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#G021

Molecular Discrepancies in Gastric Cancer between Asians and White Populations

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Background

Gastric cancer is a malignant tumor arising from the stomach lining. Gastric cancer's increased prevalence among Asian peoples has long been attributed to infections by Helicobacter Pylori and high nitrate and salt diets. With efforts to screen the public in Asian countries and improved gene mapping, molecular differences in gastric cancers between Asians and Whites may reveal new gene targets for therapy.

Objective

The molecular landscape of Asians and Whites were compared to identify any potential actionable alterations that were present in one subgroup but not the other.

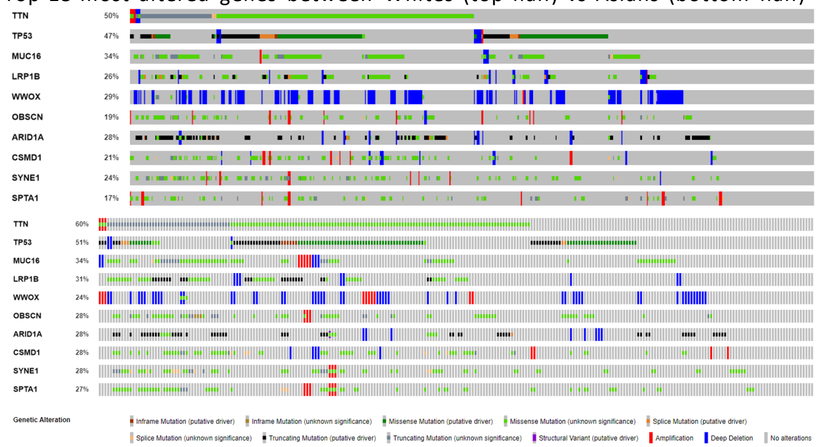
Design/Methods

A composition of 3 TCGA studies (Firehose Legacy, Nature 2014, PanCancer Atlas) were analyzed in cBioPortal to discern differences between Asians (n = 255) and Whites (n = 728). Molecular characteristics including alterations (mutations, deletions, amplifications), overall survival, and mRNA expression vs. copy number variation (CNV) were analyzed. Significant differences were noted, and OncoPrints and survival curves were generated. Statistics such as p-value (p), hazard ratio (HR), and 95% confidence intervals (CI) were used.

Molecular Gene Findings

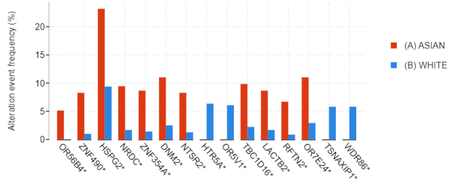
A. OncoPrint

Top 15 most altered genes between Whites (top half) vs Asians (bottom half)



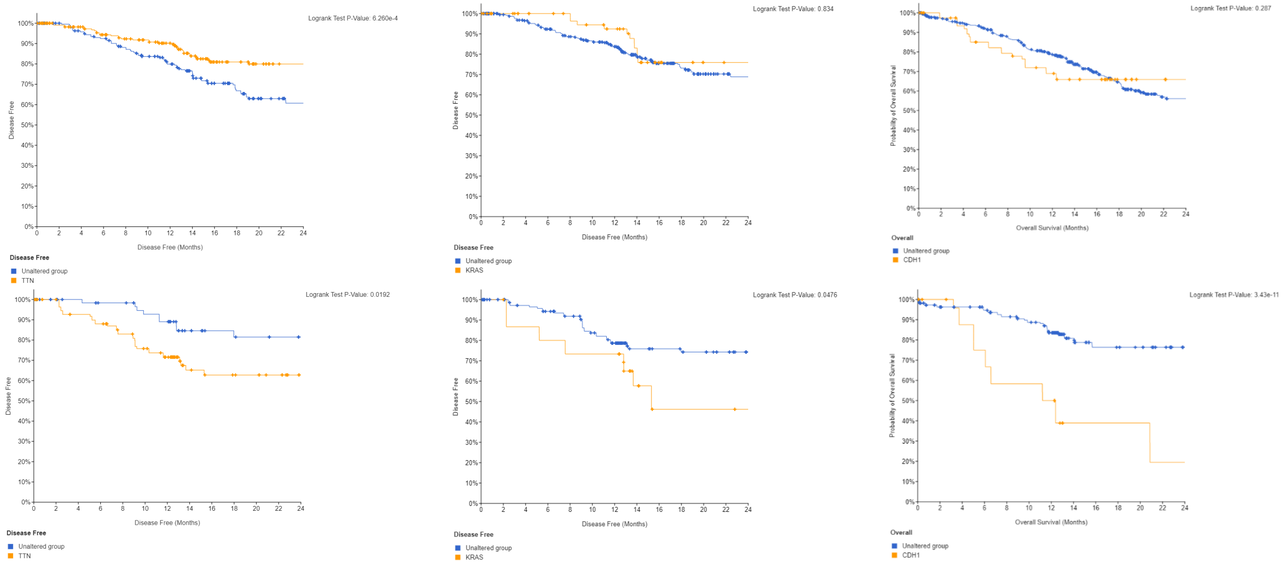
B. Top 15 most significant p-value genes

15 genes where the p value between Whites and Asians are most significant



C. Survival Curves

TTN 2-year DF, KRAS 2-year DF, CDH1 2-year OS of Whites (top 3 images) and Asians (bottom 3 images)



Results

The 2-year overall survival via cBioPortal depicted Asians having greater survival (p-value = 0.0301). The top 10 highest alteration frequency genes showed similar alteration rates between Asians and Whites, although differences were depicted between race and specific genes. Certain alterations increased the probability of 2-year disease free survival for whites, such as TTN (p = 0.0219, HR = 0.5198, CI = [0.3549, 0.7612]) and ERBB2 (p = 2.673e-3, HR = 0.3497, CI = [0.1706, 0.7167]). Genetic alterations for 2-year overall survival for whites include CDKN2A (p = 0.0117, HR = 0.6377, CI = [0.4481, 0.9074]) and BRCA2 (p = 4.628e-3, HR = 0.4551, CI = [0.2602, 0.796]). These all had significant survival for whites, but non-significant or opposite effects for Asians.

Multiple altered genes also had significant effects for Asians only. Of the 2-year disease free survival for Asians, differences included TTN (p = 0.0192, HR = 2.232, CI = [1.12, 4.447]), BRCA2 (p = 6.087e-3, HR = 2.42, CI = [1.261, 4.644]), and KRAS (p = 0.0476, HR = 1.942, CI = [0.996, 3.786]). For 2-year overall survival, TP53 (p = 0.0209, HR = 0.5336, CI = [0.3103, 0.9175]) and CDH1 (p = 3.43e-11, HR = 5.4793, CI = [3.115, 9.639]) were noted.

Conclusion

Certain genetic mutations may improve survival for Whites such as TTN, ERBB2, and CDKN2A whereas for Asians the same genes either show no significant improvement or worsen survival, namely in the case of TTN. Asians also showed significantly worse disease-free outcomes that were not seen in Whites with mutations in BRCA2 and KRAS but notably had improved survival with TP53 mutations that were not seen in Whites. CDH1 alterations in Asians depicted the largest significance in overall survival, where individuals with this alteration did far worse than unaltered individuals; this highlights the urgent need for targeted interventions and personalized treatment strategies to improve outcomes in these separate subgroups.