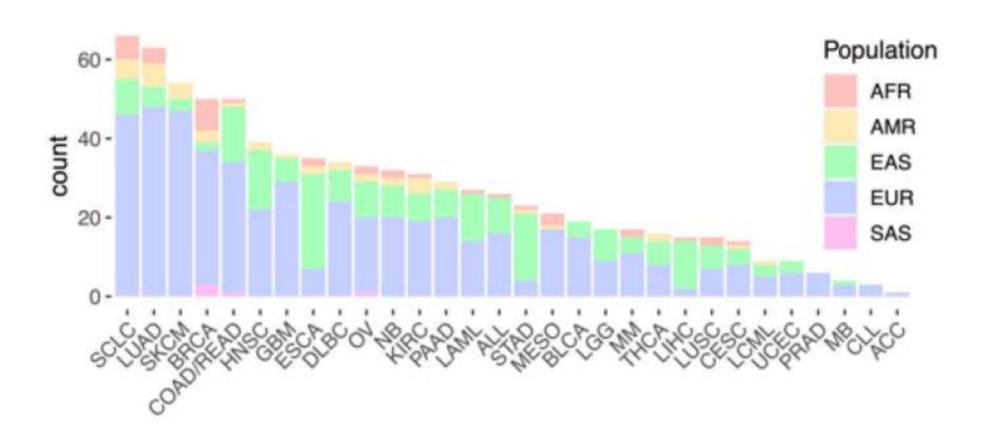
# Ancestral Bias in Pre-clinical Cancer Research Models

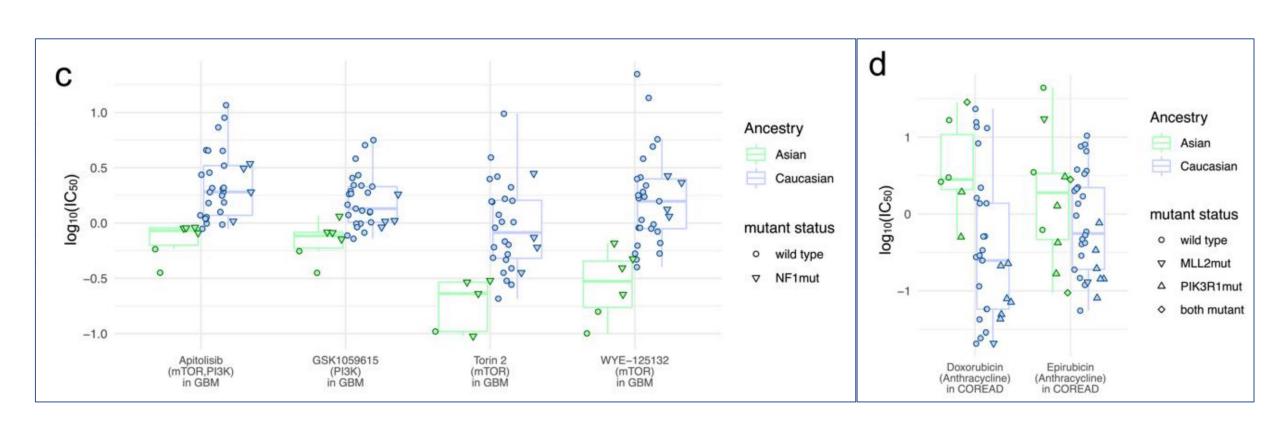
Measuring Diversity and Differentiation in the Tumor Suppressor Gene TP53 in Thousand Genomes Project Populations

