Exploring the Relationship Between Trauma, Smoking, and Leukocyte Telomere Length (LTL) in Minority and Caucasian Non-small Cell Lung Cancer Patients

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ABSTRACT

Background: Lung Cancer is the one of the deadliest, and most common cancers in the United States. Non-small cell Lung Cancer accounts for approximately 13% of all new cancers in the United States according to the American Cancer Association. Lung Cancer is also the leading cause of cancer deaths in the United States among both men and women[1]. [More people in America will die from Lung cancer than prostate, colon, and breast cancer combined[1].]Many factors contribute to the likelihood of developing Lung cancer, including smoking habits, levels of stress, ethnicity, and instances of trauma in one's life. Leukocyte telomere length is a marker of cellular aging that has been associated with both chronic stress and disease mortality[2].

Method: This study explores the potential relationships between stress and instances of trauma, and telomere length in minority versus white non-small cell lung cancer patients (n=65). [The 65 Participants of this study were recruited from the James Brown Cancer Center on University of Louisville's Health Science Center Campus in Louisville, Kentucky. All of the participants were diagnosed with non-small cell lung cancer.] Participants were sent home with Questionnaires to asses psychological status, ethnicity, and instances of trauma. Participants also had their blood drawn and assessed by a trained phlebotomist. Following data collection, Leukocyte Telomere Length was assessed at UCSF in the laboratory of Dr. Elizabeth Blackburn).

Results: Results demonstrated a high correlation between smoking and telomere length in both Caucasian and Minority patients. It was also found that despite vastly different smoking habits among Caucasian and Minority lung cancer patients, and difference in TL length, they were similar in disease severity. This leaves with further question as to why this may be the case.

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INTRODUCTION

Lung Cancer is one of the deadliest cancers in the United States. According to the Lung Cancer Foundation, lung cancer will take the lives of 422 Americans each day[3]. Mounting evidence has shown that minorities are diagnosed with lung cancer at a disproportionate rate in comparison to other demographic groups in the United States. Not only do minorities have a higher risk of developing lung cancer, but they also have higher mortality rates when diagnosed with lung cancer, despite similar smoking habits[4]. Scientists are becoming more interested in studying the biological markers that could be associated with the disproportionate survival and diagnostic rates of lung cancer patients, one of them being leukocyte telomere lengths.

Telomeres have become increasingly relevant in cancer research. Studies show that shorter leukocyte telomere lengths are associated with higher risk and higher mortality rates in non-small cell lung cancer specifically.[5] Telomere length has been used as a predictor of how early an individual will develop cancer and can be used as a biological marker for physicians to use to devise personalized treatment plans for their patients[6]. Scientists are exploring psychological and physiological factors that may contribute to telomere shortening, one of them being exposure to trauma. The focus of this study is to explore the associations between minority status, instances of trauma, smoking behavior, and the potential links between these factors and leukocyte telomere shortening.

HYPOTHESIS

- Instances of trauma, as determined by the Traumatic History Questionnaire (THQ), will occur more frequently in individuals that identify as a minority.
- Instances of trauma, as determined by the Traumatic History Questionnaire (THQ), will be associated with telomere shortening in lung cancer patients
- Smoking history will be associated with shorter Telomeres in both minorities and non-minorities.
- Minority Patients, as determined by the Multigroup Ethnic Identity Measure (MEIM), will have shorter telomeres, predisposing them to faster tumor progression

METHODS

Participants: Participants were recruited from the James Brown Cancer Center and met the following criteria: diagnosed with non-small cell lung cancer within 5 years of the study entry, between the ages of 18-85, lived within 120-mile radius, had no medical diagnoses that could influence a six-month survival, no psychiatric hospitalization or substance abuse, and no immune compromising condition. There was a total of 65 individuals that fit this criteria (N=65).

Procedure: Participants were given questionnaire packets to asses psychological state; one to be completed in one sitting, and one to be completed each morning and night for 10 days. Participants had their blood drawn to assess telomere length. Blood samples were collected in K2 EDTA purple top tubes during baseline appointments and were kept on ice at the Cancer Center until sent to the laboratory by study personnel. Blood samples were put in a centrifuge at 1300 RCF for 10 min at 4°C. The layer of plasma at the top was transferred via pipette into 1.5 mL microcentrifuge tubes and were kept on ice, as well as remaining blood pellet at the bottom. All tubes were frozen to -80°C. All frozen tubes were transferred to Dr. Elizabeth Blackburn's laboratory at the University of California San Francisco. Dr. Jue Lin of Dr. Blackburn's Laboratory, conducted telomere length assays using an adapted protocol (Lin et al., 2010) from methodology originally outlined by Cawthon (2002)

Measures:
- Multigroup Ethnic Identity Measure (MEIM)[1]
- Traumatic History Questionnaire (THQ)[2]
- Leukocyte Telomere Length

