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Evaluating Cancer Rates, Cancer Types, and Variant Hotspots Between Different Races and Ethnicities in Individuals with Li-Fraumeni Syndrome

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Background

- Li-Fraumeni Syndrome (LFS), caused by pathogenic/likely pathogenic (P/LP) variants in *TP53*, is a cancer predisposition syndrome that increases the risk for numerous cancer types in both children and adults.
- Many studies have shown that cancer rates can vary between races and ethnicities.
  - 2024 Cancer Statistics published by the American Cancer Society reported the incidence for breast cancer to be highest for White individuals and lowest for Hispanic/Latino individuals.
  - Ariffin et al 2015 showed East Asian individuals were more frequently diagnosed with gastric cancer compared to North Americans and Europeans.
  - Other studies identified P/LP *TP53* variants associated with specific populations, such as the South and Southeast Brazil founder variant, p.Arg337His.
- However, there lacks extensive research on the variable expressivity of cancers within the LFS population, based on genotype, race, and/or ethnicity.
- This study aims to describe the specific *TP53* germline variants, cancer rates, and cancer types among individuals of different racial and ethnic groups diagnosed with LFS.

Study Aims

Aim 1: Describe the cancer rates and cancer types diagnosed among individuals of different racial and ethnic groups with a confirmed *TP53* variant.

Sub-aim 1: Compare the cancer rates and types among different populations.

Aim 2: Describe the specific regions of the *TP53* gene commonly mutated within specific races and ethnicities.

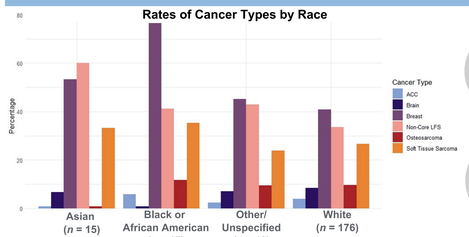
Methods

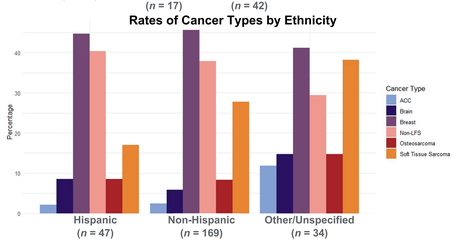
- A retrospective chart review of individuals with germline P/LP *TP53* variants at the University of Texas MD Anderson Cancer Center was completed.
- Data collected includes race, ethnicity, number of cancer diagnoses, cancer types, and location of the *TP53* variant (exon and codon).
- Individuals with a suspected somatic *TP53* variant were excluded from this study.
- Racial groupings included Asian, Black or African American, White, and Other/Unspecified. Ethnicity was categorized as Hispanic, Non-Hispanic, and Other/Unspecified.
- There were also six cancer type categories: adrenocortical carcinoma, brain cancer, breast cancer, osteosarcoma, soft tissue sarcoma, and non-core LFS cancers.
- Descriptive and statistical analyses, including chi-squared or Fisher's exact tests and pairwise comparisons, were performed using R software (v4.4.1).

Results

Characteristic (N = 250)	n	Percentage
Mean age (range), years	39.9 (1-78)	
Sex		
Female	181	72.4%
Male	69	27.6%
Race		
Asian	15	6.0%
Black or African American	17	6.8%
White	176	70.4%
Other/Unspecified	42	16.8%
Ethnicity		
Hispanic	47	18.8%
Non-Hispanic	169	67.6%
Other/Unspecified	34	13.6%

Rates of Cancer Types





Breast cancer was the most commonly diagnosed cancer type for all races, **except** Asian where **Non-Core LFS cancers** were most common.

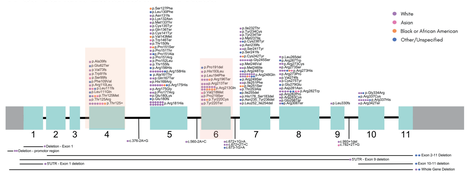
Rates of breast cancer were significantly different between racial groups (p = 0.037) with the **highest frequency in Black or African American individuals**.

Breast cancer was the **most commonly** diagnosed cancer type for all ethnicities.

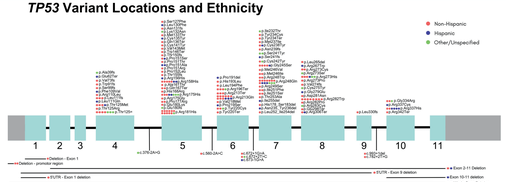
ACC was the **least frequently** diagnosed cancer type for all ethnicities.

TP53 Gene Variant Location

***TP53* Variant Locations and Race**



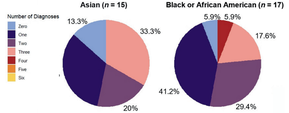
***TP53* Variant Locations and Ethnicity**



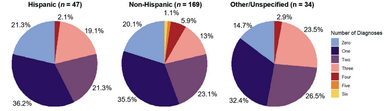
- There was a significant difference in rates of **exon four variants and race** (p = 0.021).
  - 33% of Asian individuals had a variant within exon four compared to <15% of individuals in other racial groups.
- There was a significant difference in rates of **exon six variants and race** (p = 0.016).
  - Pairwise comparison found a significant difference between Black or African American and Other/Unspecified individuals with variants more common in Black or African American individuals (35.3% vs 2.9%) (p = 0.022).
- There was not a significant differences in rates of variant locations and ethnicity.

Rates of Cancer Diagnoses

Rates of Cancer Diagnoses by Race



Rates of Cancer Diagnoses by Ethnicity



- The majority of individuals in each racial and ethnic group were diagnosed with **one primary cancer**.

Conclusion

- This study highlights similarities in the rates and types of cancers seen across racial and ethnic groups within a cohort of individuals with LFS.
- However, this study also identified potential differences in the rates of breast cancer and variant location across racial populations within the cohort.
- The results of this study provide information that can lead to more personalized counseling for patients and train risk models to accurately predict cancer risk for individuals with LFS of differing races and ethnicities.
- One limitation of this study is limited information regarding ethnicity or ancestry and further studies incorporating this information would be beneficial.

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