BIOL1435 Final Project Spring 2023

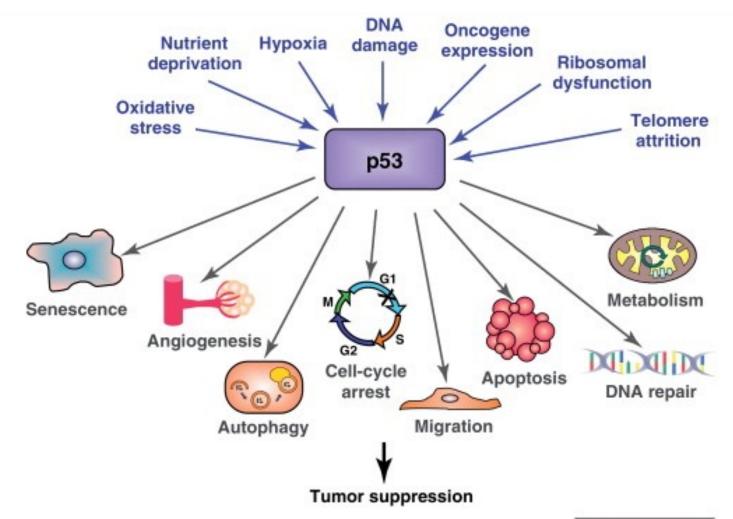
## Distribution of Inferred Ancestries of Cell Lines across Cancer Types

