prostate (9.2%)	Colorectal Cancer (9.8%)

Precision Oncology as a **Framework for Patient Care**



Biopsy

Sequencing

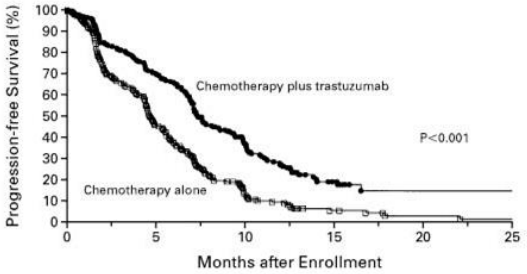
Tumour Molecular Board

Treatment

- Logistics
- Cancer Heterogeneity
- Magnitude of Clinical Benefit

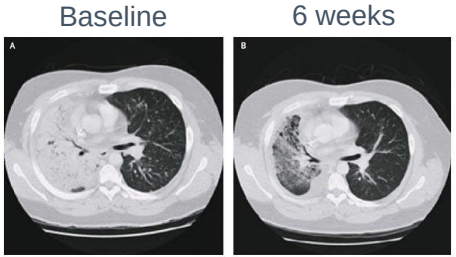
Molecularly-Targeted therapies

Trastuzumab in HER2-positive



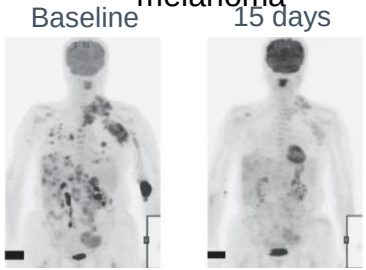
Slamon DJ, et al. N Engl J Med. 2001;344(11):783-92

Gefitinib in EGFR-mutated NSCLC



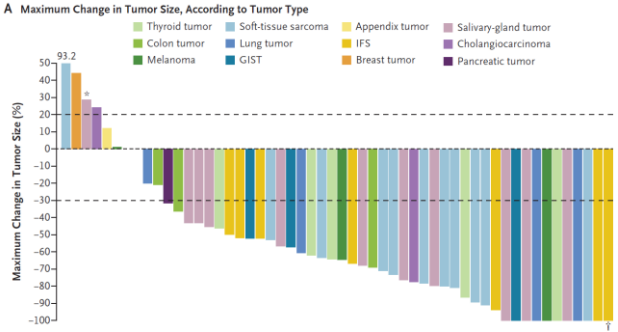
Lynch TJ, et al. N Engl J Med. 2004;350(21):2129-39

Vemurafenib in **BRAF V600E-**mutated melanoma



Flaherty KT, et al. N Engl J Med. 2010;363(9):809-19

Larotrectinib in TRK fusion-positive cancers



Drilon A, et al. N Engl J Med. 2018;378:731-39

JAMA Oncology | Brief Report

Racial/Ethnic Disparities in Genomic Sequencing

Daniel E. Spratt, MD; Tiffany Chan, MA; Levi Waldron, PhD; Corey Speers, MD; Felix Y. Feng, MD; Olorunseun O. Ogunwobi, MD, PhD; Joseph R. Osborne, MD, PhD

Individual patient data from 5,729 samples TCGA

- **12% were Black**
- **3% were Asian**
- **3% were Hispanic**

Due to limited number of racial/ethnic minorities detection of mutational frequencies of 5% were not identified for any cancer type analyzed (vs. *NHW that mutations with 5% frequency were identified for all cancers*)

Precision Oncology Alliance

- POA created to collect and share molecular data for analysis
- UPR joined the POA in July 2019 as the 28th Institution that joined the Alliance
- In 2020 submitted a Letter of Intent to evaluate the tumors from PR using de-identified data

Interrogating The Molecular Profile of Solid Tumors in Puerto Rican Hispanics

METHODS:

- Study Design: ***retrospective descriptive study***

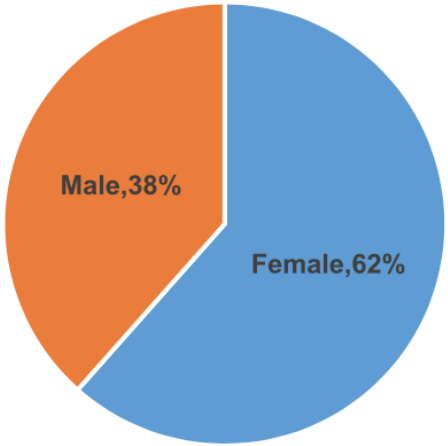
- Participants: **931 patients from Puerto Rico** whose tumors were analyzed by Next Generation Sequence platform by Caris Life Sciences © between the years **2015 to 2020**

- Data Source: CARIS Life Sciences © Next Generation Sequencing (NGS) provides the data used in this study