[1]Phinney, J. (1992). The Multigroup Ethnic Identity Measure: A new scale for use with adolescents and young adults from diverse groups. Journal of Adolescent Research, 7, 156-176
[2]Lisa M. Hooper, Patricia Stockton, Janice L. Krupnick & Bonnie L. Green (2011) Development, , and Psychometric Properties of the Trauma History Questionnaire, Journal of Loss and Trauma, 16:3, 258-283
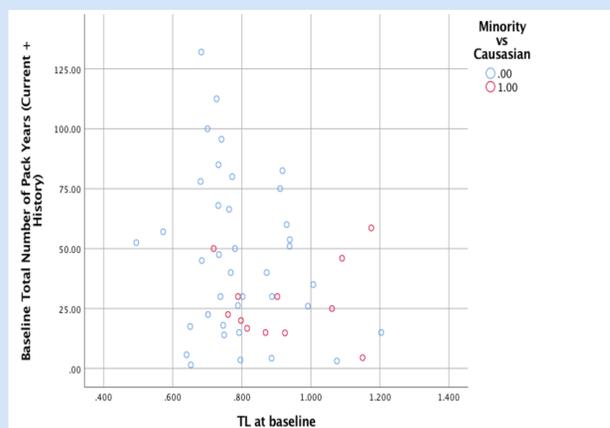
Statistical Analysis:
- Data preprocessing: Data preparation and analysis and preparation was conducted using SPSS v25.0 (SPSS IBM. Armonk, NY, 2017).

Table 1	N	%
Male	20	33.9
Female	39	66.1
Race/Ethnicity		
Non-Hispanic White	45	67.2
African American	12	17.9
Hispanic	1	1.5
Mixed race	1	1.5
Stage		
I	15	22.4
II	8	11.9
III	28	41.8
IV	16	23.9
Treatment		
Previous Radiation	38	56.7
Previous Chemotherapy	48	71.6
Current Radiation	3	4.5
Current Chemotherapy	21	31.3
	Mean	SD
Age at Diagnosis	59.57	8.91

RESULTS

Surprisingly, LTL Length was found to be shorter in Caucasians than among Minority patients. We explored confounding factors that may have contributed to this counterintuitive finding, including gender and smoking history. In this sample, Caucasians had significantly higher pack years than minorities (R= -0.244 p = .041 N=52). High pack years is also strongly correlated with Telomere Length shortening (R = -0.258 p = .032 N= 52).
Disease severity did not vary significantly across ethnicities (p = .225). Traumatic history was not significantly correlated with TL length (p = .419).
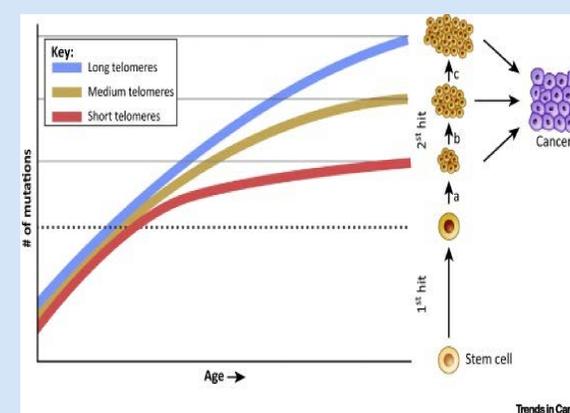

DISCUSSION

Due to the exploratory rather than confirmatory nature of this study, a number of questions remained unanswered and warrant further investigation. Shorter telomere length in the Caucasian subsample may be explained by their higher smoking.
Despite significant differences in smoking habits among Minorities and non-minorities, there was no significant difference in disease severity among the different ethnicities, raising the question of what other factors may contribute to disease severity, i.e., why did minorities have similar disease severity as Caucasians in this study, despite having lower pack years? A reason why there might have been no difference in disease severity among ethnic groups is because our minority data set consisted of mainly women: According to the American Cancer Society, Black men are 20% more likely to develop lung cancer than white men, whereas black women are 10% less likely to develop lung cancer than white women. Lastly, another contribution as to why some hypothesis were not proven may be that this is a relatively small data set.

FUTURE DIRECTIONS

- What other health behaviors can negatively impact telomere length in Lung Cancer patients besides smoking?
- What other psychological factors negatively impact lung cancer survivorship besides trauma?
- Explore why, despite shorter telomeres and higher pack years, why Caucasians had similar disease severity as minority cancer patients.
- Explore the different psychological factors that impact Telomere length.

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[2]Cleal, K., Norris, K., & D., Baird. (2018). Telomere Length Dynamics and the Evolution of Cancer Genome Architecture. International Journal of Molecular Sciences,19(2), 482. doi:10.3390/ijms19020482

[3]Common Cancer Sites - Cancer Stat Facts. (n.d.). Retrieved from https://seer.cancer.gov/statfacts/html/common.html

[4]Ethnic and Racial Differences in the Smoking-Related Risk of Lung Cancer. The New England Journal of Medicine,354, 354-4. Retrieved June 13, 2019, from https://www.nejm.org/doi/pdf/10.1056/NEJMoa033250?articleTools=true#nav.

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