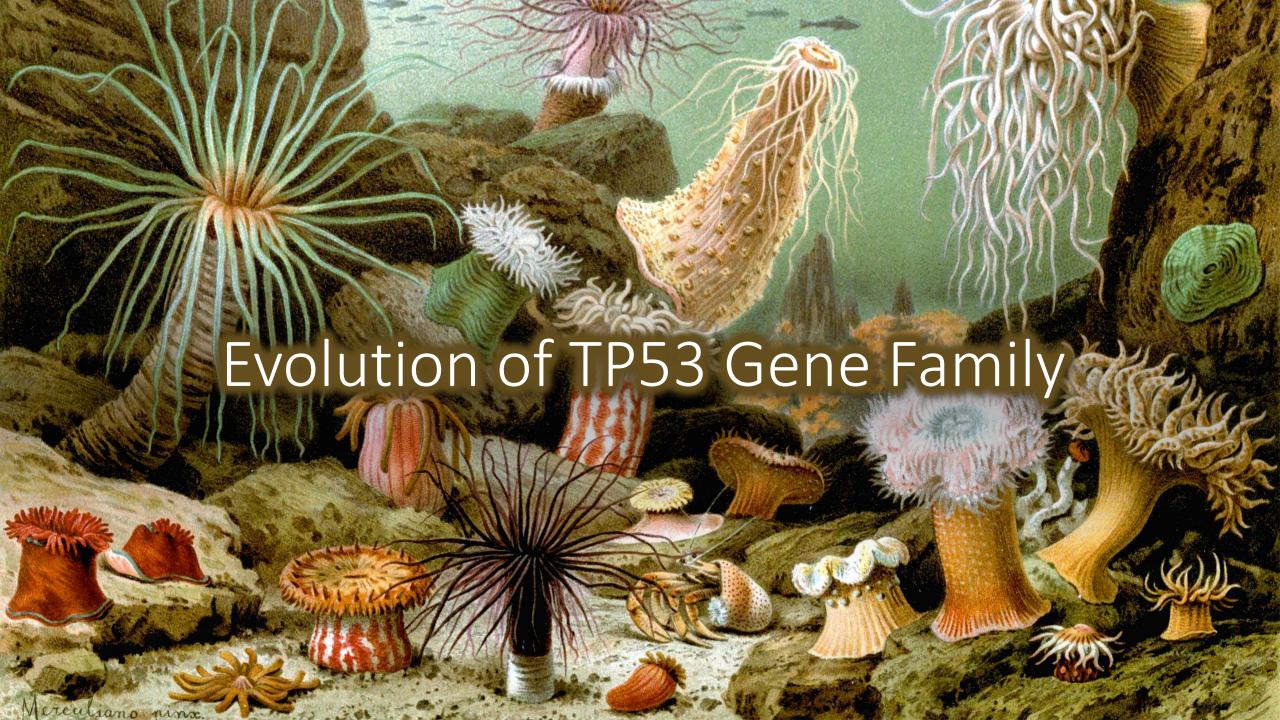


### Inferred Ancestral Origin of Cancer Cell Lines Associates with Differential Drug Response



#### TP53: "Guardian of the Genome"





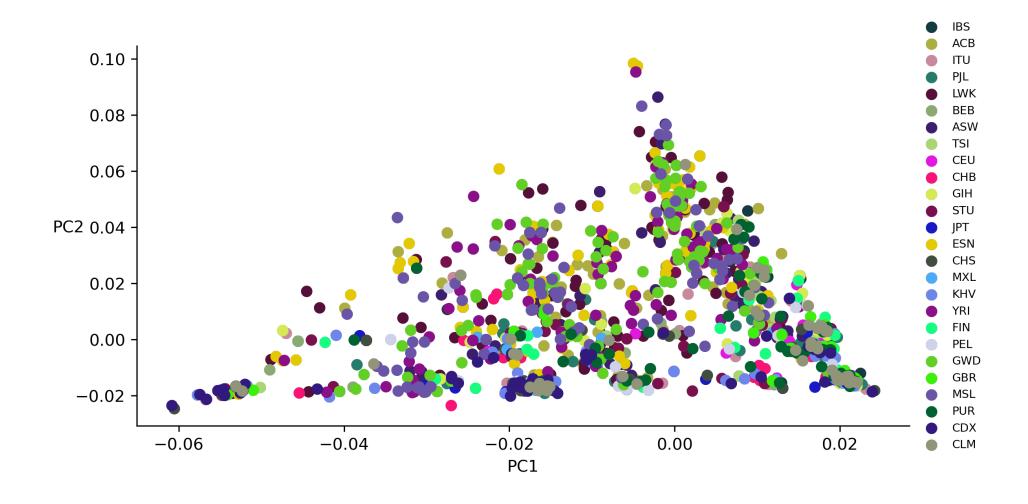
#### Motivation

- 1. Disparity in ancestral representation in preclinical cancer research models
- 2. Structural and functional conservation of cancer therapeutic targets
- 3. TP53 is an ideal locus to investigate

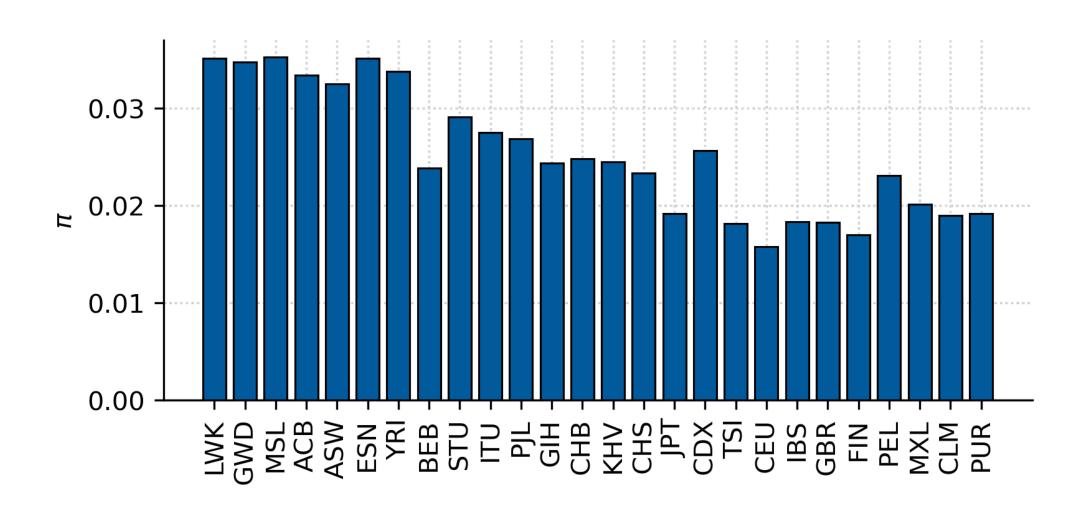
#### Hypothesis

Since TP53 is a very conserved gene among all vertebrates and deleterious variation within TP53 leads to cancer transformation, I hypothesized that TP53 diversity and differentiation is low in all populations.