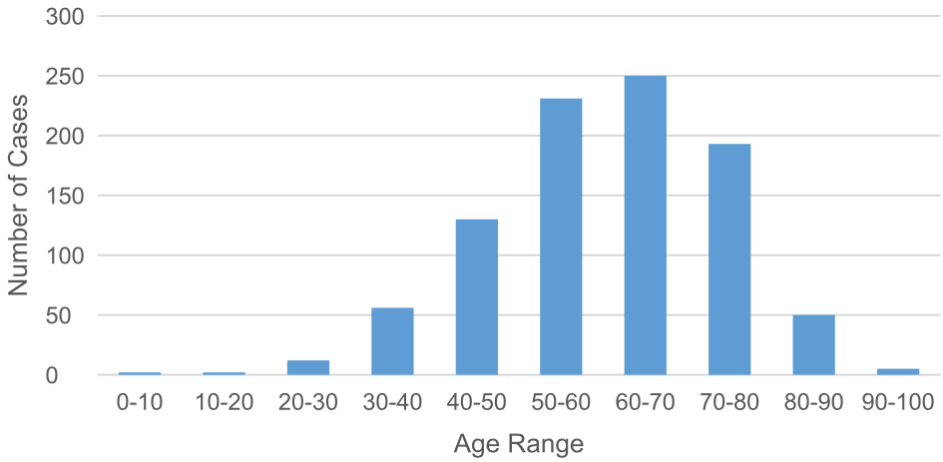
  We collected the tumor type, primary tumor location, presence of a pathogenic mutation and type of mutation

Molecular Characterization of PR Hispanics

Number of Cancer Cases by Gender (n=931)



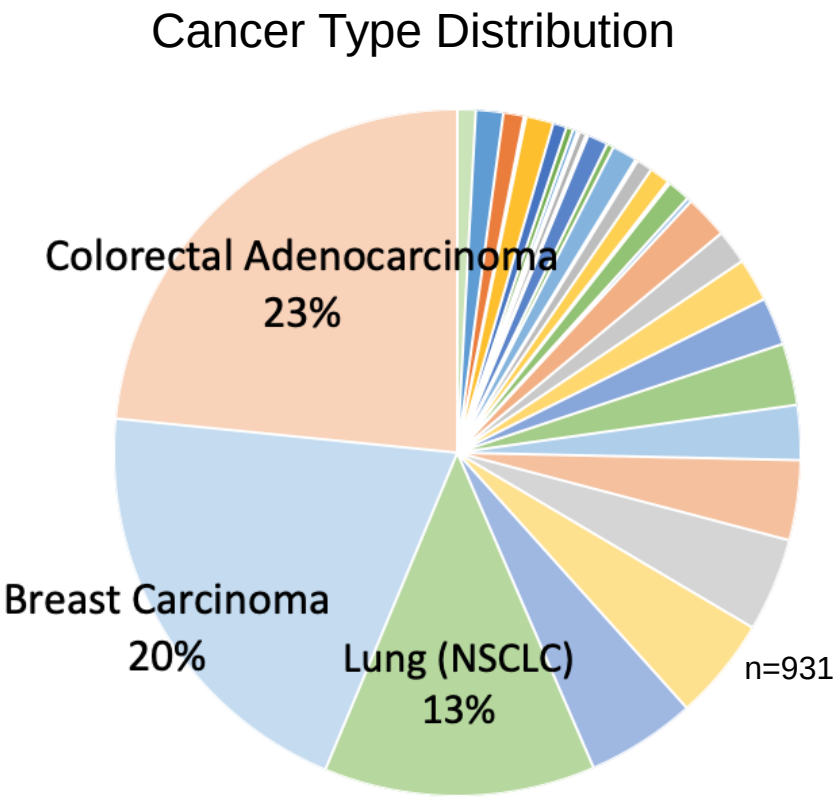
Number of Cancer Cases by Age Range (n=931)



