

Lack of racial and ethnic diversity in lung cancer cell lines contributes to lung cancer health disparities

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Abstract/ Background

Lung cancer is the leading cause of death in the United States¹ and worldwide², and a major source of cancer health disparities³. Lung cancer cell line models provide key *in vitro* models for molecular studies of lung cancer development and progression, and pre-clinical drug testing. To ensure health equity it is imperative that cell lines representing different lung cancer histological types, carrying different cancer driver genes, and representing different genders, races, and ethnicities should be available. This is particularly relevant for cell lines from Black men, who experience the highest lung cancer mortality in the United States⁴.

Based on some studies that reported using one lung cancer cell line derived from a Black man (NCI-H23), we undertook a review and asked how many lung cancer cell lines reflect different histological subtypes, gender, race, and ethnicity⁵. This information will allow us to understand if the treatments and therapies that are developed are reflective of the appropriate populations.

Methods

We used data from the Surveillance, Epidemiology and End Results (SEER) program <https://seer.cancer.gov> that is a US-based registry with 331 million patients from 17 regions to assess cancer mortality for different races/ethnicities for the main histological subtypes. (2000-2019)

Mortality differences in lung cancer subtypes

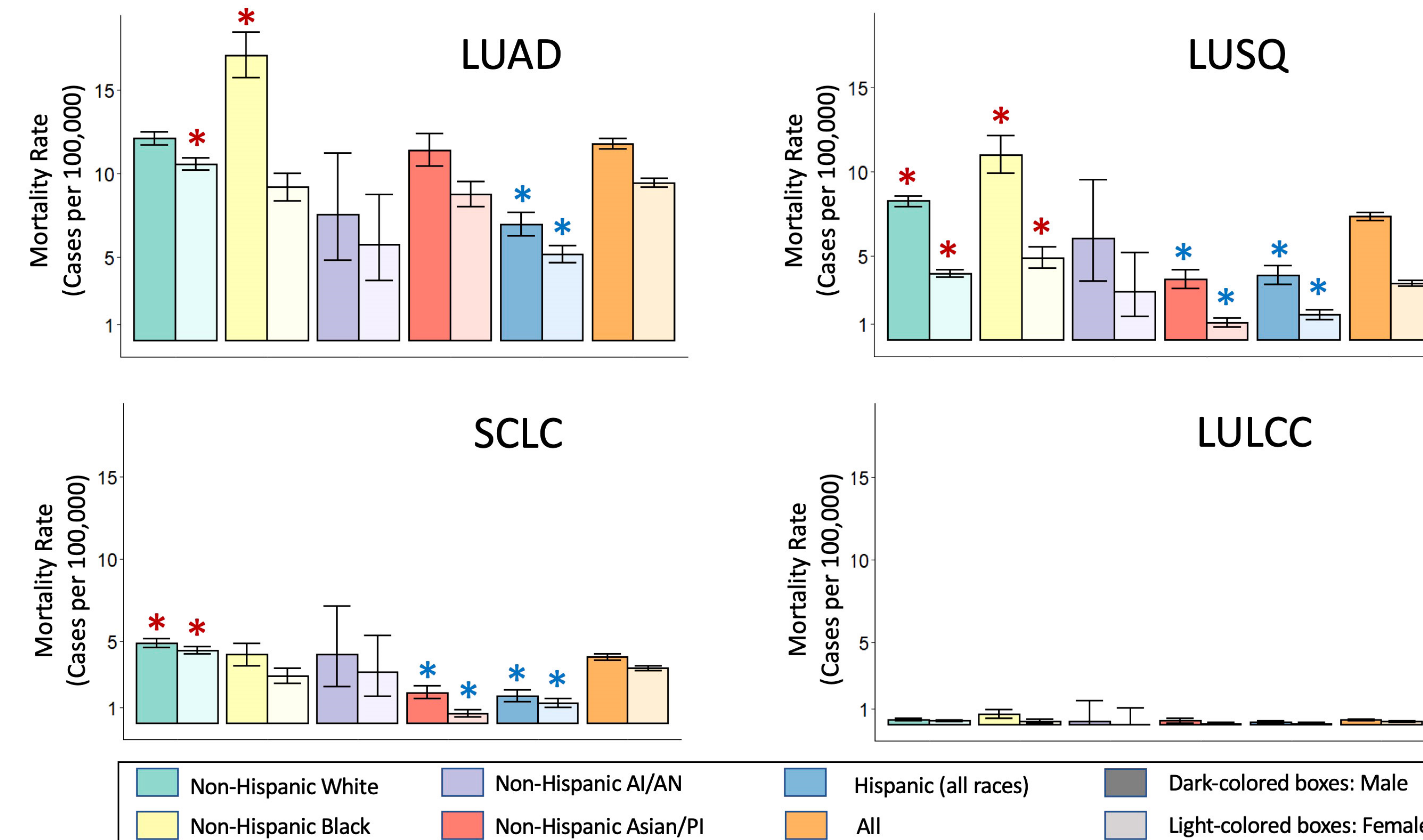


Figure 2. Race and ethnicity-specific mortality data for lung cancer histological subtypes from SEER. Mortality rates calculated via incidence-based mortality (IBM) for each group per 100K individuals. ICD-O-3 morphologic codes were group together to from the histologic subtypes⁵.