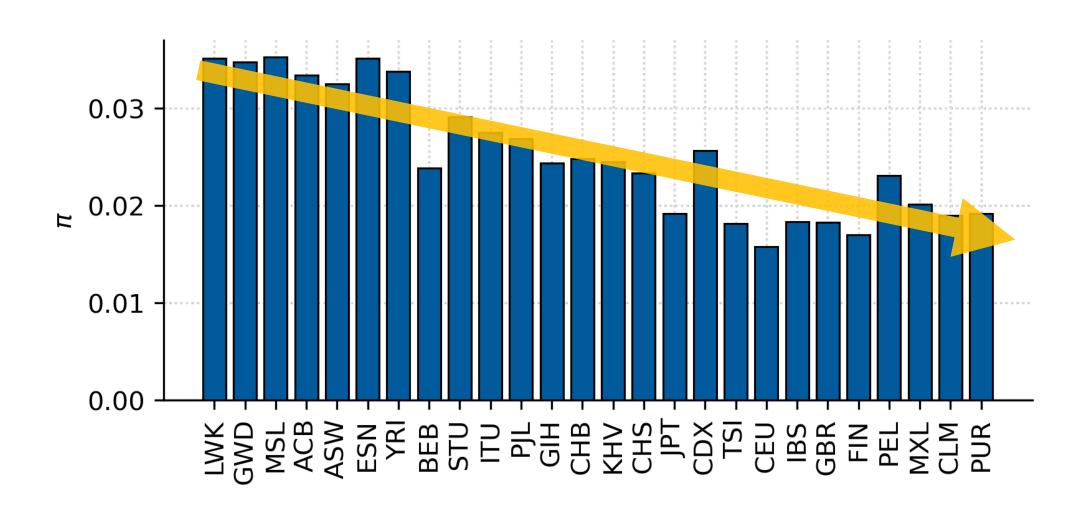
#### PCA of TP53 Biallelic SNPs



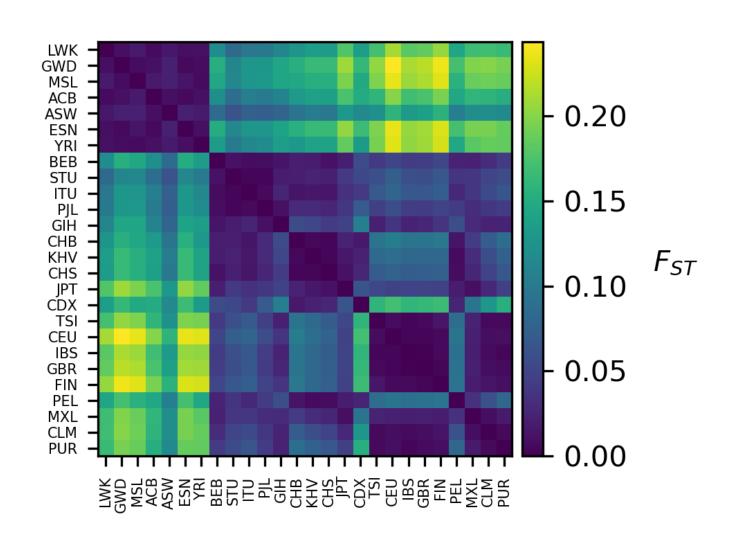
TP53 Nucleotide Diversity (Pi) Follows Trend of Human Population Dispersal "Out of Africa"



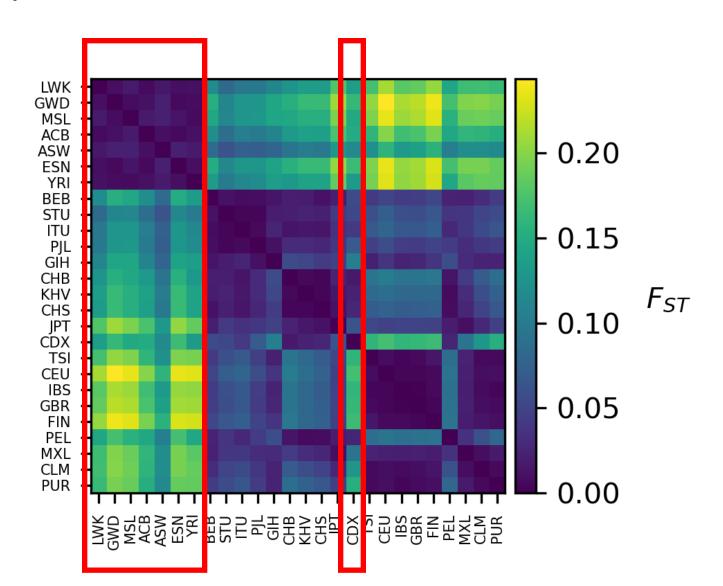
TP53 Nucleotide Diversity (Pi) Follows Trend of Human Population Dispersal "Out of Africa"