CARIS POA
PRECISION ONCOLOGY ALLIANCE

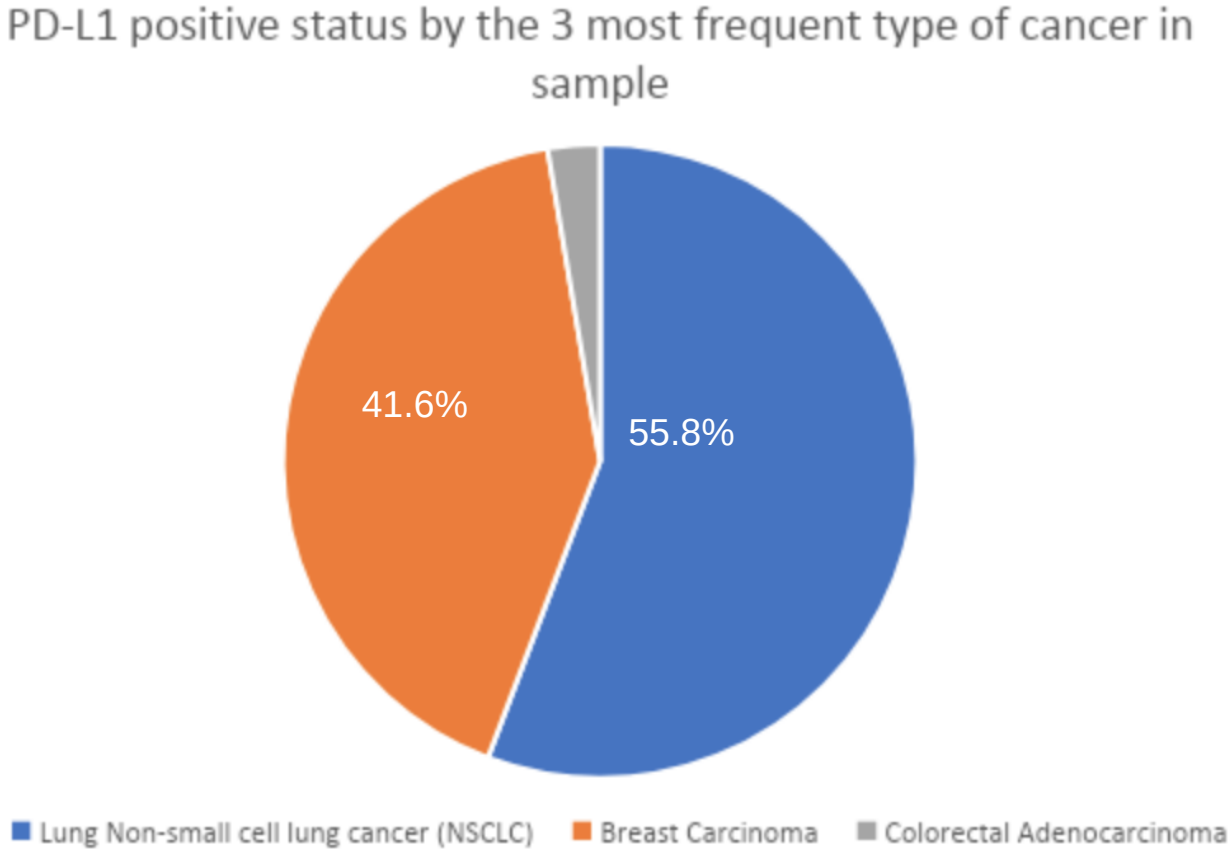
Cruz-Correa, AACR 2021

Preliminary Results



Type of Cancer	Percent (%)
Colorectal Adenocarcinoma	23.4
Breast Carcinoma	20.3
Lung Non-small cell lung cancer (NSCLC)	12.8
Pancreatic Adenocarcinoma	5.2
Ovarian Surface Epithelial Carcinomas	4.8
Female Genital Tract Malignancy	4.4
Cancer of Unknown Primary	3.8
Cholangiocarcinoma	2.9
Gastric Adenocarcinoma	2.6
Soft Tissue Tumors	2.3
Esophageal and Esophagogastric Junction Carcinoma	2.0
Prostatic Adenocarcinoma	1.6
Cervical Cancer	1.3
Head and Neck Cancers	1.3
Neuroendocrine tumors	1.2

PDL1 Expression



Comparison of TCGA, GENIE and POA datasets for the detection of clinically actionable alterations in Hispanics with Colorectal Cancer

Ingrid M. Montes-Rodríguez PhD, Hilmaris Centeno-Girona MS, Camila Rivera-Lynch BS[2], Marievelisse Soto-Salgado DrPH, MS, Noridza Rivera MD, Marcia Cruz-Correa MD, PhD

Cancer Databases Studied

The Cancer Genome Atlas (NCI)

Genomics Evidence Neoplasia Information Exchange (GENIE)

Precision Oncology Alliance

Demographics Characteristics of Cohorts

	PRH (n=218)		TCGA (n=594)			GENIE-NON-H (n=9,427)			GENIE-H (n=724)		
Characteristics	N	%	N	%	p-value	N	%	p-value	N	%	p-value
Sex											
Men	121	**55.5**	312	**52.5**	0.45	5,143	**54.6**	0.79	406	56.1	0.88
Women	97	**44.5**	280	**47.1**	0.50	4,277	**45.4**	0.79	318	43.9	0.88
Unk	0	**0.0**	2	**0.3**	0.39	7	**0.1**	0.64	0	0.0	-
Age at which sequencing was reported											
Mean	58.5		66.1			58.0			57.9		

Actionable Biomarkers in Colon Adenocarcinoma (n=218)