Cell lines from Black Patients

Name	Sex	Age	Histol. Type	Smoking	% African	Mutations
201T	M	68Y	LUAD	U	89	TP53
HCC1195	M	47Y	LUAD	U	70	TP53, NRAS
HCC122	M	48Y	LUAD	U	U	U
NCI-H23	M	51Y	LUAD	U	68	TP53, KRAS, STK11, ATM
NCI-H1373	M	56Y	LUAD	SM (30 py)	72	TP53, KRAS
NCI-H1648	M	39Y	LUAD	SM	69	TP53
NCI-H125*	M	61Y	LUADSQ	U	U	TP53
NCI-H513	M	61Y	LUADSQ	U	84	U
HLF-a**	F	54Y	LUSQ	U	91	U
NCI-H1385	F	49Y	LUSQ	SM (33 py)	69	KRAS
HCC15	M	47Y	LUSQ	U	77	TP53, RB1, NRAS, EP300, CTNNA1
HCC1897	M	47Y	LUSQ	U	77	U
NCI-H64	F	48Y	SCLC	SM (30 py)	68	TP53
NCI-H128	M	60Y	SCLC	U	70	TP53
NCI-H220	M	51Y	SCLC	NS	U	U
NCI-H250	M	34Y	SCLC	NS	91	TP53, RB1
NCI-N390	M	49Y	SCLC	U	U	U
NCI-H748	M	62Y	SCLC	SM (30 py)	86	TP53, BRCA2
NCI-H1048	F	53Y	SCLC	NS	70	TP53, RB1, PIK3CA
NCI-H1339	F	49Y	SCLC	U	71	TP53
NCI-H1963	M	56Y	SCLC	U	56	TP53, RB1
NCI-H2107	M	36Y	SCLC	U	U	TP53
NCI-H2108***	M	36Y	SCLC	SM (26 py)	U	U
NCI-H835	F	48Y	LUCART	NS	80	U
HCC1359	F	55Y	LUGCC	U	86	TP53
HCC3051	M	63Y	LULCC	U	U	U
NCI-H810	M	51Y	LuLCC	U	82	TP53, DDR2
NCI-H292	F	32Y	LUMEC	U	81	NF2
EMC-BAC-1	M	U	NSCLC	U	74	TP53, STK11
NCI-H2110	U	U	NSCLC	NS	83	U
NCI-H2172	F	U	NSCLC	NS	82	U

Table 4. Lung cancer cell lines (31) from black patients⁵. * Cell line discontinued; ** Cell line reported to be contaminated; *** Duplicate cell line (H2107); Sex: M=Male, F=Female; Age: Y=Years; Subtype: LUAD, LUADSQ=Lung adenosquamous carcinoma, LUCART=Lung carcinoid tumor, LUGCC=Lung giant cell carcinoma, LULCC=Lung large cell carcinoma; LUMEC=Lung mucoepidermoid carcinoma, LUSQ=Lung squamous cell cancer, NSCLC, SCLC. Smoking: NS=non-smoker, SM=Smoker, py=pack years, U=Unknown; % African: Percentage African ancestry, U=Unknown; Mutations: known mutations are indicated; U=Unknown

General Lung Cancer Subtype Properties

Histol. Type	Classification	WHO 2014	General Location	General Properties
LUAD	Lung Adenocarcinoma	LUAD	Alveoli	Subtypes: lepidic, acinar, papillary, micropapillary, and solid
LUSQ	Lung Squamous Cell Carcinoma	LUSC	Central or airways	Subtypes: keratinizing, nonkeratinizing, and basaloid
SCLC	Small Cell Lung Cancer	NE	Airways	Very aggressive, NE: ASCL1(A), NEUROD1(N) NE-: POU2F3(P), CD8/PDL1(I)
LULCC	Large Cell Lung Carcinoma	NE	Anywhere, generally periphery	Poorly differentiated NE morphology: LCNEC Non NE: reclassified

Table 1. General properties of lung cancer cell subtypes. NE = neuroendocrine⁵.