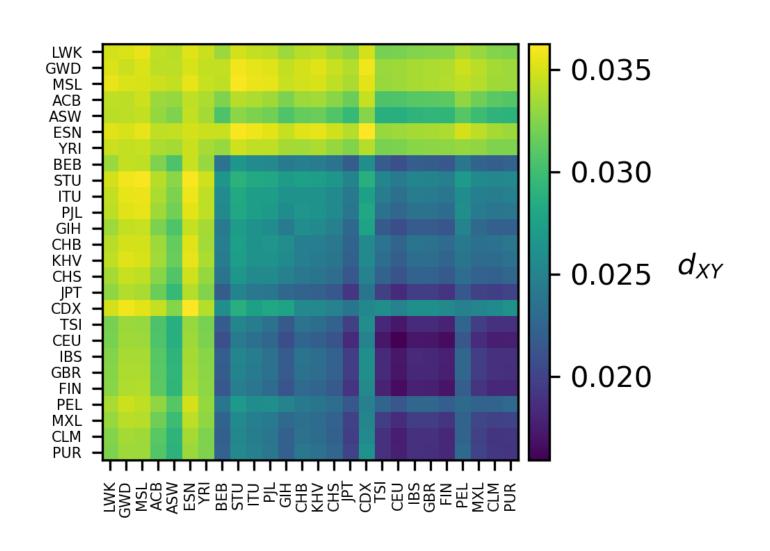
#### TP53 Sequence Fst Between 26 TGP Populations



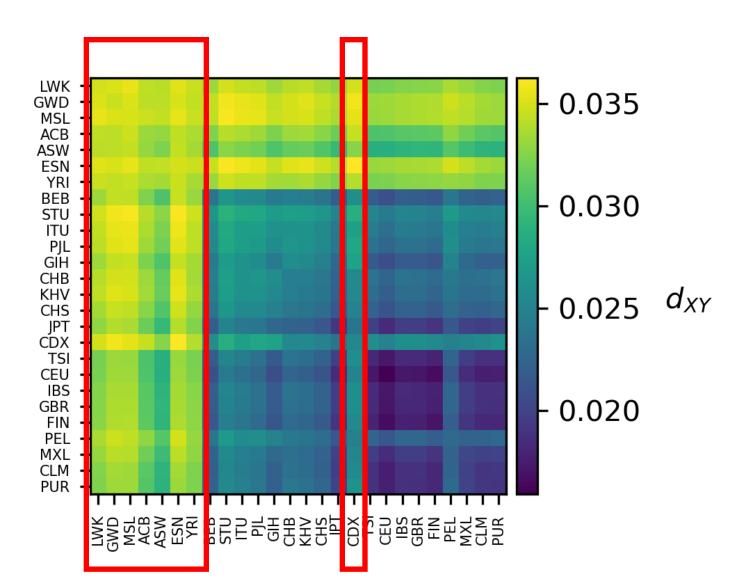
#### TP53 Sequence Fst Between 26 TGP Populations



#### TP53 Sequence dXY Between 26 TGP Populations



#### TP53 Sequence Dxy Between 26 TGP Populations



## Example of clinically relevant TP53 nucleotide diversity specific to African populations

#### rs1800371:

- Germline nonsynonymous single-nucleotide polymorphism in *TP53*
- Exists in African-descent populations
- Associated with high cancer incidence
- Exhibits decreased cancer drug response

#### Conclusions and Impact

High diversity and differentiation suggest the structural differences in p53 between populations

These findings may explain differential drug response and disparities in cancer treatment effectiveness

Equal representation of all population ancestries in cancer cell line development will require pan-institutional action