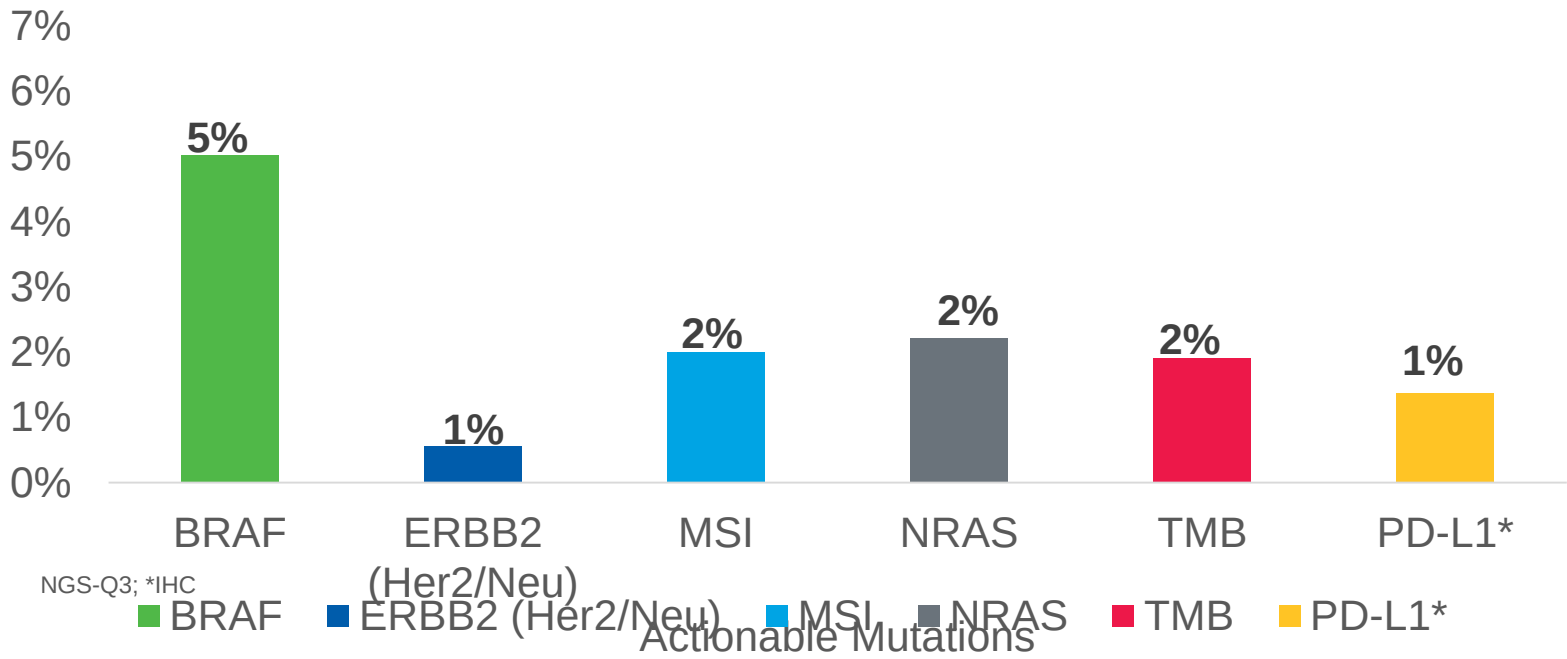
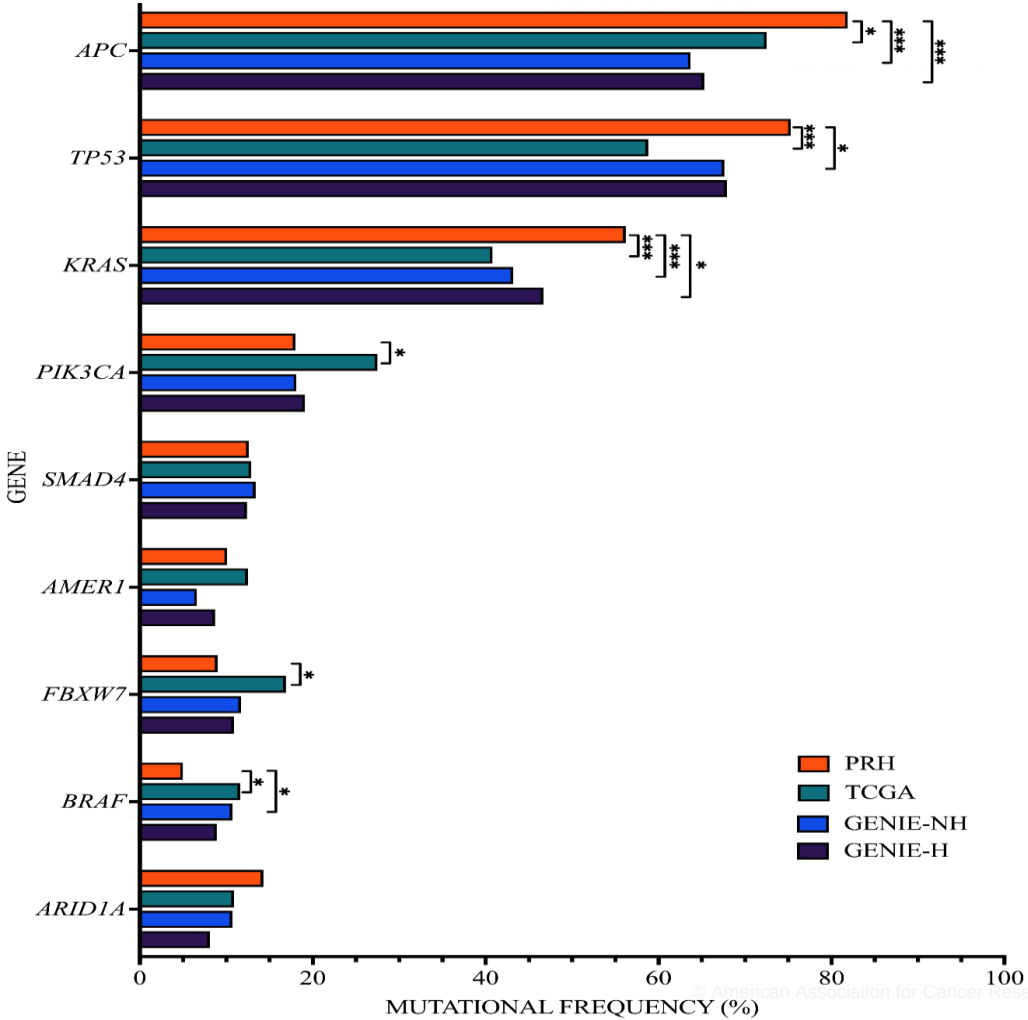
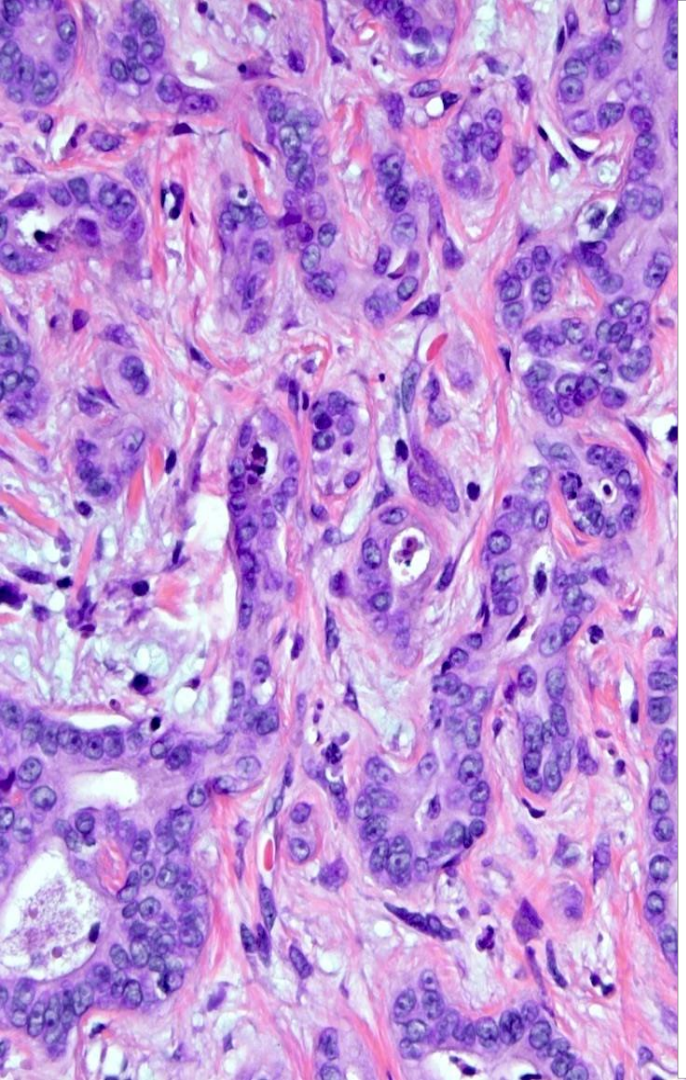