Lung Cancer Histological Subtypes

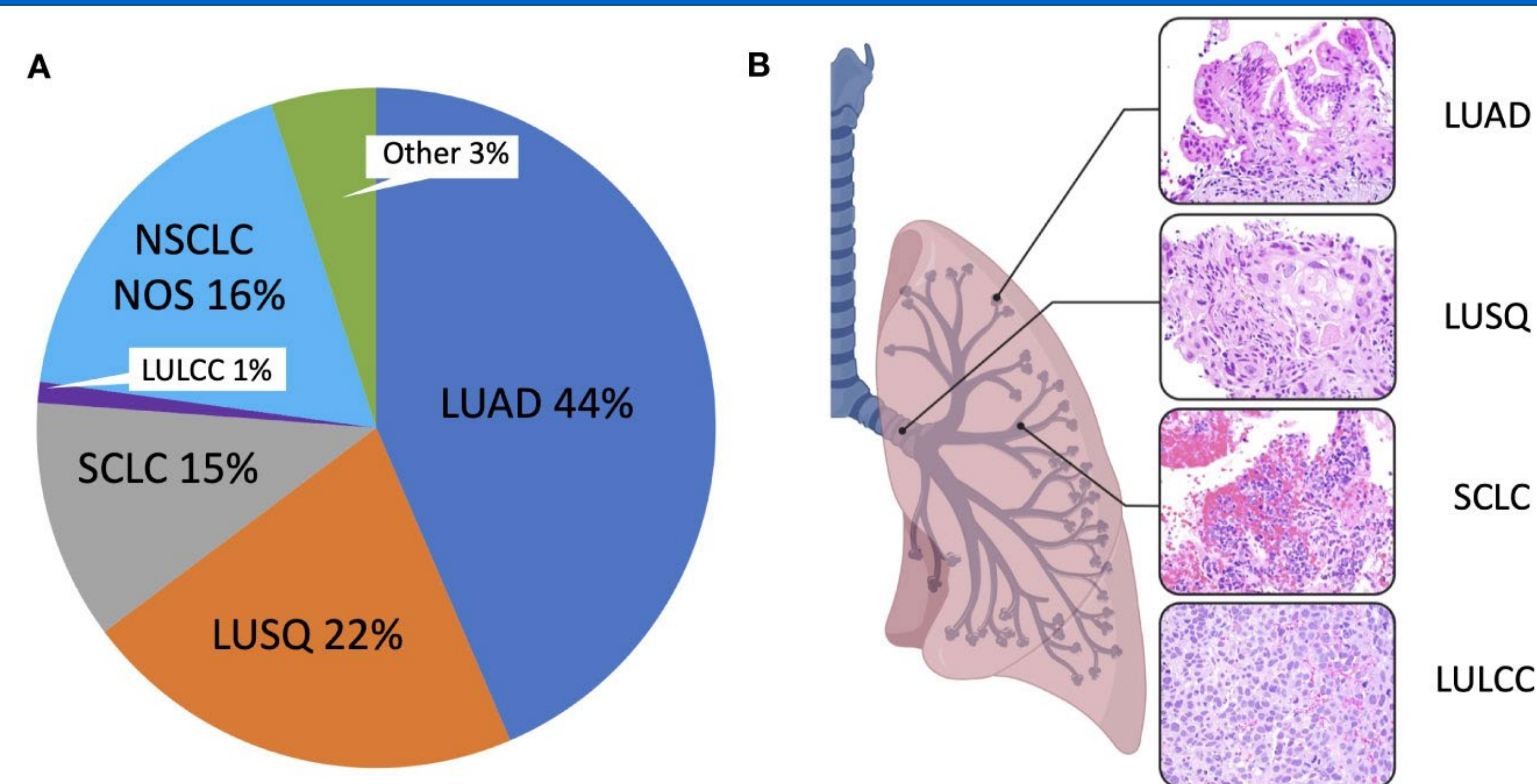


Figure 1. Major lung histological subtypes⁵. **A)** Pie-chart showing mortality data indicating the proportion of different histological subtypes. Data obtained from SEER 200-2019. LUAD; LULCC; LUSQ; NOS, Lung cancer, not otherwise specified. **B)** Hematoxylin and eosin-stained sections of different lung cancer types at 400x mag.

Cell line verification

Goal	Web Site
Identify cell lines	https://www.atcc.org/search-str-database
Identify cell lines	https://www.cellosaurus.org/
Identify cell lines	https://www.dsmz.de/services/human-and-animal-cell-lines/online-str-analysis
Find mislabeled cell lines	https://www.atcc.org/the-science/authentication/reclassified-cell-lines

Table 2. Websites used to verify lung cancer cell lines⁵.

Cell line information

Resource Name	Web Site
ATCC: The Global Bioresource Center	https://www.atcc.org/
cBioPortal for Cancer Genomics	https://www.cbioportal.org/
Expaty - Cellosaurus.	https://www.cellosaurus.org/
Wellcome Sanger Institute. Cell model Passports. A Hub for Preclinical Cancer Models.	https://cellmodelpassports.sanger.ac.uk/passports?tissue=lung

Table 3. Websites used to identify lung cancer cell line information⁵.

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Summary/Conclusions

- LUAD is most common across all gender and race/ethnic categories, with Black men and White women having greatest age-adjusted mortality rates.
- LUSQ is 2nd most common subtype, with Black men and women having highest age-adjusted mortality rates.
- Of over 800 cell lines, 200 were from White, 390 from Asian, only 31 from Black (1 possible duplicate), and 0 from Hispanic/Latino, American Indian/Alaskan Native, and NHOPI patients respectively. Almost 300 cell lines had unknown race/ethnicity.
- Cell lines representing men were 2-fold greater than women, but 7 times greater in Asian individuals.
- Ethnicity should be captured for all cells, and diverse populations should be better represented. Without diverse cell lines, therapies will continue to be ineffective.

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