Figure. Mutational frequencies of *APC, TP53, **KRAS**, **PIK3CA**, SMAD4, AMER1, FBXW7, **BRAF*** and *ARID1A* in PRH, TCGA, GENIE-NH and GENIE-H.

*Significant differences between PRH and other populations are denoted with an asterisk (*p< 0.05, **p< 0.01, and ***p< 0.001).*





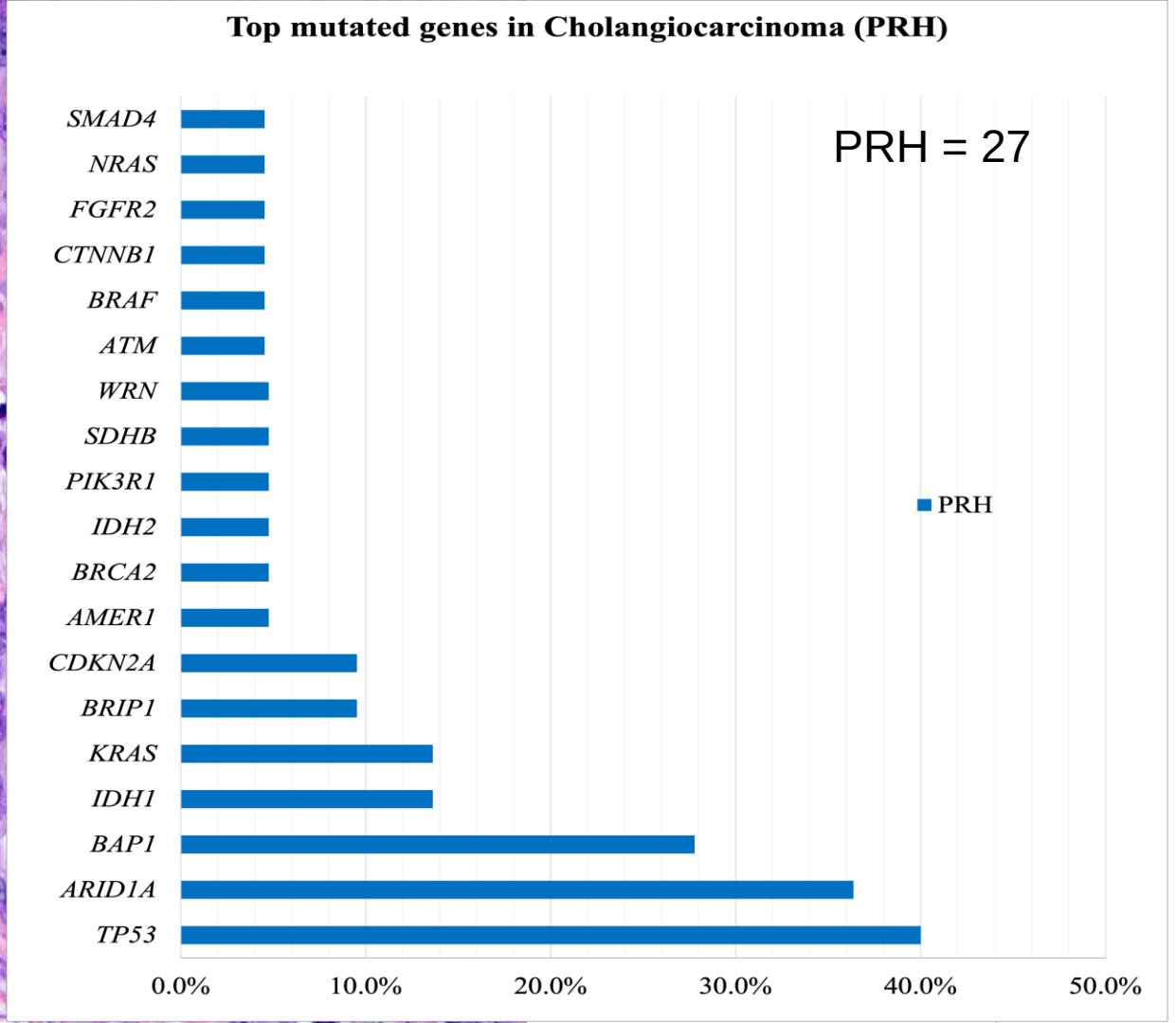
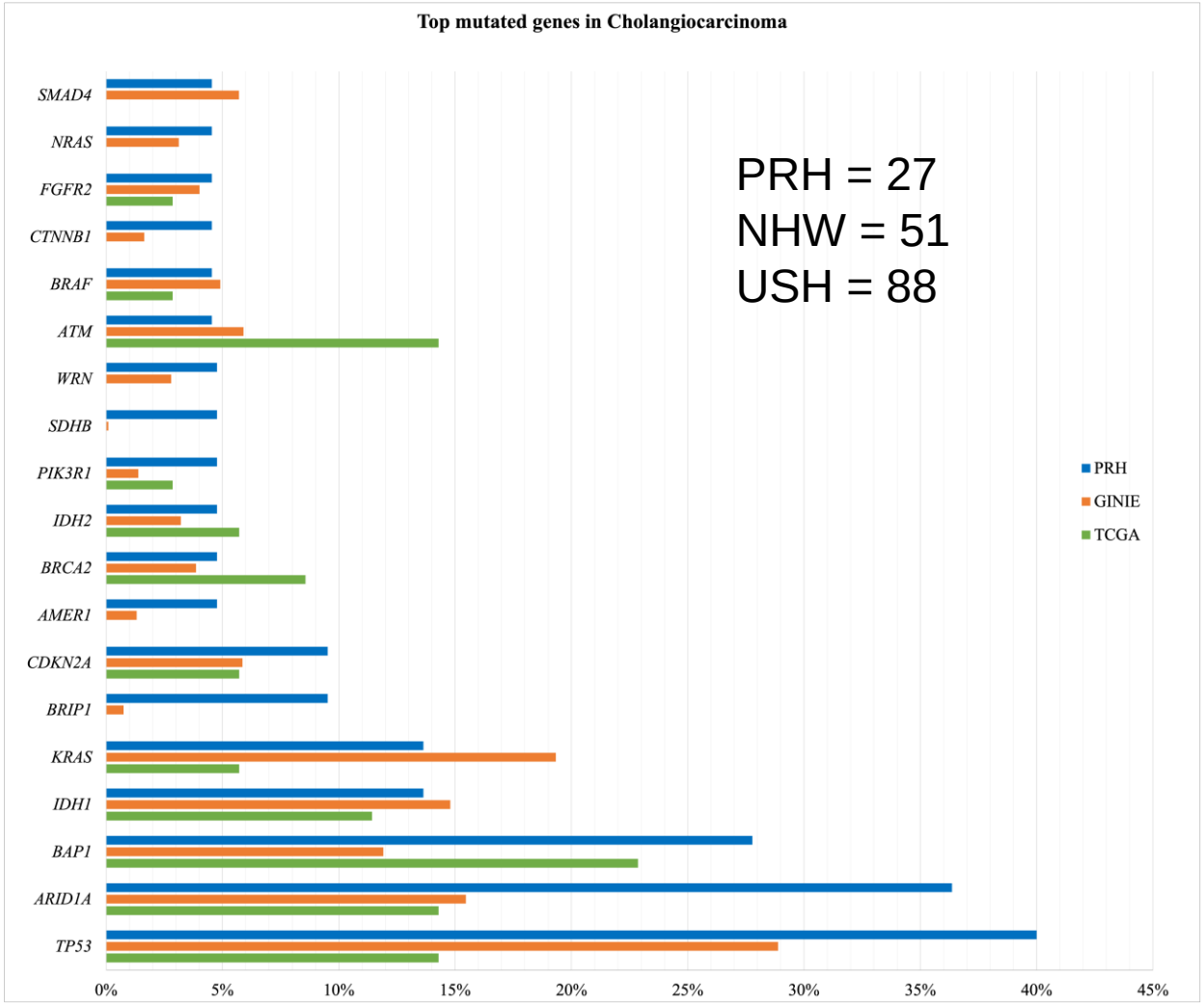
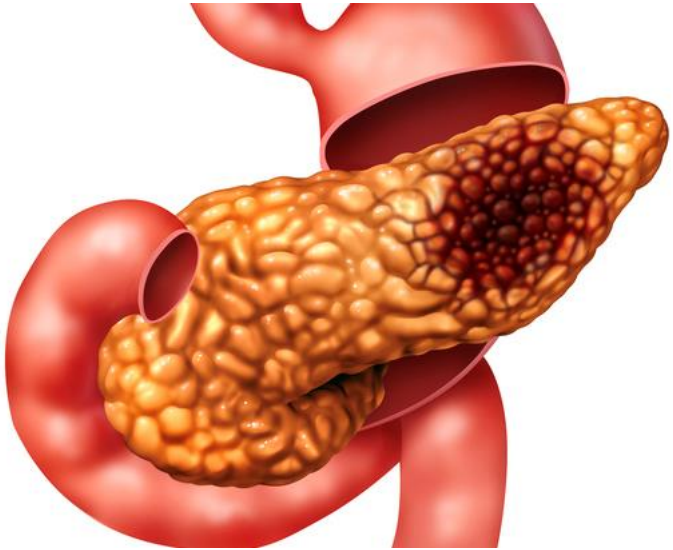

Top mutated genes in Cholangiocarcinoma (PRH)
PRH = 27
SMAD4
NRAS
FGFR2
CTNNB1
BRAF
ATM
WRN
SDHB
PIK3R1
IDH2
BRCA2
AMER1
CDKN2A
BRIP1
KRAS
IDH1
BAP1
ARID1A
TP53
PRH
0.0%
10.0%
20.0%
30.0%
40.0%
50.0%

Figure. Mutations in actionable genes were seen in:

IDH1 (14%)
FGFR2 (5%)
HRD genes ***(****ATM, BRCA2, CDKN2A****)***





PRH = 48 patients

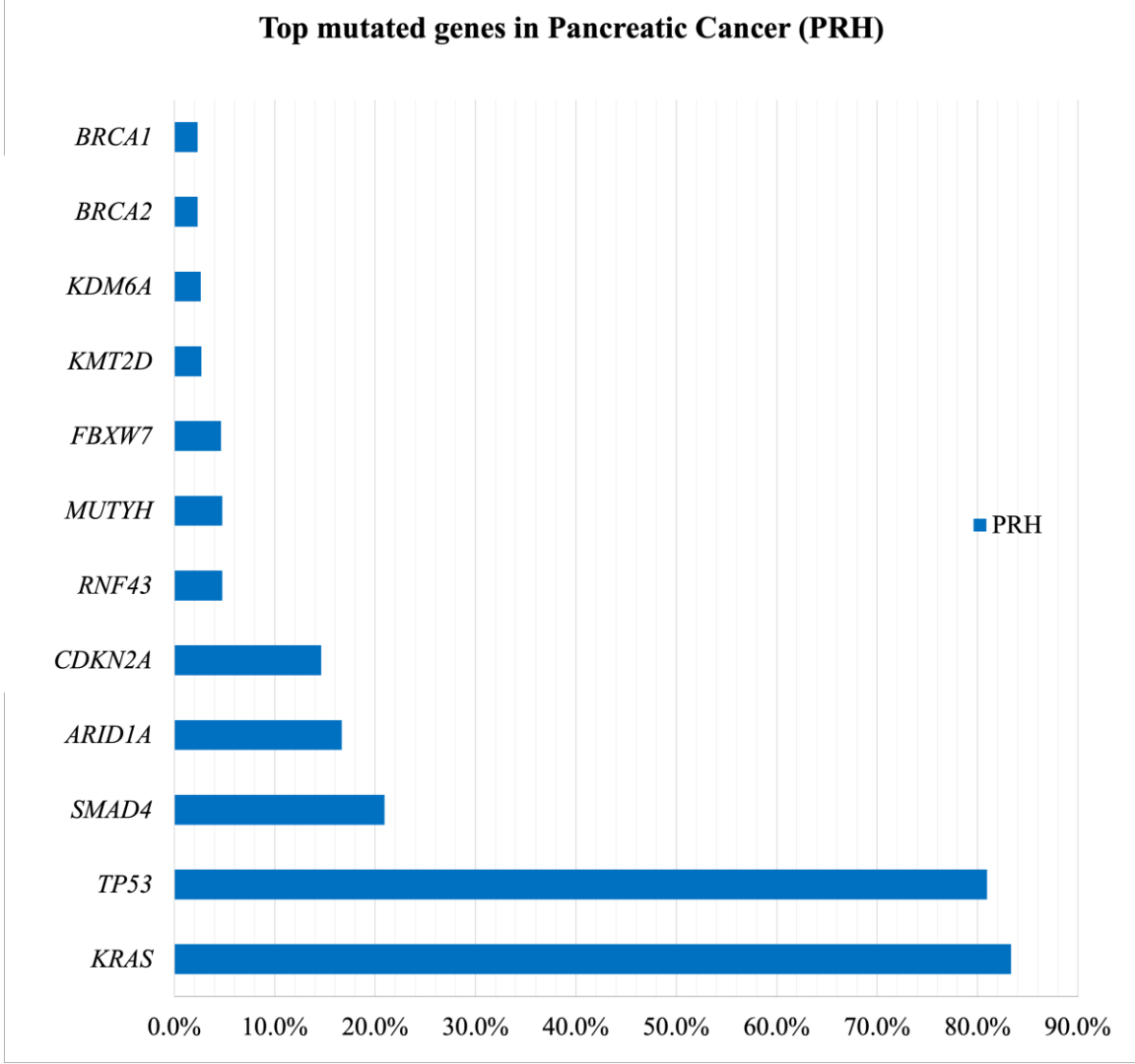
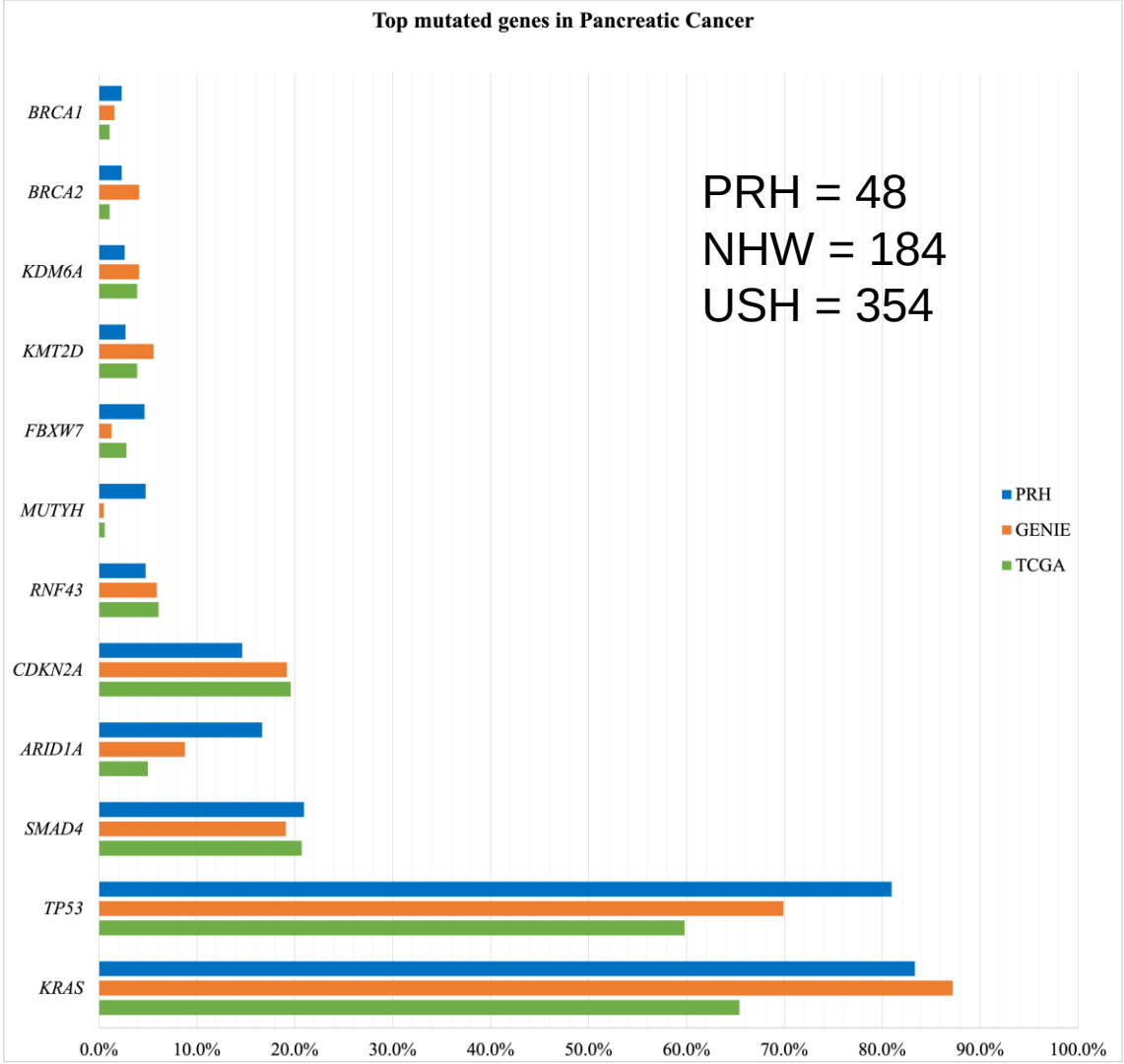


Figure. Mutational Frequencies of ***KRAS, TP53, SMAD4, P16, MUTYH, BRCA1/2***

No alterations in actionable biomarkers MSI, NTRK1-3

Significant differences between PRH and other populations were detected for *TP53, KRAS and P16 (p <0.001)*



Conclusions

- **Integration** of NGS technologies into clinical management of cancer patients is an integral part of precision oncology (NCCN guidelines)
- **Defining** the ***molecular profile of PRH*** will inform clinicians, scientists and health policy stake-holders about actionable mutations to guide research, treatment and health policy efforts
- **Collaboration** between ***private industry, community and academic sectors*** is key to accelerate translation of scientific discoveries into clinical practice

"IF WE DIDN'T HAVE GENETIC MUTATIONS, WE WOULDN'T HAVE US. YOU NEED ERROR TO OPEN THE DOOR TO THE ADJACENT POSSIBLE."

STEVEN JOHNSON